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Annual Report
2021-22

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DIRECTOR GENERAL MESSAGE

It gives me immense pleasure to present the Annual Report of the Indian Council of Medical Research (ICMR) for the year 2021-22. During this period, A total of 13 products were commercialized, the notable ones that will assist in TB elimination are Truenat™, C-Tb, TB detect and standard treatment workflow for paediatric pulmonary TB & extra pulmonary TB.14 products including mosquito feeder, mosquito ovitrap, mosquito larvicidal formulation, etc, which will help in vector control, are in the process of commercialization, whereas 45 new products have been developed & applied for patenting. A total of 8 patents were granted, significant being, plasmodium detection technique & chikungunya inhibition agent. A total of 995 publications were done out of which approximately 40 were published in journals with impact factor more than 20. Several important projects were completed during this period; as an example, a large implementation Research project, India Hypertension Control Initiative (IHCI), was successfully implemented in 104 districts of 21 states; received a UN award and its learnings have been incorporated into NPCDCS National program.

Several state of Art infrastructure facilities were provided to the country, significant being, rabies lab, polio essential facility lab, antenatal screening for hemoglobinopathies, etc.Interventions of Nationwide utility like mobile app MosquiTracker, Red cell panels for rare blood donors, BCI tool for smokeless tobacco quitting, Neuro Cognitive Tool box (ICMR-NTB),Tuberculosis Verbal Autopsy Tool, etc, were developed. Plenty of studies contributed to National programmes like National TB Prevalence Survey, IHCI, DEC fortified salt for filariasis, ICMR STEMI ACT, Mobile Stroke Unit, Stroke Care Pathway, etc.

The The inauguration of new state-of-the art building of ICMR-RMRC, Gorakhpur was done by Hon'ble Prime Minister, Shri Narendra Modi on 7th December 2021 to expand research activities in eastern UP.

A Commemorative postal stamp on COVID-19 vaccine (BBV-152) was released by Dr Mansukh Mandaviya, Hon'ble Union Minister of Health and Family Welfare, Govt of India, on the occasion of anniversary of COVID-19 Vaccination Drive on 16th January 2022. The i-DRONE study was first of its kind in the South Asian region where drones were used for delivering COVID-19 vaccines from land to island. The first drone sortie between Bishnupur District Hospital to Karang Primary Health Centre was launched by Hon'ble Health Minister. The State-of-the art Make in India 'Mobile BSL-3 Laboratory' was inaugurated by Dr. Bharati Pravin Pawar, Hon'ble Union Minister of State for Health & Family Welfare, Govt. of India, on 18th February 2022 at Nashik.

I congratulate all ICMR Scientists for their commitment and accomplishments in Health Research.

Rajiv Bahl

(Dr. Rajiv Bahl)
Secretary to Government of India,
Department of Health Research &
Director General, Indian Council of
Medical Research, New Delhi

MOST IMPORTANT OUTCOMES (2021-22)

NEW HEALTH TECHNOLOGIES

A. PRODUCTS COMMERCIALIZED

- A point of care rapid detection kit for semi-quantitative estimation of CC16 in human samples was developed. The technology has been transferred to two companies (Axiva Sichem Biotech-Delhi and Acrannolife Genomics Pvt. Ltd, Chennai).
- Nipah Point of Care Assay in collaboration with Mol Bio Diagnostics Pvt. Ltd, Goa, for the detection of Nipah viral RNA from clinical samples was developed.
- KFDV Point of Care Assay in collaboration with Mol Bio Diagnostics Pvt Ltd, Goa, for detection of KFD viral RNA from clinical samples was developed.
- Truenat™, an indigenous molecular test has been validated for TB, MDR TB, Extra pulmonary TB (EPTB) and Paediatric Pulmonary TB (PPTB) and is currently being used under National TB Elimination Programme. The test has also been recommended by WHO for detection of TB and MDR-TB.
- C-Tb (New Skin test for Latent TB): ICMR validated more specific new skin test C-Tb for detection of latent TB in adult population (18yrs and above) for use under the NTEP.
- TB Detect for improved smear microscopy to strengthen microscopic detection at periphery has been validated. It has better sensitivity as compared to conventional microscopy and has been recommended for use under NTEP.
- ICMR developed Standard Treatment workflow for paediatric pulmonary TB and Extra-pulmonary TB for all levels of health care system to facilitate management of Tuberculosis under NTEP (Till date no such thoroughly prepared document for peripheral health setup is available on TB). The document, posters and the App was launched on World TB day on March 24th 2022 by MoHFW.
- ICMR deposited "RD-Knockout polio non-permissive cell line" using CRISPR Cas9 to ATCC, USA. The development of CD155 (poliovirus receptor) gene knockout cells from the RD cell line can be widely used for virus culture of non-polio enteroviruses without the fear of poliovirus growth as inadvertent contamination.
- The technology for rapid, simple and cost-effective lateral flow immunoassay for the diagnosis of severe Haemophilia A and von Willebrand disease was developed and transferred for commercialization to Bhatt Biotech and has been approved by CDSCO for marketing. The World Federation of Haemophilia has shown keen interest in this technology and will promote it in other developing countries.
- X-ray based AI tool for COVID-19 diagnosis was validated. Indian Novel Claim Portal *inovecop* was developed.
- ICMR in collaboration with IMGENEX INDIA Pvt. Ltd. developed and performed the clinical validation of an indigenous SARS CoV2 Antigen detection kit (Im-CoV-Ag™). The kit is commercialized and presently in market.

- A technology to diagnose the cause of male infertility (Y chromosome microdeletions) was handed over to the industry partner APS Lifetech.
- ICMR has developed and transferred Bti- a mosquito bio-larvicide technology to the public sector undertaking - Hindustan Insecticides Ltd.

B. PRODUCTS IN PROCESS OF COMMERCIALIZATION

- An Artificial blood free Diet formulation has been developed for adult mosquitoes. It will be helpful in control of dengue, Chikungunya, Zika and Yellow Fever.
- ANM Mosquito Feeder-A microcontroller device has been developed for artificial diet/blood-feeding for mosquito rearing in the laboratory. This device reduces cost, space requirement and is very handy to use.
- Invention of a cost-effective mosquito attractant and lethal non-electric ovitrap was done.
- There was development of portable Protein Gel Electrophoresis Unit.
- A Mechanical Aspirator for the Safe Transfer of Mosquitoes was made.
- A novel process was developed for the production of a mosquito larvicidal formulation based on Solid-State Fermentation (SSF) of *Bacillus thuringiensis* var. *israelensis* (serotype H14) which is potentially a cost cutting technology with high commercial value.
- Immunodiagnostic kits were developed for detection of aspergillus fumigatus in sera of patients with bronchial asthma and pulmonary tuberculosis.
- Colorimetric isothermal (RT-LAMP) assay for rapid detection of Nipah virus infection has been developed. It does not require a thermal cycler and can be performed using a single-temperature heating device within 40 minutes.
- There was development of Nipah virus-specific IgM & IgG ELISA for screening of human serum samples.
- A functional food formulation for diabetic complications has been developed. This formulation is currently under preclinical safety evaluation. A MoU is signed with an industry for developing the products for clinical trials.
- A sensitive and easy-to-adopt assay to detect BPA in urine, milk and water samples has been developed and optimized.
- ICMR validated a novel point-of-care Hb measurement in pooled capillary blood by a portable autoanalyzer which has better Hb estimates than conventional methods being used.
- A new indigenous sputum transportation kit for bio-safe sputum transportation at room temperature was validated. It has been recommended for use under NTEP.
- ICMR validated quality of the Handheld X-rays with comparison to that of the standard X-rays, which was found to be at par and can be used for screening of TB under NTEP.

NEW INTERVENTIONS WITH IMPLICATIONS FOR PUBLIC HEALTH OR CLINICAL PRACTICE

- ICMR has developed a combo assay for the detection of SARS CoV 2, Influenza A, B and RSV in a single tube, which will be helpful in early diagnosis and better clinical management of respiratory infections.

- Target Product Profiles for the rapid diagnosis of sepsis in adults and neonates were developed to detail the criteria for performance and operational specifications of a "fit-for-use test" as per needs of healthcare in India.
- The *i*-DRONE study was first of its kind in the South Asian region where drones were used for delivering of COVID-19 vaccines from land to islands of Manipur and Nagaland. These drones delivered 21,000 units of medical supplies including multivitamin tablets, syrups, COVID-19 vaccines and routine vaccines.
- WHO-ICMR-Solidarity trial highlighted little / no effect of remdesivir, hydroxychloroquine, lopinavir and interferon regimes on hospitalized patients with COVID-19. These findings formed the basis for revised clinical management guidelines for COVID.
- A phase 2/3, multicentric randomized controlled study was implemented by ICMR to determine the safety and immunogenicity of COVOVAX in Indian adults. Emergency use authorization for vaccination in adults was accorded to COVOVAX by WHO and DCGI in India.
- Study for detection of anti-SARS-COV-2 IgG antibodies among unvaccinated HIV-infected individuals (PLHIV) attending ART Centre showed an estimated seroprevalence of 54.6% in unvaccinated, asymptomatic PLHIV. These findings highlighted the need of COVID-19 vaccination among this vulnerable group.
- ICMR has prepared 'Red cell panels' suitable for Indian population and have distributed them to >70 centres across India. This will help in accurate identification of rare donors and improve transfusion medicine services in India.
- A quasi-experimental pilot study among 138 mild to moderate anaemic (Hb <12 g/dl) adolescent girls (aged 17-19) supplemented with 100 gm/day pearl millet-peanut chikki for 3 months, showed that there was 23.9 % reduction of anaemia without any adverse events.
- Evaluation was done of immunogenicity and protective efficacy after vaccine interchangeability in a selected population of Eastern UP.The findings suggested that immunization with a combination of Covishield and Covaxin was not only safe but also elicited better immunogenicity.
- The mobile app "MosquiTracker" was developed for remote area entomological collection, monitoring and analysis. This can have major implications for the vector control strategies in the region.
- Tuberculosis Verbal Autopsy Tool was developed and validated. This tool will help to estimate the deaths occurring in the community due to Tuberculosis with high accuracy and will help the NTEP to understand the mortality due to TB.
- Visceral Leishmaniasis cases co-infected with HIV may be treated with AmBisome and Miltefosine combination with reduced treatment duration i.e. 14 days instead of 38 days. It has been accepted as treatment guidelines in the National Program / WHO.
- Digital autopsy with CT scanning was developed for dignified management of dead.
- Mutational analysis in MODY & NDM helped in changing treatment from insulin to OHA. IDRS (Indian Diabetes Risk Score) was evaluated across the nation and is found to be suitable, for cost effective screening for diabetes in Asian Indians.
- ICMR-INDIAB study recommended for using age-specific cut-offs while utilizing HbA1c to diagnose diabetes and pre-diabetes, so as to minimize the risk of over diagnosis and unnecessary initiation of treatment in elderly people, who could have physiological increase in HbA1c levels.

- ICMR-INDIAB study recommended reduction in carbohydrates and an increase in protein, for both, T2D remission and for prevention of progression to T2D in pre-diabetes and individuals with normal glucose tolerance, hence, underlining need for new dietary guidelines that recommend appropriate changes in macronutrient composition for reducing the burden due to diabetes in South Asia.
- Guidelines for Management of 20 cancer sites in the body were published, which will serve as a guidance document for treating physicians.
- Integration of ICMR e-Mor cause of death module with Tamil Nadu CRS software was completed and implemented in September 2021. This is of public health significance as it strengthens MCCD-CRS system to provide cause specific mortality statistics in the state.
- Framework for audit of Medical Certification of Cause of Death (MCCD) at Health Facility was developed by ICMR in collaboration with CBHI-DGHS and WHO. Implementation of this framework by hospitals would help minimize errors and ensure completeness of MCCD forms at the hospital.
- Based on the need for standard data collection on stroke for assessment of quality of care, the data fields from the Hospital based stroke registry core form of the National Stroke Registry Programme (NSRP) of ICMR-NCDIR have been identified and are being included in the Ayushman Bharat Transaction management database. Recording of standard data on stroke management in the AB–empanelled hospitals can facilitate data analysis of patterns of care and outcomes of stroke.
- Situational analysis of childhood cancer care services in India was conducted using a cross-sectional survey design. The most frequent challenge which patients and their caregivers faced was, treatment denial and treatment abandonment, for which, financial constraint was the most commonly cited reason. It is recommended to formulate a National Childhood Cancer Policy, as well as integrate childhood cancer in RBSK, ICDS and other child health welfare schemes.
- Due to absence of proper diagnostic measures for enteric viruses, diarrhoea with viral aetiology is misdiagnosed as bacterial, leading to irrational prescription of antibiotics. ICMR has developed a conventional RT-PCR assay for detection of 4 major viruses, Group A Rotavirus, Human enteric adenovirus species F, Astrovirus and Norovirus GI/GII.
- There was development and testing of a Behavioural Change Intervention (BCI) tool for smokeless tobacco quitting. The tool encompasses interactive booklet for healthcare providers which includes details related to different types of smokeless tobacco products, chemical compositions, its effect on human health & wellbeing and advantages of quitting smokeless tobacco.
- There was Establishment of Utility of Blood as the Clinical Specimen for the Molecular Diagnosis of PKDL.
- There was development of improved lid of underground tanks where *An. stephensi* used to breed (20-40%) that prevented *An. stephensi* from breeding in Western Rajasthan.
- ICMR developed an intervention package for smokeless tobacco (SLT) cessation among tribal women in Manipur that consists of 4 sessions delivered on one to one basis to women SLT users, at home, over a duration of 4 weeks.
- There was development of Behaviour Change Communication (BCC) intervention for improving utilization of Maternal and Child Health (MCH) Services through Male Participation among Saharia Tribes in selected districts of Madhya Pradesh.

- HTA study on linking HIV and Family Planning services to promote dual contraceptive use among women living with HIV (WLHIV) demonstrated that it was not only cost-effective but could avert many unintended pregnancies, abortions, maternal deaths and infections among newborns.
- Mass distribution of DEC double fortified salt (Diethylcarbamazine (DEC) at 0.2% w/w and iodine) was implemented in two phases in Nancowry group of islands, sublimating to ongoing MDA. This resulted in elimination of persistent foci of diurnally sub-periodic Wuchereria bancrofti among Nicobarese tribe in the entire group of Nancowry group of islands , a lone focus in India.
- ICMR developed food-based recipe using an indigenous flower called Mahua for tribal pregnant women. The results showed increase in haemoglobin levels when compared to control group. The recipe is under consideration with Govt. of Telangana.
- Studies on the Impact of *Salmonella* killing lytic bacteriophages on probiotic microbiota showed that the administration of lytic bacteriophages will not harm the probiotic microbiota and are likely to be safe for use in food preservation.
- Active case finding in severely malnourished children admitted to Nutritional Rehabilitation Centres (NRCs) has shown very high (5%) incidence of TB. Case detection was improved with proper training and providing point of care diagnostic tests under National Programme. The intervention has potential to increase quality and yield of the TB case detection at NRCs.
- Based on recently concluded study by ICMR, for screening of TB in High-risk groups (all patients aged 60 years or more, diabetic, living with HIV, & admitted to medical wards), current diagnostic algorithm (2 spot and one overnight sputum sample) can be simplified by limiting sputum collection to a single spot sample only.
- The White Paper on "Infectious Diseases Beyond COVID-19" highlights the measures needed to tackle other infectious diseases during the current pandemic. This paper intends to create awareness among healthcare professionals regarding the need to focus on the other infectious diseases in such unprecedented times, and to minimize the impact of COVID-19 pandemic.
- ICMR developed a comprehensive neuropsychological and behavioural test battery, the Multilingual Dementia Research and Assessment Toolbox (MUDRA—previous name) ICMR Neuro Cognitive Tool box (ICMR-NTB), in five different Indian languages that can be used to assess cognitive impairment due to stroke and other dementias in different populations within India.

IMPLEMENTATION RESEARCH THAT LED TO HIGHER COVERAGE AND/OR QUALITY OF HEALTH PROGRAMS

- India Hypertension Control Initiative is a large implementation project which has been implemented in public health facilities in 141 districts of 25 states. Best practices of IHCI have been integrated into the NPCDCS program. This project has received a UN Award.
- National TB Prevalence Survey for prevalence of national and state-wise data on TB and latent TB along with health seeking behaviour has been concluded by ICMR and the report shared with CTD. This mega survey is a significant contribution towards tackling TB elimination Programme of India.
- A study on introduction of quality management system with well-defined modules and processes under National programme laboratories has shown significant improvement in quality of TB diagnosis and increased yield of TB cases at these facilities. This will have a larger impact on quality of TB diagnosis under the National Programme.

- ICMR constituted an Expert Committee to review the indicators used in the Global Hunger Index (GHI). The Committee concluded that the four indicators used in the GHI [undernourishment, stunting, wasting, and child mortality] do not measure hunger per se, as these are not the manifestations of hunger alone. The deliberations of the Expert Committee were published in Indian Journal of Medical Research as a White Paper entitled "Global Hunger Index does not measure hunger - An Indian perspective."
- Field feasibility evaluation of one kit based rapid diagnostic test (Rapidogram) for UTI detection provided evidence on its usefulness in peripheral healthcare settings with 99.6% specificity, 90.6% sensitivity, 96.7% PPV, 98.9% NPV and 98.7% test accuracy. Diagnostic test was recommended to National Health Systems Resource Centre (NHSRC) under NHM for pilot study.
- Cost effectiveness assessments of two indigenously developed rapid diagnostics for diagnosis and management of uncomplicated symptomatic UTI among women provided evidence on the test associated cost-efficient clinical decision-making. Net Monetary Benefit of ₹ 37,715 (RightBiotic) and ₹ 37,281 (Rapidogram) were obtained for using these diagnostics based on GDP per capita income of ₹1, 45,679 in 2022.
- For lymphatic filariasis, ICMR is advocating DEC fortified salt (cooking salt) as an adjunct tool which when consumed by endemic communities, accelerates elimination of microfilaremia from the communities. There is in principle agreement to adopt the DEC salt (DECIDE – DEC and Iodine fortified salt) in the National policy.
- Impact of Anti-retroviral therapy (ART) under National AIDS Control Programme (NACP) was evaluated and free ART programme was found to be cost-effective. Issues highlighted for future action include focus on ageing HIV population, co-morbidities, retention, establishment of more centres in underserved states, immediate linkage to ART and improved CD4/viral load monitoring.
- Seroprevalence of Hepatitis B virus (HBV) and Hepatitis C virus (HCV) among High-Risk Groups and Bridge Population in India at regional and national level was conducted. This resulted in evidence-based planning for the National Viral Hepatitis Control Programme (NVHCP) in India.
- It was recommended that Vitamin D3 is efficient than Vitamin D2 in improving the reduced vitamin D levels, thereby, Vitamin D3 supplementations may be given rather than the vitamin D2 supplements.
- In a recent nationwide survey of Indian children, it was found that only 7 states had a prevalence of Vitamin A Deficiency (> 20%) requiring a VAS program. This raises the need for considering a targeted state-based VAS program, unlike the nation-wide VAS program that is currently the norm. An additional reason is that there may be an overlap of ongoing vitamin A fortification (oil and milk) and VAS program in India, resulting in hazardous effect by exceeding the upper limit of vitamin A. Based on this, the current universal VAS program is being considered for a revision by the Child Health Division of Ministry of Health & Family Welfare.
- School students/Public bus conductors were used as TB Ambassadors for creating TB awareness to increase diagnostic coverage in the country. There was usage of Nutrition supplement to increase adherence and treatment completion in TB patients in Jharkhand state (RATIONS study).
- Adverse Events Monitoring for COVAXIN vaccine for the entire state of Tamil Nadu was undertaken by ICMR.
- During the evaluation phase of the Sickle cell disease project, it was observed that the patients could take their medication from the PHCs itself instead of going to DHH, which saved them from out-

of-pocket expenditure. Given the success of the project, it will be undertaken to the entire CHCs of Kandhamal district, Odisha.

- During ICMR surveys, it was noted that the coverage of livestock vaccination against anthrax was very minimal, so the vaccination was made free of cost for all livestock by District Collector, Koraput District, Odisha. In the last 2 years, there are no outbreaks of Anthrax or mortality due to Anthrax disease in the district.
- There was reporting of massive shortage of Long Lasting Insecticide Treated Nets (LLINs), villagers sleeping without any bednet protection, expiry issues of existing LLINs, and vector and malaria caseload increase in very remote Tribal areas to the authorities, prompting the district authorities to distribute Insecticide Treated Bednets (ITNs) in all malaria endemic villages of Dhalai District, Tripura.
- Constant monitoring of the malaria surveillance system by ICMR, assisted by the Fever Tracker app, led to the identification of several gaps and continuous feedback to the District Health Authorities.
- Scrub typus prevalence and the risk factors responsible for the spread in the endemic foci of Tamil-Nadu and Kerala was identified. An educational pamphlet was prepared, both in English and Malayalam and handed over to the DHS, Kerala for creating awareness among the public.
- The productive period of a malarial larval habitat was estimated, enabling target larval sources to reduce adult populations. It was noted that implementing larvicidal strategy before monsoon season is presumably the most cost-effective strategy. The output can be utilized for environmental monitoring of mosquito breeding risk in other malaria endemic areas, particularly where medium/large water bodies are the predominant breeding sites for malaria vectors.
- A rapid study was carried out to assess the nutritional status of the children in litchi growing areas of Muzaffarpur district of Bihar, where an outbreak of Acute Encephalitis Syndrome (AES) was reported. Most children reportedly consumed Litchi fruits and were exposed to hot sun during summer. Litchi fruits contain hypoglycin A or Methylene cyclopropylglycine (MCPG) known to cause hypoglycemia and metabolic derangement. Therefore, parents were sensitized not to allow their children to skip the night meal and not to play outdoors in hot sun.
- ICMR STEMI ACT has helped to improve the thrombolytic rate in STEMI patients in Hub (Medical College in a District) and Spoke model (CHCs, Civil hospital, District hospital). STEMI ACT has been initiated in 8 districts and 7 states and successfully implemented in Shimla, (HP) and Ludhiana, (Punjab) districts. The STEMI guidelines under NPCDCS are being modified to incorporate the ICMR-STEMI ACT model.
- Stroke Care Pathway is being developed through stroke unit at medical college hospital level and Mobile Stroke Unit (ambulance equipped with CT scanner, telemetry, small laboratory facility, and provision of giving thrombolytic therapy under supervision of a neurologist or a physician) at community level. A stroke code/green channel was implemented at hospital emergency to provide thrombolysis to ischemic stroke patients. Door-to-CT time and door-to-thrombolysis time in government colleges improved following establishment of stroke unit and implementation of stroke code.
- ICMR demonstrated for the first time that the two existing rotavirus vaccines in public health program in India (Rotavac & Rotasiil) can be used in an interchangeable dosing schedule safely and effectively for routine immunization. It aided in overcoming vaccination shortages and supply chain challenges. The findings were translated into policy decisions for vaccination delivery by India's health ministry.

- Typhoid Conjugate Vaccine (TCV)mass vaccination campaigns were found as effective population-based tools to prevent typhoid fever. The vaccine has been recommended in the NTAGI meeting to be included in public health program.
- There is strengthening of Early Detection of Breast Cancer, involving Strategic Education and Awareness Among Women, as a joint program of ICMR and State Government. A total of 47,943 women (30-65 years) from Jalore, Pali, and other Jodhpur districts of Rajasthan were covered. After the knowledge assessment, women (age of >18 years) were trained in breast self-examination (BSE). Suspected cases of breast cancer were suggested to visit the tertiary care centre. The women trained in BSE were followed up periodically to reinforce BSE.
- Screening of Sickle Cell Anaemia was carried out by ICMR, jointly with Rajasthan State Medical and Health Department. A total of 43,908 population was screened for Sickle Cell Anaemia and prevalence of 7.49% (3365) was reported. Sickle status card was distributed to the participants along with counselling.
- Referral system for silicosis suspects has a potential to improve clinical assessment and certification of patients with suspected silicosis and improve awareness among sandstone miners and mine owners about the silicosis. It will help in diagnosing silico-tuberculosis in light of National Strategic Tuberculosis Elimination Program of India which has a Goal of Tuberculosis Elimination by 2025.
- ICMR developed and validated discriminatory concentrations of nine insecticides with bottle bioassay and 2 insecticides with filter paper test against *Aedes aegypti* (first time) and *An. stephensi* mosquitoes, which are currently in use or under evaluation for various vector control applications (IRS, LLIN, space spray, household products, etc).This information is key to establish the baseline susceptibility of vector populations to the new insecticides and to detect any change in phenotypic resistance after their deployment. It will help the national programme in monitoring of insecticide susceptibility of mosquito vectors of public health importance. Results were included in a report published by WHO in March 2022.
- It was established that adding Tranexemic Acid to the management of all cases of PPH saves more lives, prevents surgical interventions or ICU admissions and is cost effective. The results were communicated to the Maternal Health division for incorporating the same into the LaQshya-Guidelines and Dakshata checklist.
- Cost-effectiveness of different Point of Care tests for diagnosing Sickle Cell Anaemia was assessed by ICMR. Since the existing costs of two clinically effective tests did not prove to be cost-effective, threshold analysis was done which showed that if the kit cost was reduced to less than Rs. 100, it would be cost-effective. The Ministry then negotiated the price with the companies and a notice was sent to all state and UT health secretaries to procure the said kits at Rs. 100 and increase coverage to sickle tests.
- A validation study commissioned by MoHFW on comparing methods assigning causes of death via verbal autopsy for non-institutional deaths was conducted by ICMR. The study findings established that the existing manual method (Physician certified verbal autopsy) being currently used are superior to automated methods (computer coded verbal autopsy). The study findings were presented to the Technical advisory committee constituted by MOHFW.
- The malaria elimination demonstration project (MEDP) was conducted by ICMR in collaboration with FDEC, India and State Govt. (in Public-Private Partnership mode) in Mandla district of M.P. The project covered population of 11.5 Lacs in 1233 villages of Mandla district and adopted T4 strategy

(Track, Test, Treat, and Track) for control and management of malaria along with vector control measures.The study demonstrated that malaria elimination in India is feasible and achievable within a stipulated timeline using existing tools.

- A study was carried out in all seven Saharia-dominated districts of Madhya Pradesh in which there is an alarmingly high TB prevalence. The interventions comprised of case detection and treatment through village TB volunteers; involvement of traditional healers & community members; Advocacy, communication, and social mobilization (ACSM) activities. A total of 5,30,002 individuals from 1,814 Saharia villages in seven districts were evaluated. The treatment success rate was above 90%. This study highlights the significance of innovative community-based approaches in controlling TB.
- A program to control of Tuberculosis among the Nicobarese of Car Nicobar was initiated with a special focus on detection of Latent TB infection among contacts, screening of hepatitis B infection in TB patients, treatment strategy based on levels of liver enzymes, follow-up of the children who were on chemoprophylaxis, counselling of parents on importance of chemoprophylaxis, and involving Traditional knowledge practitioner (TKPs) in surveillance . The efforts resulted in the decline of occurrence of new cases per year and mortality due to pulmonary TB.
- A screening model, along with an Andoid-based registry, was developed and instituted locally to screen Sickle cell disease (SCD), and subsequently treat the patients through PHC doctors. So far, the screening and treatment for SCD are available only at tertiary care hospitals. This intervention study has influenced the state health departments and made them to supply hydroxyurea and other drugs for SCD care to SCD endemic areas. Some of the intervention components can be incorporated into the forthcoming National programme.
- ICMR-NIN proposed revision to nutrition norms for schedule II of the NFSA, 2013 for energy and protein. Further, the centre provided norms for protein quality and micronutrients such as calcium, iron, zinc, vitamin A, dietary folate and vitamin B12, for beneficiaries of Poshan 2.0 and PM Poshan Programme.
- A 2-minute film was developed to showcase the journey of Covaxin development and other achievements of ICMR in tackling COVID-19. The film was showcased in Geneva during ‘Going Viral’ Book launch and Postal stamp Launch.

INFRASTRUCTURE AND CAPACITY BUILDING

- There was inauguration of Made in India ‘Mobile BSL-3 Laboratory’ by Dr. Bharati Pravin Pawar, Hon’ble Union Minister of State for Health & Family Welfare, Govt. of India at Nashik on 18th February 2022.
- There was establishment of the Polio essential facility (PEF) at ICMR-NIV, Pune, as per the Global Action Plan III guidelines.
- A state-of-the-art Rabies Laboratory offering the full range of molecular and serological tests for antemortem and post-mortem diagnosis of human rabies has been established by ICMR.
- The Department of Neurosurgery at ICMR-BMHRC, Bhopal, has started carrying out “awake craniotomy” surgeries. This enables the Neurosurgeon to ensure minimal damage to normal brain tissue during surgery. The outcomes are much better as compared to traditional surgeries.
- The Department of Cardiac Surgery at ICMR-BMHRC, Bhopal, has started carrying out “minimally

invasive coronary artery surgery" (MICAS). The procedure is as effective as the traditional method, but there is a much faster recovery time.

- Under the DBT UMMID initiative, ICMR has established facilities of antenatal screening for hemoglobinopathies and newborn screening for six inherited diseases in 'Aspirational District' Nandurbar, Maharashtra.
- Under the DBT UMMID initiative, ICMR has been recognised as the training centre for genetic diseases and started a fellowship program in 'Clinical genetics' for in-service clinicians aimed at focused training in the diagnosis of various inherited haematological and immunological disorders.
- Under the multicentric study on Systemic Lupus Erythematosus (SLE) from the North-Eastern (NE) region of India, diagnostic facilities for autoimmune diseases have been established in 5 centres in the region.
- ICMR developed effective intervention model for the Sickle Cell Disease (SCD) patients in tribal areas for accessing government health care system and capacity building in terms of knowledge, skill and training of the health care workers at different levels of health system for prevention and management of SCD.
- Mobile pictorial app for real-time surveillance and drug compliance monitoring was prepared with Dashboard in collaboration with North Eastern Space Applications Centre (NESAC).
- ASHAs empowered for establishing chain for diagnosis and referral mechanism in Cachar, Assam.
- ICMR developed Interventions on control of Anthrax in endemic district of Koraput, Odisha, using One Health approach. Three capacity building & training modules for different stakeholders as well as audio content in local tribal language for creating awareness were developed.
- Three regional trainers workshops were conducted on the 'National Guidelines for Data Quality in Surveys', developed by ICMR, for building capacities of researchers engaged in implementing surveys. These guidelines have the potential to improve data quality in demographic, health, and nutrition surveys conducted in India.
- The 'Education for Effective Nutrition in Action (ENACT) and Food Systems' modules were developed in coordination with FAO. Six e-learning modules on "Nutrition and Food Systems" were also developed and six universities were contacted to include these modules in the undergraduate curriculum.
- ICMR developed and released 3 volumes of "Contribution of ICMR to world science literature in the area of COVID-19" containing consolidated research articles on COVID-19 published in peer-reviewed journals by ICMR and its institutes.
- A total of 27 Scientists and young researchers were awarded in 24 different ICMR Awards/Prizes categories in the field of biomedical research.A total 3,690 Adhoc proposals, 3,220 Fellowships, and 1,126 special call proposals were processed. Under ICMR-MD/MS/DM/MCh/DNB/DrNB/MDS thesis support program, 101 proposals have been selected for financial support**.** 21 students have joined ICMR JR fellowship programme, whereas 12 students joined Post Doctoral fellowship programme.
- The Clinical Trial registry of India has registered around 50,000 clinical trials till date. ICMR developed Customized dataset items for Ayurveda studies in CTRI portal. The National COVID Registry has registered more than 55,000 cases and provides information to the MoHFW for development of policies and programmes.

SELECTED HIGH IMPACT PUBLICATIONS

1	Ella R, Reddy S, et al; COVAXIN Study Group. Efficacy, safety, and lot-to-lot immunogenicity of an inactivated SARS-CoV-2 vaccine (BBV152): interim results of a randomised, double-blind, controlled, phase 3 trial. Lancet. 2021 Dec 11;398(10317):2173-84.	202.7
2	Fleming KA, Horton S, et al.The Lancet Commission on diagnostics: transforming access to diagnostics. Lancet**.** Oct 2021; 398: 1997-2050.	202.7
3	Zhou B, Carrillo-Larco RM,et al. Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. Lancet. 2021;398(10304):957-80.	202.7
4	Saxena N, Singh S. South Africa's Health: Traditional healers in South Africa: a parallel health care system connecting tribal healers to primary health care: A dire need to alleviate health of indigenous and tribal populations. BMJ Mar 2022. https://www.bmj.com/content/310/6988/1182/rr-0	93.3
5	Shrivastava S, Verma AK, Saha KB. South Africa's Health: Traditional healers in South Africa: a parallel health care system connecting tribal healers to Primary Health Care: A purpose stride, but difficult to accomplish. (Lettertoeditor).BMJ Jan2022. https://www.bmj.com/content/310/6988/1182/rapid-responses	93.3
6	Yadav PD, Kumar S. Global emergence of SARS-CoV-2 variants: new foresight needed for improved vaccine efficacy. Lancet Infect Dis. 2022 Mar;22(3):298-9.	71.4
7	Ella R, Vadrevu KM, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial. Lancet Infect Dis. 2021;21(5):637-646.	71.4
8	Murhekar MV, Kamaraj P, et al; ICMR Serosurvey Group. Immunity against diphtheria among children aged 5-17 years in India, 2017-18: a cross-sectional, population-based serosurvey. Lancet Infect Dis. 2021 Jun;21(6):868-875.	71.4
9	Thomson KM, Dyer C, et al; BARNARDS Group. Effects of antibiotic resistance, drug target attainment, bacterial pathogenicity and virulence, and antibiotic access and affordability on outcomes in neonatal sepsis: an international microbiology and drug evaluation prospective substudy (BARNARDS). Lancet Infect Dis.2021 Dec;21(12):1677-1688.	71.4
10	Dhar MS, Marwal R, et al. Genomic characterization and epidemiology of an emerging SARS-CoV-2 variant in Delhi, India. Science.2021 Nov 19;374(6570):995-999	63.7
11	GBD 2019 Adolescent and Young Adult Cancer Collaborators. The global burden of adolescent and young adult cancer in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Oncol.2022 Jan;23(1):27-52.	54.4
12	Sarin SK, Prasad M, et al. Integration of public health measures for NAFLD into India's national programme for NCDs. Lancet Gastroenterol Hepatol. 2021 Oct;6(10):777-778.	45.0

13	GBD 2019 Diabetes Mortality Collaborator. Diabetes mortality and trends before 25 years of age: an analysis of the Global Burden of Disease Study 2019.Lancet Diabetes & Endocrinol. 2022 Mar 1;10(3):177-92.	44.8
14	Anjana RM, Unnikrishnan R, et al and ICMR-INDIAB collaborators. Achievement of guideline recommended diabetes treatment targets and health habits in people with self-reported diabetes in India (ICMR-INDIAB-13): a national cross-sectional study. Lancet Diabetes &Endocrinol. 2022; 10 (6):430-441.	44.8
15	Sapkal G, Srivastava RK, et al. Immune responses against different variants of SARS-CoV-2 including omicron following six months of administration of heterologous prime-boost COVID-19 vaccine. J Travel Med. 2022May 31;29(3):taac033.	39.1
16	Kant R, Dwivedi G, Zaman K, Sahay RR, Sapkal G, Kaushal H, Nyayanit DA, Yadav PD, Deshpande G, Singh R et al: Immunogenicity and safety of a heterologous prime-boost COVID-19 vaccine schedule: ChAdOx1 vaccine Covishield followed by BBV152 Covaxin. Journal of travel medicine 2021. Dec 29;28(8):taab166	39.1
17	India State-Level Disease Burden Initiative Neurological Disorders Collaborators. The burden of neurological disorders across the states of India: The Global Burden of Disease Study 1990–2019. Lancet Glob Health 2021 Aug;9(8): E1129-44.	38.9
18	Mandal S, Arinaminpathy N, et al. Responsive and agile vaccination strategies against COVID-19 in India. Lancet Glob Health. 2021 Sep; 9(9): e1197–e1200	38.9
19	Murhekar MV, Bhatnagar T, et al. SARS-CoV-2 antibody seroprevalence in India, August-September, 2020: findings from the second nationwide household serosurvey. Lancet Glob Health.2021 Mar;9(3):e257-e266.	38.9
20	Murhekar MV, Kumar MS. Reaching zero-dose children in India: progress and challenges ahead. Lancet Glob Health. 2021 Dec; 9(12): e1630-e1631.	38.9
21	Faizi N, Kaur J. Insecticide resistance and ITNs in India. Lancet Glob Health. 2021 Oct;9(10):e1370.	38.9
22	Rajamanickam A, Kumar NP, et al. Latent tuberculosis co-infection is associated with heightened levels of humoral, cytokine and acute phase responses in seropositive SARS-CoV-2 infection. J infect. 2021;83(3):339-46	38.6
23	Thangaraj JWV, Yadav P, et al. Predominance of delta variant among the COVID-19 vaccinated and unvaccinated individuals, India, J Infect. 2022 Jan; 84(1): 94–118.	38.6
24	Rubeshkumar P, John A, Narnaware M, M J, Vidya F, Gurunathan R, et al. Persistent Post COVID-19 Symptoms and Functional Status after 12-14 weeks of recovery, Tamil Nadu, India, 2021. J Infect. 2022 May; 84(5): 722–746.	38.6
25	Thangaraj JW, Kumar MS, Kumar CG, Kumar VS, Kumar NP, Bhatnagar T, Ponnaiah M, Sabarinathan R, Sudharani D, Nancy A, Jagadeesan M. Persistence of humoral immune response to SARS-CoV-2 up to 7 months post-infection: Cross-sectional study, South India, 2020-21. J Infect. 2021 Sep; 83(3): 381–412.	38.6

26	Global Burden of Disease 2019 Cancer Collaboration. Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019-A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol2022 Mar 1;8(3):420-444.	33.0
27	Sands K, Carvalho MJ, et al; BARNARDS Group, Walsh TR. Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries. Nat Microbiol. 2021 Apr;6(4):512-523.	30.9
28	Parai D, Dash GC, et al. Antibody response to SARS-CoV-2 infection among health workers: a report from India. Eletter. Science Immunology 2021.	30.6
29	Paradkar MS, Devaleenal DB, et al. Randomized Clinical Trial of High Dose Rifampicin with or without Levofloxacin versus Standard of Care for Paediatric Tuberculous Meningitis: The TBM-KIDS Trial. Clinical infectious diseases. 2022. Clin Infect Dis. 2022 Nov 1; 75(9): 1594–1601.	20.9
30	Longley AT, Date K, et al. Evaluation of Vaccine Safety After the First Public Sector Introduction of Typhoid Conjugate Vaccine-Navi Mumbai, India, 2018. Clin Infect Dis. 2021 Aug;73(4):e927-e933	20.9
31	Burza S, Mahajan R, et al.AmbBisome monotherapy and combination AmBisome – miltefsoine therapy for the treatment of visceral leishmaniasis in patients co-infected with HIV in India: a randomized open label, parallel arm, phase 3 trial. Clin Infect Dis.2022 Oct 12;75(8):1423-1432	20.9
32	Elhence A, Singh A, et al. Real-world re-treatment outcomes of direct-acting antiviral therapy failure in patients with chronic hepatitis C. J Med Virol.2021 Aug;93(8):4982-4991.	20.6
33	Dash GC, Subhadra S, et al. Breakthrough SARS-CoV-2 infections among BBV-152 (COVAXIN®) and AZD1222 (COVISHIELD™) recipients: Report from the eastern state of India. J Med Virol. 2022 Mar;94(3):1201-1205.	20.6
34	Deval H, Behera SP, et al. Genetic characterization of dengue virus serotype 2 isolated from dengue fever outbreaks in eastern Uttar Pradesh and western Bihar, India. J Med Virol. 2021 Jun;93(6):3322-9.	20.6
35	Chandra P, Lo M, et al. Genetic characterization and phylogenetic variations of human adenovirus-F strains circulating in eastern India during 2017-2020. J Med Virol. 2021 Nov;93(11):6180-6190.	20.6
36	Aranha C, Patel V, et al. Cycle threshold values in RT-PCR to determine dynamics of SARS-CoV-2 viral load: An approach to reduce the isolation period for COVID-19 patients.J Med Virol. 2021 Dec;93(12):6794-6797.	20.6
37	Mahajan NN, Gajbhiye RK, et al. Co-infection of malaria and early clearance of SARS-CoV-2 in healthcare workers.J Med Virol.2021 Apr;93(4):2431-2438	20.6
38	Parai D, Choudhary HR, et al. Single-dose of BBV-152 and AZD1222 increases antibodies against spike glycoprotein among healthcare workers recovered from SARS-CoV-2 infection. Travel Med Infect Dis.2021 Nov-Dec;44:102170.	20.4

39	Ganeshkumar P, Muthappan S, et al. Syndromic surveillance during religious mass gatherings, southern India 2015–2018. Travel Med Infect Dis.2022 May-Jun; 47:102290.	20.4
40	Shukla P, Singh KK. Uncovering mitochondrial determinants of racial disparities in ovarian cancer. Trends Cancer. 2021 Feb;7(2):93-97.	19.1

PATENTS

A total of 26 Indian patent applications, 1 design application, 5 copyright applications, 10 PCT applications and 6 International patent applications were filed during this period. 5 Indian patents and 3 International patents were granted.

Table 1: Patent Applications.

S N	Title of Invention	Patent Application No.
1.	An Assay And Method For Detection of SARS-CoV-2 From Human Respiratory Samples	202111015708
2.	Fluorescent Polystyrene Based Nanohybrid Array For Estimation Of Circulating Cell-Free MiRs	202111031427
3.	Screening assay for detection of epidemiologically important SARS-CoV-2 variants	202111032470
4.	A pharmaceutical composition with a recombinant fragment of human surfactant protein-D for pulmonary infection including SARS-COV-2	202111030956
5.	Novel method for concentration of polio viruses and other entero viruses from sewage	202111037829
6.	Development of microneedle patch for trans-scleral administration of triamcinolone acetonide to enhance choroid, retinal and vitreal concentration	202111042201
7.	A simple user friendly method for extraction of nucleic acids	202111043228
8.	Fever tracker app for the health workers	202111049722
9.	Development of HEK293 knock-out cell line of EV-A71 receptors SCARB2 and PSGL1 genes	202111048030
10.	Human Monoclonal antibodies against SARS-CoV-2 and a method of generation thereof	202111052088
11.	Simple, novel and cost effective Lateral Flow Immunoassay for diagnosis of Glanzmann thrombasthenia	202211003648
12.	Compositions for metabolic reprogramming of cells by modulating the expression of Tumor Suppressor Candidate 1 (TUSC1)	202211003978
13.	Fiber optic nano antenna based excitation of whisper gallery mode resonator and various sensing applications	202211004683
14.	A nano -dentritic cell construct for selective targeting of tumor cell	202211005691
15.	Hydroxyapatite-responsive cell-attachable and stable surface-active biocompatible mats	202211009698

16.	Suture resistant antimicrobial biodegradable and biocompatible fibrous patch constructs	202211008790
17.	Portable Protein gel Electrophoresis Unit	202211008794
18.	Probiotic Bael based nutraceutical for remission of ulcerative colitis	202211012630
19.	VCRC-ANM Mosquito Feeder-A microcontroller-based device for artificial diet/blood feeding for mosquito rearing in the laboratory	202211016261
20.	Development of universal method for simultaneously detection of diseases caused by inter and intra species using Hybrid LAMP kit	202211019752
21.	Vaginal Lactobacilli for urogenital health	202211019761
22.	Hydroxyapatite-responsive cell-attachable and stable surface-active biocompatible mats	202211009698
23.	Invention of a cost effective mosquito attractant and lethal non-electric ovitrap	202211015554
24.	Suture resistant antimicrobial biodegradable and biocompatible fibrous patch constructs	202211008790
25.	A probiotic bael based nutraceutical and a process of preparation thereof	202211012630
26.	Biomarker panel to diagnose the malaria severity with statistical predictive model method	202211014867
27.	Mobile Application based System for Adherence to prescribed analgesics and adjuvants in Cancer patients receiving palliative care - Part 2	21105/2021-CO/SW
28.	Mobile Application based System for Adherence to prescribed analgesics and adjuvants in Cancer patients receiving palliative care- Part-1	21107/2021-CO/SW
29.	Health Diary	22461/2021-CO/L
30.	Sehat ki Diary	22462/2021-CO/L
31.	Fever Tracker App for the Health Workers	1826392/2021-CO/SW
32.	A Mechanical Aspirator for the Safe Transfer of Mosquitoes	348640-001
33.	A rapid and sensitive method for detecting SARS-CoV-2	PCT/IN2021/050549
34.	Herbal Composition for the treatment of menopausal syndrome	PCT/IN2021/050592
35.	A paper disc based method for determining the drug susceptibility of Mycobacterium tuberculosis	PCT/IN2021/050414
36.	A diagnostic device and method for differentiating Asthma-COPD Overlap Syndrome (ACO) from Asthma and COPD	PCT/IN2021/050793
37.	A method for developing a rapid immunochromatographic assay for identifying hepatitis E infection	PCT/IN2021/050758
38.	An assay and method for detection of SARS-CoV-2 from human respiratory samples	PCT/IN2022/050173
39.	RT-LAMP assay for detection of human β-actin housekeeping gene	PCT/IN2022/050183
40.	A pharmaceutical composition with a recombinant fragment of human surfactant protein-D for pulmonary infection including SARS-CoV-2	PCT/IN2022/050237

41.	Rapid LAMP assay for detection of *Corynebacterium diphtheria*	PCT/ IN2022/050276
42.	Fluorescent polystyrene based nano-hybrid array for estimation circulating cell-free MiRs	PCT/ IN2022/050239
43.	Device for Germfree and gnotobiotic mosquitoes	i) Indonesia App. No. awaiting ii) Singapore App. No. 11202202863Q
44.	Apparatus, Method and Kit for Detection of Von Willebrand Factor and Factor VIII	
45.	Biomarkers for predicting malaria severity and methods thereof	

Table 2: Patents granted

S. No	Title of invention	Application No
1	A PCR method for the detection of *Chlamydia Trachomatis*	362608
2.	Rapid detection of drug resistant *Plasmodium falciparum* through a novel approach using loop mediated isothermal amplification	380417
3.	Method of processing of feeder cells suitable for adult stem cell proliferation	385296
4.	Water re-circulated garment for auxiliary body cooling for protection against high heat exposure	384530
5.	A process for the preparation of a fibrinolytic enzyme	391961
6	A novel molecular diagnostic technique for detecting the different species of plasmodium	Congo Democratic Republic 373/2016
7	RNAi agent for inhibition of chikungunya virus	Australia AU 2014285701
8	Alginate Chitosan Nanoformulation of OmpA - a Shigella Protein Subunit	US 11,298,415

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CONTENTS

COMMUNICABLE DISEASES

Communicable and infectious diseases pose serious public health problems. ICMR research efforts in the area of communicable diseases were made by 16 institutes/ centres including Regional Medical Research Centres (RMRCs) and their field stations located in different parts of the country as well as by granting adhoc projects in extramural mode in universities/ medical colleges and other organizations. The research activities carried out by different ICMR Institutes and their outcome for the year 2021-22 are detailed in this chapter.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF VIROLOGY (ICMR-NIV), PUNE

Diagnostic real-time RT-PCR for screening of samples for SARS-CoV-2

- The ICMR-NIV (including the units) overall tested 8,14,556 samples for SARS-CoV-2.
- Clinical samples (n=8,14,556) were investigated using SARS CoV-2 real time RT-PCR. SARS-CoV-2 positivity of 15.23%was detected at National Influenza Centre (NIC), Pune, 29.46% at ICMR-NIV Kerala unit, 6.5% at ICMR-NIV Bangalore Unit, and 8.08% at the ICMR-NIV Mumbai Unit.
- ICMR-NIV indigenously developed and standardized one-tube SARS-CoV-2 RT-qPCR assay and transferred it to industry for commercial production.
- ICMR-NIV developed and standardized a one-tube combo RT-qPCR kit for simultaneous detection of SARS-CoV-2 and influenza viruses and distributed to VRDL network.
- ICMR-NIV acted as the central hub and distributed real-time RT–PCR kits, VTM, RNA extraction kit, and NGS sequencing kits to Government laboratories.
- ICMR-NIV has achieved a major feat by qualifying the WHO-EQAS panel in 2021 with 100% concordance. ICMR-NIV also dispatched WHO SARS CoV-2 EQAS panel to 649 different labs all over India.
- Under the 'Atmanirbhar Bharat' program, ICMR-NIV evaluated SARS-CoV-2 real time RT-PCR kits (n=80), RNA extraction kits (n=25), VTMs (n=15) and swabs and did batch testing before distribution to various laboratories.
- Pan India epidemiological, virological and genomic surveillance for human influenza and SARS CoV-2 through DHR-ICMR VRDL Network was established in which 18,158 samples tested for influenza and SARS CoV-2 by 28 VRDL laboratories.
- As evident from SARS-CoV-2 diagnostic data, second wave peaked in April-May 2021 and the third wave peaked in January 2022 as shown in fig. 1. Influenza viruses were detected in 4384

(4.34%) samples, influenza A/H3N2 virus in 2551 (2.53%), influenza A/H1N1pdm09 virus in 206 (0.20%) and influenza B in 1627 (Fig. 1).

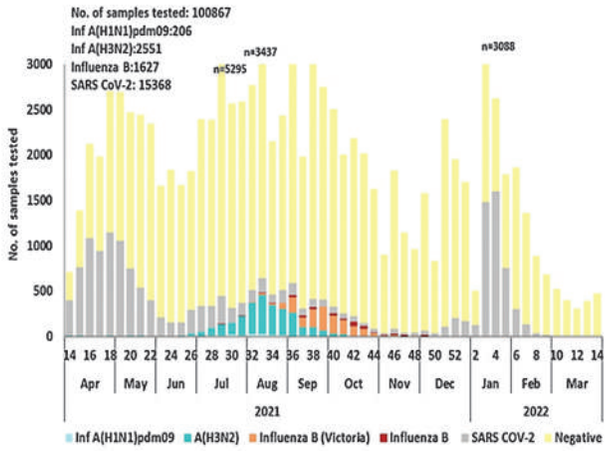


Fig. 1: Samples tested for SARS CoV-2, influenza A and B viruses at NIC, ICMR-NIV, Pune.

Evaluation of immunogenicity and protective efficacy after vaccine interchangeability in a selected population of eastern UP

Study on heterologous vaccination of COVISHIELD followed by COVAXIN demonstrated safety and better immunogenicity in vaccines. Post six months follow-up showed significant reduction in neutralizing antibody (Nab) titers against Omicron variant in vaccines.

Neutralization potential of COVID-19 vaccines against SARS-CoV-2 Variants of Concern (VOC)

- The waning immune response post seven month of vaccination and immune evasion leading to breakthrough and reinfection was observed with the Delta and Omicron variants. An increase in the COVID-19 cases was also observed due to Delta and Omicron variants. Delta and Omicron variants were supplied to BBIL, Hyderabad to improve the vaccine composition.
- The immune response generated with COVISHIELD and COVAXIN partially rescue the protection against Beta, Delta and Omicron variants. However, it could still effectively neutralize these VOCs.
- Studies conducted to understand the antibody responses during SARS CoV-2 infection and vaccination clearly suggests efficacy in neutralizing the emerging SARS CoV-2 VOCs including B.1, Alpha, Beta, Kappa, Delta, Delta Plus, Omicron. The data was helpful in implementing the evidence-based public health policy to undertake second dose of booster vaccination. The COVID-19 sero-diagnostic tools developed at ICMR-NIV added the strength to evaluate the antibody dynamics and longevity post infection and vaccination.

Isolation of new SARS-CoV-2 variants and characterization using cell culture and animal model

- Considering the potential threat from emerging SARS-CoV-2 variants and the rising COVID-19 cases, SARS-CoV-2 genomic surveillance is ongoing in India. Different variants of SARS-CoV-2 were propagated using cell culture as well as laboratory animals and characterized.
- The Brazil variant P2 lineage (B.1.1.28.2) isolated from clinical specimens of travelers returned to India from the United Kingdom and Brazil using in vitro method. Pathogenesis studies in hamsters demonstrated increased disease severity and neutralization reduction as compared to the B.1 variant.
- Studies on Kappa variant demonstrated higher pathogenicity in hamsters as evident from reduced body weight, higher viral load in lungs and pronounced lung lesions as compared to the B.1 variant.
- SARS-CoV-2 Delta variant pathogenesis and host response studies in Syrian Hamsters demonstrated presence of high levels of SARS-CoV-2 sub-genomic RNA in the respiratory tract for 14 days with lung disease of moderate severity. In addition, isolation of SARS-CoV-2 Beta and Eta variants from clinical specimens of international travelers was performed in cell culture.
- Pathogenesis studies of the Omicron variant in hamsters demonstrated moderate to severe

lung disease similar to that of the Delta variant. However, the sera showed poor neutralizing ability against Delta and earlier VOCs which suggest the possibilities of increased reinfection.

- Studies on re-infection of hamsters with Delta variant shows that prior infection with the B.1 variant could not produce sterilizing immunity but it can reduce disease severity in case of reinfection.

Molecular epidemiological analysis of SARS-CoV-2 circulating in different regions of India

- A total number of 19,953 whole genome SARS CoV-2 sequences were analysed during the period (April-2021 to March-2022) through the NIC and including six other laboratories. The distribution of SARS-CoV-2 lineages and WHO VOCs/ VOIs during the period between April-2021 to March-2022 (Fig 2), revealed the predominance of Delta and Omicron BA.2 lineages.
- Predominance of the Delta variant in SARS-CoV-2 infections of pediatric cases during the second wave highlights the importance of genomic surveillance in children.
- Two doses ChAdOx1 vaccine regime found to be effective against the delta and delta derivatives in the community-based cohort study in Chennai during the second wave.

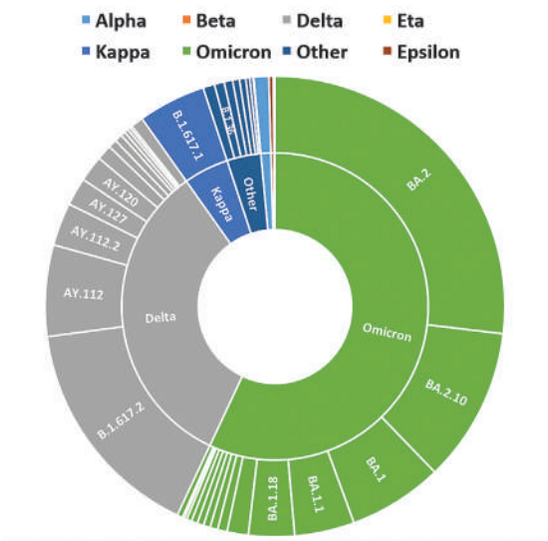


Fig. 2: Distribution of SARS CoV-2 lineages circulating in Indiaduring April-2021 to March-2022.

ANTI-VIRAL STUDIES

In vitro antiviral assays against SARS-CoV-2 showed Indomethacin possessing potential anti-SARS-CoV-2 activity in Vero CCL-81 cells with CC50 of ~490 mM, IC50 of 12 mM and selectivity index of 40.

Study on feaces of SARS-CoV-2 positive cases as possible route of virus transmission and potential role of cases in persistent fecal viral shedding in the environment

- To assess the presence and concentration of SARS-CoV-2 RNA in stool and urine samples of positive cases, 107 paired samples from cases with mild, moderate, and severe disease, were compared the detection sensitivity of RT-qPCR with the next-generation PCR method (ddPCR). All the stool samples showed 100% positive concordance by both the methods while in case of urine samples, 27.1% tested positive by ddPCR and only 1.81% tested positive by RT-qPCR (average Ct 36.41) suggesting higher sensitivity of ddPCR. The virus was detectable in faeces of a SARS-CoV-19 case.
- Presence of SARS-CoV-2 in 37/104 sewage samples was also demonstrated by ICMR-NIV Bangalore unit using RT-qPCR.

Nipah outbreak containment and response, September 2021, Kozhikode, Kerala

- Nipah outbreak was reported during Aug-Sep 2021 in the Chathamangalam Panchayat Kozhikode, with an encephalitis case in a 12-year old boy who succumbed to infection.
- Quick outbreak containment responses including establishment of an onsite Nipah virus (NiV) diagnostic facility by Kerala state, ICMR and central team could restrict the outbreak.
- NiV sequences retrieved from the clinical specimen of the index case formed a sub-cluster with the earlier reported NiV-I genotype

sequences from India with more than 95% similarity.

- Anti-NiV IgG positivity detected in 21% of *Pteropus medius* **and 37.73% of** *Rousettus leschenaultia* **surveyed from the epicenter areas.**
- The DCGI has approved the PoC for emergency use during Nipah outbreak 2021.
- The high-power committee decided to modify the algorithm for Acute Encephalitis Syndrome with inclusion of the NiV diagnosis, which would enhance the human surveillance.

Investigation of Hepatitis A virus (HAV) outbreak in rural area of Satara, Maharashtra

HAV outbreak investigation revealed that ~42% of the people in the age group of 15-25 years did not have IgG antibodies. This suggests that the decline in this population may have started 15-25 years ago. Countries in 'intermediate transmission' should consider need of HAV vaccination.

Outbreak of acute watery diarrhea in village Top, Kolhapur district of Maharashtra

An investigation performed with the help of the local rapid response team identified *Vibrio cholerae* O1 Ogawa biotype El Tor as cause of diarrheaoutbreak in Kolhapur district of Maharashtra. The source of infection identified to be the drinking water pipelines in which leakages detected close to the shallow drainage areas. Public health measures were implemented to successfully contain the outbreak.

Entomological investigations during arboviral outbreaks

Entomological investigations carried out during outbreaks resulted in isolation of a novel strain of chikungunya virus from the Dehu village, Pune district. Investigations also performed during the dengue outbreaks reported from Rajegaon village and Alandi Taluka of Pune district and the Zai village in Palghar disctrict where a confirmed Zika casewas identified.

HUMAN INFLUENZA

Virological data from 1,15,646 clinical samples including positives composed of 236 influenza A(H1N1) pdm09, 2735 A(H3N2), 1767 Influenza B was submitted to Global Influenza Surveillance and Response System (FLUNETPLUS). Influenza isolates (n=77) (H1N1pdm09: 14, H3N2: 32, Influenza B: 31) were submitted to WHO CCs, CDC, Atlanta and Melbourne Australia.

AVIAN INFLUENZA

Gene pool analysis of avian influenza H9N2 viruses isolated from India showed that the viruses have undergone inter- and intra-subtype assortments revealing a gradual shift towards mammalian adaptation.

Prospective investigation of transmission of Crimean Congo Hemorrhagic Fever (CCHF) amongst close contacts of confirmed CCHF cases

- A total of 44 cases and 20 deaths reported due to CCHF in 2019, 2020 from Gujarat and Rajasthan states with Case Fatality Ratio of 45.45%.
- Investigations first time identified circulation of the re-assorted strain of Asian-African genotype and Asian genotypes of CCHF in India.
- A total of 705 close contacts of CCHF cases were followed, of these 44 CCHF positive cases and only one asymptomatic close contact showed anti-CCHF IgM and anti-CCHF IgG antibodies positivity after 14 days, suggestive of very low subclinical infection (1/705 [0.14%]).

ZIKA SURVEILLANCE ACROSS THE COUNTRY

Surveillance of Zika virus in different parts of the country performed at different time intervals identified positivity in different states and UTs of India (Fig. 3). Strengthening of laboratory

capacity and human resource development for Zika diagnosis helped to detect Zika cases in newer areas including Kerala, Uttar Pradesh and Maharashtra.

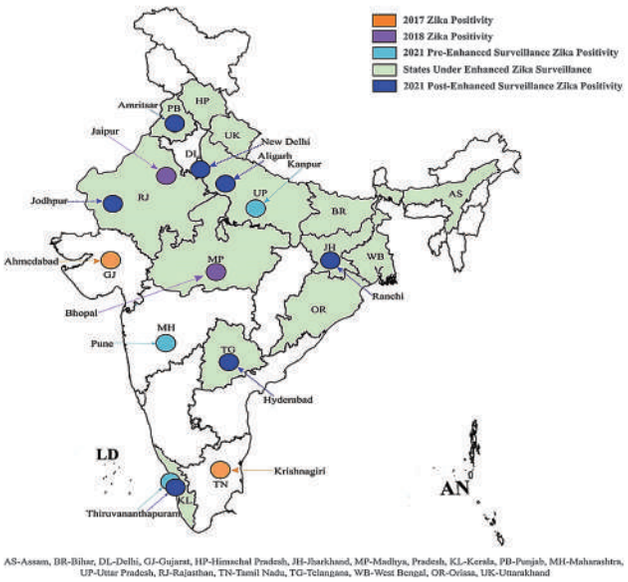


Fig. 3: Geographical distribution of Zika positive cases in India. ZIKV activity documented in Assam (AS), Bihar (BR), Delhi (DL), Gujrat (GJ), Himachal Pradesh (HP), Kerala (KL), Punjab (PB), Maharashtra (MH), Uttar Pradesh (UP), Rajasthan (RJ), Tamil Nadu (TN), Telangana (TG), West Bengal (WB), Orrisa (OR) and Uttarakhand (UK).

VIRAL ENCEPHALITIS

Laboratory investigations of 574 AES cases identified infections with Japanese encephalitis virus (JEV) in 08, dengue virus (DENV) in 26, Chandipura virus (CHPV) in 12, herpes simplex virus (HSV-1) in 05 and enterovirus (EV) infection in 02 cases. Studies on domestic animals to detect prior exposure with JEV and CHPV established infection of buffalos, bulls, cows, dogs, donkeys, goats, horses and pigs by JEV but not CHPV.

DENGUE AND CHIKUNGUNYA

- Investigation of suspected dengue cases (n=2352) from Maharashtra by real-time RT-PCR identified dengue infection in 468 cases with predominance of DENV-2 serotype in all the states including Telangana, Andhra Pradesh, Goa, and Sikkim. Sequence analysis of DENV from cases revealed circulation of Asian and American African genotypes of DENV-1, cosmopolitan genotype (GIV) of DENV-2 and DENV-3 genotype III.
- Investigation of suspected Chikungunya cases (n=1967) by IgM ELISA identified CHIKV infection in 719 (36.5%) cases. Genetic analysis of genome amplified from clinical samples and CHIKV isolated from cases revealed that all the isolates belonged to the Indian Ocean lineage of East Central South African genotype.

Development and evaluation of multiplex RT-qPCR assay for simultaneous detection of dengue, chikungunya and zika viruses in clinical samples

Developed a tetraplex RT-qPCR assay to detect dengue, chikungunya, and zika viruses along with the internal control (B-actin) standardized. The assay had a sensitivity of 96% (90.3 to 98.9) for detection of DENV and 100% (89.2-100) sensitivity for detection of CHIKV.

Development of Polio Essential Facility in line with the Global Action Plan III at ICMR-NIV, Pune to support work on Polio

Physical changes with respect to the construction renovation for establishment of the Polio Essential Facility (PEF) at ICMR-NIV, Pune has taken a leap forward with preparation of the Laboratory and facility documents, which includes Standard Operating Procedures, risk assessments, Policies, Plans and Executive Procedures as per the Global Action Plan III guidelines and progressing for its certification by the WHO.

National Laboratory for testing Polio, Measles and Rubella virus under WHO-SEARO network

- ICMR-NIV Bangalore Unit achieved 100% score in WHO proficiency panel for Polio Virus Isolation and Molecular testing for human and sewage samples. The unit also achieved 100% score in serology testing of Measles and Rubella virus and passing score in Measles and Rubella virus RT-PCR testing. Tested 4874 AFP samples and confirmed 73 samples in Virus Isolation and 49 samples for Sabin 1 or 3 like virus.

- As a WHO Global Specialized Laboratory for polio, ICMR-NIV Mumbai unit working on the National Polio Surveillance Project showed absence of wild type poliovirus confirming polio-free status of India. The country is leading globally in iVDPV study by including 21 major hospitals across India and training more than 150 clinicians in phase II of the iVDPV research study initiated in Jan 2022 (Fig. 4). The Phase I of research study on iVDPVs investigated 150 children with Primary immunodeficiency (PID) and revealed the involvement of combined immunodeficiency not antibody deficiency as the major factor in poliovirus clearance.

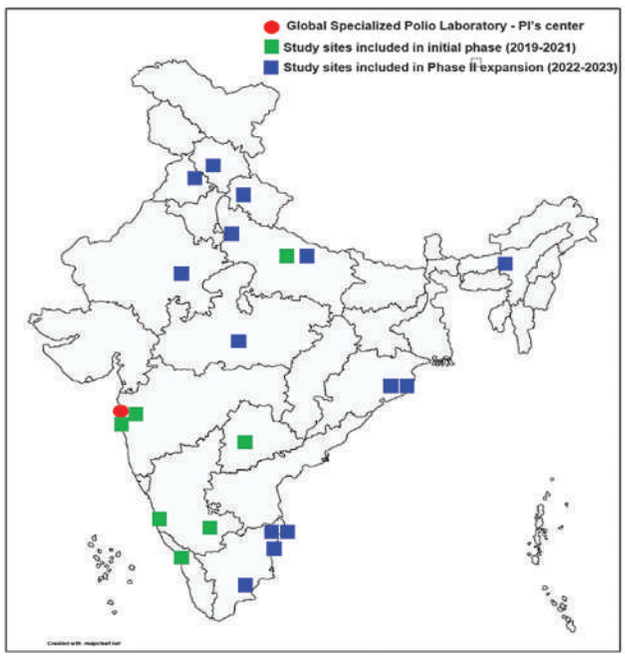


Fig. 4: Map of India depicting the iVDPV study sites of Phase-I, Phase-II and the PI's Institute.

Screening of non-polio enteroviruses [NPEV] in respiratory samples: A Pilot study

- Study revealed the presence of NPEVs in 35.23% and 31.08% of the acute respiratory illness [ARI] and severe acute respiratory infection [SARI] cases, respectively, with prevalence of Rhinovirus species A-C and Echovirus in ARI cases. Predominance of Rhinovirus C followed by Rhinovirus A documented in the SARI cases.
- EV71 sero-prevalence study with three genotypes isolated in India showed lowest sero-positivity (23.24%) in the age group of 1 to 5 years as compared to the age group 1-15 years (68.3%) indicating need of EV71 outbreak preparedness.
- As a WHO reference laboratory for sequencing, work on measles and rubella surveillance showed predominance of D8 genotype.

Measurement of virus specific IgM antibody, IgG antibody and neutralizing antibody levels in suspected measles and rubella cases

Study performed to understand the qualitative and quantitative correlation of IgM, IgG, IgG-avidity and Nt-antibodies to Measles virus (MeV) and Rubella virus (RuV) in pediatric fever cases with skin-rash. MeV and RuV past/reinfection detected in 58.6% and 72.6% cases.

Genetic characterization of clinically suspected Measles, Mumps, Rubella and Chickenpox cases reported to the local hospitals

- During Feb 2022, chickenpox cases reported from Surangi village (PHC Amboli, Dadra & Nagar Haveli). All cases showed presence of VZV specific IgM antibodies.
- Genetic characterization of measles and mumps virus isolates carried out by two different methods (Sanger's and next generation sequencing) to compare the differences in outcome. Among the 14 isolates of each virus, complete genome sequence of four isolates each was not resolved by NGS due to low virus titer.

Establishment of a State Level VRDL and 'Model Rural Health Research Unit' in Kerala

The ICMR-NIV Kerala Unit established a state level laboratory to support investigations of viral diseases. Referred clinical samples (n=4863) investigated for viral diagnosis. Out of 1924 human influenza cases, H3N2 infection detected in 104, pandemic H1N1 infection in one case, and influenza

B infection in 33 cases. Out of 150 cases, 3 tested positive for both measles and rubella infections. Acute gastroenteritis outbreak investigations revealed association of norovirus GII. Zika virus RNA detected in 09/271 referred cases. Leptospira DNA detected in 108/536 cases.A memorandum of understanding to establish MRHRU signed between Kerala state government and ICMR-NIV to establish the unit.

Hospital based surveillance of rota virus in children with acute gastroenteritis

Hospital based study conducted in Pune city confirmed the predominance of rota virus A (RVA) followed by norovirus, adenovirus and astrovirus among acute gastroenteritis patients.

Pertussis seroepidemiology, maternal immune status and missed diagnosis among young infants in India - a multi-centric study

Out of 340 samples (from Bhubaneshwar, Jodhpur and Puducherry) tested by ELISA, maternal seropositivity for anti-pertussis toxin IgG was detected in 7.05% (95% CL 4.79 -10.29). *B. pertussis, B holmesii* and *B. parapertussis* confirmed in one of the cases among 45 infants with severe respiratory infections.

In-vitro antiviral activity of different extracts/ compounds/formulations against dengue virus type 2 and chikungunya virus

- *Carica papaya* leaves based silver nanoparticles and supercritical fluid extract of *Carica papaya* leaf formulations showed significant inhibition of dengue virus (DENV) while papaya leaves in powder form showed significant reduction of chikungunya virus (CHIKV).
- Phytosterol and chromane terpenoid rich *Sauropus androgynus* L. Merr. leaf extract which exerted antiviral activity against DENV-2 and identification of the bioactive compounds in the extracts might help in developing a phytopharmaceutical against dengue.
- Chebulinic acid (CA) from the plant *Terminalia chebula* andCarpaine, a major alkaloid of *Carica papaya* plant exerted virucidal activity/ anti DENV activity against DENV-2. Molecular docking of CA and carpaine with structural and non-structural DENV-2 proteins revealed strong binding affinity with envelope protein and multiple virus proteins, respectively.

Repurposing of drugs against dengue and chikungunya viruses using systems biology approach

Transcriptomics-based bioinformatics approach adopted for identification and *in-vitro*/ *in-silico* screening of FDA-approved drugs for repurposing for their prophylactic, virucidal and therapeutic effects against dengue and chikungunya viruses. Investigations on selected sixteen drugs showed anti-DENV activity of elvitegravir and anti-CHIKV activity of Emetine. Resveratrol lomibuvir and enalaprilat showed activity against both viruses. Molecular docking studies indicates interaction with protein targets including the NS5 RdRp, NS2B-NS3 protease, and NS5 methyltransferase of DENV and nsP3 macro domain of CHIKV.

Role of Histidine residues of envelope protein in membrane fusion of Japanese encephalitis virus (JEV)

Among the 13 histidine residues in the JEV envelope protein, the study identified the role of His319 in pH sensing and triggering conformational changes necessary for membrane fusion. JE virus like particles carrying mutations in different His residues succeeded in undergoing membrane fusion like the parental JEV while VLP carrying His319 mutation failed. The information may be useful for development of antivirals blocking viral entry.

Antiviral activity of favipiravir against Chandipura virus

- Favipiravir (T-705, Avigan), a broad-spectrum antiviral was found to be a promising drug against CHPV infection in Vero cells as complete inhibition was observed at 160µM concentration with selectivity index of 37. *In*

vivo studies confirmed its therapeutic potential as complete protection in CHPV challenged mice (CD1) was obtained with 300mg / kg / day oral dose for 07 days. For humans, 1600 mg oral dose twice a day followed by 800 mg twice a day for 07 days was recommended.

- Molecular docking of CHPV RdRp (L protein) revealed binding of T-705 with L protein priming loop residues (Ser1152, Gln1155, Glu1158, Lys1159 and Ser1161) located at active site of capping domain forming seven intermolecular H-bonds with binding affinity ΔG= -5.5kcal/mol (Fig. 5). These priming residues projects into the polymerase domain cavity forming contact with the minor groove of the nascent product to enhance fidelity and coupling of capping for initiation of polymerization.

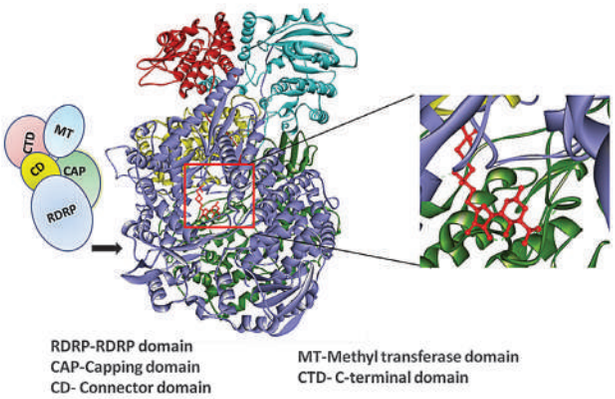


Fig. 5: *In silico* analysis of the interaction of Favipiravir (T-705) with CHPV large protein (RNA dependent RNA polymerase). Prediction identified interactions with Thr551, Ser1152, Gln1155, Glu1158, Lys1159 and Ser1161 residues located on the polymerase domain cavity of RdRp.

Mobile application for immunization data in India (MAIDI)

The mobile application was found feasible and helpful for healthcare workers for tracking on-time vaccination. The delay in vaccinations can be addressed by sensitizing beneficiary parents and healthcare workers along with assurance on infection control practices.

Production and Supply of MAC ELISA kits

ICMR-NIV supplied 12946 MAC-ELISA kits comprising 9285 Dengue, 2974 Chikungunya and 687 JE for detection of IgM antibodies, to sentinel surveillance hospitals/ centres under national program (NCVBDC), DHR-VRDLs and some national institutes in the country.

Animal House at ICMR-NIV

Renewal of the registration was accorded by the CPCSEA, based on last five years inspection reports and records. The registration validity is until July 2027. Ten strains of mice (Inbred: BALB/c (Jax and CRL), C57BL/6, DBA/2, C3H, Outbred: CD-1, Immuno-deficient: CD-1 nu/nu, BALB/c nu/nu, RAG-1 KO and AG129) and Golden Syrian hamsters were maintained and bred for supply under in house research projects.

Computational drug repurposing approach for the development of therapeutics against Hepatitis E virus

Screening of drugs using *in vitro* enzymatic activity assays showed significant inhibition of HEV polymerase by Ribavirin, Sofosbuvir (SOF), daclatasvir (DAC), acarbose (ACA), miglitol (MIG), metformin (MET) and voglibose (VOG). These drugs also inhibited HEV helicase enzyme. HEV inhibitory activities of these drugs were, SOF and DAC, 61% and 77% respectively, antidiabetic drugs MET, ACA and MIG, 56, 44 and 65% inhibition respectively. Interestingly, these drugs also showed inhibition of genotype 3 HEV (HEV-3), which is known to cause chronic infections. Considering that these drugs have inhibitory activity against two important HEV genotypes causing human infections, they deserve further evaluation in animal model.

Assessment of risk factors for the development of cardiovascular disease (CVD) in patients with active HCV infection

Among the HCV infected patients, compared to 3.8% prevalance in healthy controls,11.9% were found to be suffering from metabolic syndrome who are significantly more prone to develop insulin resistance and liver fibrosis including cirrhosis, and showed raised IL-10 and IL-1β cytokine levels.

Metagenomic analysis of viromes of Aedes aegypti mosquitoes in India

An insect specific virus, Phasi Charoen-like virus (PCLV) from *Phenuviridae* family was detected in mosquitoes from Maharashtra, Assam, Tamil Nadu and Karnataka by next generation sequencing approach. Comparison of the sequences from Maharashtra showed close genetic relationship with the Rio (Brazil) isolate of PCLV.

VECTOR COMPETENCE

- Studies performed to understand the kinetics of replication of dengue and chikungunya virus co-infection in *Aedes aegypti* mosquitoes highlights comparatively efficient replication of CHIKV over DENV-2. Superinfection of CHIKV infected mosquitoes with DEN-2 showed increase in titres of both; however, CHIKV showed predominance, while in reverse situation, both viruses showed similar levels of replication.
- Infection of *Culex quinquefasciatus* and *Cx. tritaeniorhynchus* mosquitoes with West Nile virus showed that both species are capable of transmitting the virus, as seen by detection of virus in saliva of both mosquitoes.

Qualitative analysis of public trust in JE vaccine acceptance and hesitancy in Alappuzha district, Kerala

Healthcare organizations and the government must take aggressive measures to soothe public fears about Adverse Event Following Immunization as it is a source of worry in the population including stringent action against false propaganda through social media.

PATENT

1. Title of patent "Development of HEK293 knock-out cell line of EV-A71 receptors SCARB2 and PSGL1 genes".
2. Title of patent "Instrument free nucleic acid extraction method".
3. Title of patent "Development of screening assays for detection of epidemiologically important SARS-CoV-2 variants".
4. Title of the patent "RT-LAMP Assay for detection of human β -Actin housekeeping gene."
5. Title of the patent "Rapid RT-LAMP assay for detection of SARS-CoV-2."
6. Title of the patent "Multiplex single tube Real Time RT PCR assay for detection of SARS CoV-2."

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS (ICMR-NIRT), CHENNAI

TREATMENT OF TB

Shorter regimens for TB are beneficial to both the patients and the health system and our Centre has been evaluating regimens of shorter duration for more than 2 decades.

- A multicentric study on various doses and duration of Linezolid in combination with Bedaquiline and Pretomanid (mBPaL study) after 26 weeks of treatment in adults with either Pre-Extensively Drug-Resistant OR Treatment Intolerant / Non-responsive multidrug-resistant Pulmonary Tuberculosis coordinated by our Centre is ongoing that has enrolled 230 patients till date.
- Prospective Cohort Study (BEAT Study) which evaluates a Combination regimen of Bedaquiline, Delamanid, Linezolid and Clofazimine in Adults with Pre-extensive and Extensively Drug-resistant Pulmonary Tuberculosis has recruited 167 patients across India and the follow-up is on-going.
- The evaluation of a Standard Treatment Regimen of Anti-tuberculosis drugs for patients with MDR-TB (STREAM – Stage 2) study in

which our Centre participated has completed the follow-up of 49 enrolled patients.

- The multi-country SHINE Study in which our Centre participated concluded that the four month treatment was as good as the standard six-month treatment for children with minimal TB and this is incorporated in the WHO treatment guidelines.
- HICON-R study which was initiated and coordinated by our Centre observed early and faster sputum culture conversion, with similar adverse events as compared to conventional dose, suggesting 25mg/kg/day Rifampicin containing regimen can be considered in the treatment of pulmonary TB patients.

PREVENTION OF TB

Research and efforts towards TB prevention are crucial to achieving the goal of TB elimination.

- Follow-up of 2214 enrolled participants is ongoing in the placebo-controlled TB vaccine which evaluates the Efficacy and Safety of two vaccines VPM1002 and Immuvac (M*w*) in preventing TB in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB patients.
- Findings from the study on Airborne Infection Control (AIC) practices done by our Centre in Chennai District among TB patients and Health Care Workers have implications for TB prevention.

TB DIAGNOSIS

- Accurate, Rapid, Robust & Economical Diagnostic Technologies for Tuberculosis (ARREST-TB) aims to develop and validate novel molecular diagnostics for the detection of Mycobacterium tuberculosis complex and multidrug-resistant TB, with seamless data interpretation, collation and 'real-time' reporting. The recruitment of study participants is ongoing. Isolation and Analysis of Mycobacterium tuberculosis-Induced-MMPs directly from sputum samples: Inhibitor synthesizing and validation is being done.
- Performance evaluation of mfloDx® MDR-TB and mfloDx® MDR-TB plus test for the detection of *M. tuberculosis* and its drug resistance from sputum samples is being conducted.
- Feasibility of using Truprep extracted DNA for LPA Testing in National Tuberculosis Elimination Programme is currently ongoing. Multicentre trial to assess the performance of centralised assay solutions for the detection of MTB and resistance of rifampicin and isoniazid is planned to be initiated.
- Development and deployment of Artificial Intelligence (AI) aided tool for screening of chest x-ray for enhanced detection of Pulmonary TB is being done by the Centre. The objective is to develop and validate a quality AI tool, integrated with online electronic systems like e-Hospital made available for use for auto-reading of chest x-ray to detect abnormalities and create appropriate testing, referral and management for supporting the National Strategic Plan for Ending TB in India.

Pharmacokinetics of anti-TB drugs

- Adequate blood drug levels are essential to achieve the desired effect of the drug. Bioavailability of fixed-dose combination (FDC) of first-line anti-TB drugs in patients with pulmonary TB is currently ongoing.
- ICMR-NIRT has developed a new validated HPLC method for therapeutic drug monitoring (TDM) of plasma linezolid (LZD) and for quantitation of anti-diabetic drug; metformin in urine.

National TB Prevalence Survey in India

ICMR-NIRT coordinated one of the world's largest TB prevalence survey in terms of its population surveyed, operations size and area covered. The survey was successfully completed from 2019 to 2021. The survey estimated the point prevalence

of microbiologically confirmed pulmonary TB (PTB) among persons aged ≥15 years in India at the national level and for 20 individual states / state groups. In addition, the health-seeking behaviour and the prevalence of TB infection were studied.

A total of 3,54,541 population was covered, of which 90.9% of the eligible population participated in the survey. Among 3,22,480 who participated, 100% had symptom screening results and 97.1% had chest X-ray results. 13% among those who participated were eligible for sputum, and 88.7% submitted at least one sample. Prevalence of Microbiologically confirmed Pulmonary TB among 15 years and above in India was 316/lakh population for the period 2021. Prevalence of TB was associated with past history of TB treatment, older age group, malnourished, known diabetics, smokers and alcohol users. The National TB prevalence to TB notification ratio was 2.84 (2.61 - 3.07). Majority (64%) of symptomatic population did not seek health care. The reasons were ignoring the symptoms (68%), not recognising the symptoms as TB (18%), self-treatment (12%) and could not afford to seek care (2%). Among the 36% of survey participants who sought care for their symptoms, there was equal preference for government and private facilities. The findings from this survey have implications for focussed interventions to reduce TB disease burden in India.

District level Annual Survey in India

The survey coordinated by ICMR-NIRT used an innovative mixed method study with a triangulation design to assess the incidence of TB at the district level in India. The quantitative component included a cross-sectional primary data collection through a survey and secondary data review (review of records from NIKSHAY notification systems and NTEP reports, utilization of drugs in public and private sector). The qualitative component involved nominal focus group discussions (FGD) and key informant interviews (KII) among chemists and private providers on anti-TB drug sale in the private sector. The Incidence of TB & decline in incidence (from 2015) of TB was calculated to understand the progress of the districts towards TB Free status. During the year 2021, 10 states/UTs and 201 district claims from NTEP were submitted for verification. 8 States/UTs and 91 districts were recommended for awards in different categories of progress towards TB free status based on the decline in incidence of TB in 2021 compared to 2015.

BASIC SCIENCE

- The immunological interactions between infectious diseases and metabolic disorders, mainly the interfaces of co-infections and multimorbidity including diabetes-latent tuberculosis, helminth-latent tuberculosis, helminth-diabetic and helminth-SARS-CoV-2 interactions are being studied. The studies conducted were 1) a cross-sectional study to estimate the influence of malnutrition, diabetes mellitus and helminth infections on bio-signaturesin latent TB in a South Indian population, 2) Regional Prospective ObservationalResearch in Tuberculosis (RePORT)- Phase, 3) A pilot study of the effects of helminth infection and SARS-COV-2 Sero-positivity on immune response and the intestinal microbiotain India. Studies focussing on immune responses and pathogenesis of SARS-CoV-2 in both paediatric and adult populations are being conducted. Molecular Analysis of Monocyte Subsets from Humans Infected with *Mycobacterium tuberculosis* revealed a differential expression of cytokines and chemokines from latency to drug-sensitive and to drug-resistance. Immunomodulation of Serum Vitamin D levels combined with circulatory proteins towards a prognostic biomarker for pulmonary TB was studied. It was observed that Vitamin D significantly correlated with IFNg, TNFa, IL17A, IL-4 and Resistin in the active TB group.
- Identification of Mycobacterium tuberculosis complex (MTBC) organisms in the lymphnode samples of slaughtered cattle in Chennai was done. Whole genome sequencing (WGS)

revealed that five of these isolates are *M. orygis* and one isolate is *M. tuberculosis* andapart from this, 72 non-tuberculous mycobacteria (NTM) have been identified.

- Identified soluble biomarkers that can predict short-term risk of progression from *M. tuberculosis* infection to active TB disease.
- Identified a seven-gene signature that can accurately differentiate between active and latent tuberculosis.
- Virologic response and HIV drug resistance (pre-treatment and acquired) in adults newly initiated on first line Antiretroviral Therapy in a representative population from Chennai
- Evaluation of immunogenicity of ChAdOx1 nCoV-19 (Covishield) vaccine in adults with Diabetes
- Supported the National Early Infant Diagnosis Program in the capacity of Regional Reference Lab for HIV-1 molecular testing.
- Supported the National Antiretroviral Treatment Program in the capacity of Regional Reference Lab for HIV-1 viral load testing.
- Supported whole genome sequencing of emerging SARS-CoV-2 strains for the Indian SARS-CoV-2 Consortium on Genomics (INSACOG).
- Central Biorepository for the RePORT India Consortium and Regional Biorepository for the National HIV Cohort Program.

DRUG DEVELOPMENT

Development of new drugs for TB is essential for effective treatment regimens to cure TB disease.

- Carnosine, a natural dipeptide was shown to have anti-inflammatory and antioxidant properties. The NIRT team had successfully developed carnosine nano rods and characterized their physiochemical properties. Preliminary work was carried out on the therapeutic potential of natural compounds through *in silico* methods identified three important lead molecules. Two adjuvant formulations from *Unani* pharmacopeia have been validated in preclinical studies.
- Two species of mangrove from Pullivasal and Kurusadai Island of Gulf of Mannar, Ramnad district and Six species of mangrove were collected form Muthupet Lagoon at Thiruvarur District under supervision of Forest range. Among 9 species of mangrove, Two of the crude extracts resulted in the inhibition of *Mycobacterium tuberculosis* H37RV strain using broth micro dilution method at 1 mg/ml. One of the extracts was not toxic to Vero, THP-1 and PBMC cells upto 2mg/ml. Eight compounds were identified by GC-MS from 9th fraction which showed inhibition at the MIC of 0.5mg/ml against Hs7RV.
- Efflux pump inhibiting potential of five small molecule inhibitors namely Ellagic acid, Methyl Stearate, Myoinositol, Rutin, and Shikimic acid that could block the Rv1819c – an ABC transporter efflux pump that confers resistance to rifampicin were elucidated in the drug resistant *Mycobacterium tuberculosis* clinical strains and recombinant *M. smegmatis* expressing Rv1819c. In-silico and in-vitro methods of toxicity testing showed evidence of non-toxicity in Myoinositol and Methyl Stearate. Based on these findings these molecules could be considered for adjunct TB therapy; however, its impact on other drugs of anti-TB regimen needs to be tested.

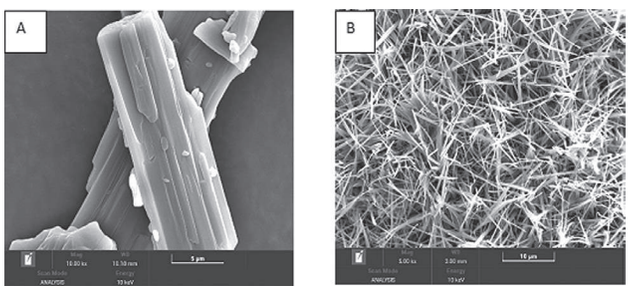


Fig 6: Scanning electron microscope imaging of A- native carnosine (scale 5µm), B-nanocarnosine (scale 10 µm).

Socio-behavioral studies in TB

- A prospective observational study among TB patients in Tamil Nadu assessed the disclosure patterns and the socio-economic consequences

of disclosure among TB patients. A total of 466 TB patients were followed-up along with their contacts and TB disclosures patterns were identified. Maximum disclosures were made with household family members (92.8%) at baseline i.e., within 15 days of TB diagnosis. The study enabled the Centre to develop a method and tool to measure TB disclosure patterns which in turn will help in facilitating positive disclosures for TB patients and thus will enable better patient support system.

- A qualitative study in exploring and understanding the psycho-social factors enabling drug-resistant patients to achieve better treatment adherence and completion was conducted by ICMR-NIRT. Based on the findings, the study was able to provide a theory of change and identify an intervention framework for addressing treatment challenges and psycho-social risks among DR-TB patients based on a self-efficacy driven treatment approach (SETA).
- A quantitative scale for measuring the patient-perceived quality of care in public and public-private mix care settings for TB has been developed and validated. The tool could be used for evaluating the quality of services for TB patients from a patient perspective. The study which explored and identified the social mixing patterns of TB patients who are alcohol users documented how social mixing could drive the TB transmission within small group of individual with unhealthy and risk behaviours. The findings could help in developing preventive strategies.
- Future research studies as part of Socio-Behavioral Research Network for TB in India to implement large scale socio-behavioral studies for TB are being planned.

Health Technology Assessment (HTA)

- Health Economics Department undertakes Health Technology assessment of various health technologies to prioritize national health spending. Further department of health economics established effective partnership with the state government of Tamil Nadu for identifying priority areas and conducting conduct HTA studies in Tamil Nadu like
- HTA for screening of Type 2 Diabetes & Hypertension in India
- HTA for screening of Hepatitis B and C at Primary Health centres
- HTA for implementation of blood counters to diagnose of dengue at PHC settings in Tamil Nadu state

COVID-19

- ICMR-NIRT has reported that Covid-19 vaccine Covaxin induces an enhanced humoral immune response, with persistence till at least 12 months post-vaccination against most SARS-CoV-2 variants. The team has also documented that single dose of Covaxin (BBV152) induced humoral immunity in previously infected individuals was equivalent to two doses of the vaccine in infection-naïve individuals.
- ICMR-NIRT completed 2 rounds of the COVID Sero survey to estimate the spread of SARS-COV-2 in Greater Chennai Corporation to understand the SARS-COV-2 transmission pattern in the city and to plan interventions for controlling the pandemic.
- National Sero Survey Round 3 and 4 was done by ICMR-NIRT to understand the seroprevalence of SARS-COV-2 among general population and among health care workers to understand the SARS-COV-2 transmission pattern in the city and to plan interventions for controlling the pandemic and the usefulness of the vaccination.
- Functioned as ICMR approved COVID testing lab and ICMR Central Depot for COVID-19 reagents.

Laboratory support for TB program

- ICMR -NIRT Bacteriology Laboratory is one of the National Reference Laboratory under National TB Elimination Programme (NTEP) - closely monitors five states (Andhra Pradesh, Gujarat, Kerala, Tamil Nadu, Telangana State) and five Union territories (Andaman & Nicobar, Puducherry, Lakshadweep, Daman & Diu and Dadra & Nagar Haveli) and provides technical support for the TB laboratory activities of NTEP. As part of service to the Tamil Nadu programmatic management of drug-resistant TB (PMDT) activities, involved in the diagnosis of drug-resistant TB.
- Testing newer drugs like bedaquiline, delamanid and prothionamide and participating in the External Quality Control (EQA) in India for the same is undertaken by the Centre. Critical concentrations of Bedaquiline,Delamanid, PA824, Moxifloxacin, Linezolid, Clofazimine and levofloxacin by broth micro dilution method were determined and were found to be dissimilar for all the drugs tested except levofloxacin when compared with the ECOFF proposed by the CRyPTIC Consortium.
- Renewal of National Accreditation Board for testing and calibration laboratories (NABL) Certificate was obtained. Approval was obtained from ICMR for expanding and upgrading the lab capacity to BSL 3 facility.

XV biennial Virtual Conference of International Biometric society - Indian Region

ICMR-NIRT hosted the XV biennial Virtual Conference of International Biometric society - Indian Region (IBS-IR) during 16-17 November 2021 & pre conference workshop on *Survival Analysis* on 15th November 2021. The theme of the conference was *Statistical challenges in clinical trials*. The conference was a valuable platform for young researchers with 40 oral presentations in seven technical sessions.

Fig. 7: XV biennial Virtual Conference of IBS-IR.

PATENT

- Filed a patent titled "A paper disc based method for determining the drug susceptibility of mycobacterium tuberculosis" partnering ICMR and IIT Kharagpur.
- Filed patent titled "Efficacy enhancement of Quinone molecules in combination with isoniazid and rifampicin".

ICMR-NATIONAL JALMA INSTITUTE FOR LEPROSY & OTHER MYCOBACTERIAL DISEASES (ICMR-NJIL&OMD), AGRA

PROJECTS

Role of ELR+ chemokines, VEGFA and solTNF in the Mycobacterium tuberculosis induced angiogenesis in granuloma and in regulating the dissemination of tuberculosis infection by increasing the drug penetration

The study revealed that treatment with Xpro1595, Motixafortide and atorvastatin either alone or as adjunct to anti-TB drugs did not reduce mycobacterial survival in the lung when compared to infected control or anti-TB treated guinea pigs group. The observations are significant in a sense that alternate day treatment with these drugs did not interfere with immunological responses and did

not compromise the control of pulmonary bacterial burden.

Proteomic profiling of exosomes for the identification of potential biomarkers for tuberculosis in HIV patients

The quantative miRNAs and proteomic analysis of serum exosomes of HIV patients with and without TB co-infection were performed using qRT-PCR and SWATH-MS method, respectively. The study identified crucial exosomal miRNAs and proteins which have highest discrimination utility for the diagnosis of patients with HIV-TB co-infection. The majority of significantly altered exosomal proteins were associated with phagocytosis, recognition, complement activation and humoral immune response.

Apart from above studies, the following three studies were also initiated at department of microbiology and molecular biology of the Institute.

- Evaluation of sensitivity and specificity of the PathoDetect™ MTB & NTM detection kit for detection of *Mycobctrium tuberculosis* (MTB) and Non tuberculosis mycobacteria in TB suspects in comparison with the gold standard.
- Evaluation of the PathoDetect™ MTB and NTM Kit.
- Identification of genetic determinants and risk factors for drug resistance to bedaquiline and delamanid in native isolates of *Mycobacterium tuberculosis* in India.

COVID-19 TESTING FACILITY

The Institute initated RT-PCR testing of COVID-19 samples in 2020 and presently the facility can test 1100 samples per day. The samples were received from nine districts (Agra, Mathura, Hathras, Firozabad, Kasganj, Farrukhabad, Auraiya, Kanpur Dehat and Etah) of western Uttar Pradesh. During the period of 2021-2022, a total of 2,88,052 samples were tested for SARS-COV-2 infection at COVID-19 diagnostic laboratory of the Institute.

TUBERCULOSIS

An Investigational Study on Mycobacteriophages and Their Enzymes as New Drugs (IND) For Treating Tuberculosis

Due to emergence of drug-resistant bacteria, bacteriophages are now being considered as the next generation therapeutics for tuberculosis (TB). 120 mycobacteriophages have been isolated so far by using double agar overlay method. Eleven mycobacteriophages were found to show lytic activity against *Mycobacterium fortuitum* NIHJ1615 and two were found to show lytic activity against clinical strain of *Mycobacterium kansasii.* Three mycobacteriophages showed activity against *M. tuberculosis* (fig 1). However, further studies are required to rule out that observed activity against *M. tuberculosis* is not due to "lysis without". Additionally, the capacity of D29 Lysin B as a therapeutic alternative to antibiotics in surfactant free condition was assessed. The genes were cloned, overexpressed and purified. Following cloning and expression/purification, antimycobacterial activities of these two lytic proteins were determined in vitro. The results showed that D29 LysB targets the M. tuberculosis irrespective of drug resistance status and can inhibit the growth of intracellular mycobacteria.

Prevalence of Microbiologically Positive Pulmonary Non-Tuberculous Mycobacterium (NTM) including Species Information under the National Tuberculosis Elimination Programme (NTEP), India (NTM Project)

The study tested the application of novel definitions for presumptive Non-tubercular mycobacterial disease. The most important of them 'Presumptive TB patients who are sputum smear positive by Microscopy (ZN/FM) and CBNAAT negative' for *Mycobacterium tuberculosis*' had a proportion of 5.7% identified as NTM and the findings suggest that this group could be potentially explored to look for NTM disease at the community level.

Strengthening Mechanisms for TB Death Reporting under the Revised National Tuberculosis Control Programme

The TB Death Audit project developed a new verbal autopsy tool for TB and validated it through robust study procedures. Its feasibility for use in the general health system was also researched. The results of the study have demonstrated an 85% accuracy for the 'TB Verbal Autopsy Tool' and the initial feasibility studies are indicative of its successful application within the general health system.

Prevalence and Determinants for TB Disease among Contacts of TB Patients – a bi-directional study

The TB Contact project estimated the prevalence of TB among the contacts of TB patients using a wider definition of contacts including the neighbourhood, relatives, workplace etc. The study finding revealed a clear higher prevalence of TB among the adult and paediatric household contacts than the general population. The other categories of contacts also had significant occurrence of TB. The findings reflect that the preventive activities of the NTEP should not be limited to the household contacts but should be inclusive of the neighbourhood, relatives, workplace and other social contacts.

Model Rural Health Research Unit, Ghatampur, Kanpur Nagar, Uttar Pradesh

The MRHRU, Ghatampur continued with the exemplary diagnostic and treatment services for TB and Leprosy. The popularity of the Unit can be ascertained from the fact that the whole of Ghatampur Tehsil accesses the services at the Unit. Patients also at times come far away from the district. A total of 13,366 patients attended the OPD in the year 2021-22 of which 9,904 were diagnosed with various skin diseases; 82 were diagnosed with filariasis; 115 were diagnosed with Leprosy; 2,563 had chest symptoms and 377 were diagnosed with TB. On the research front, the Unit had 6 projects underway/completed.

Model Rural Health Research Unit, Haroli, Una, Himachal Pradesh

The MRHRU at Haroli, Una, Himachal Pradesh is functional under the scheme of Department of Health Research, MOHFW/GOI. It had 12 projects underway/completed during this period.

National Tuberculosis Prevalence Survey

The project was coordinated by NIRT, Chennai and was implemented across the nation by various ICMR Institutes, State TB Offices, STDCs and the CTD, MOHFW/GOI. The ICMR-NJIL&OMD undertook the survey in the States of Uttar Pradesh, Himachal Pradesh, Jammu & Kashmir and Uttrakhand. The project has been completed and the results have been made public. The objective of the project was to estimate the point prevalence of microbiologically confirmed pulmonary TB among persons aged ≥15 years in India at National level and to estimate the point prevalence of microbiologically confirmed pulmonary TB among persons aged ≥15 years individually for 20 states / state groups. The prevalence of TB for the country for all forms of TB for all ages was 312 per lakh population. The prevalence of TB disease in India varied widely, with 70% of the burden contributed by 9 states. P:N ratio suggests missing TB patients nationally. Higher prevalence was observed in participants with past history of TB treatment, elderly, males, malnourished, known diabetics, smokers, and alcohol users compared to those who did not have these characteristics. These findings will be useful in making informed decisions for newer interventions to end TB in India.

National Reference Laboratory (NRL) at the ICMR-NJIL&OMD

The NRL at ICMR-NJIL&OMD has been entrusted with two states – Uttar Pradesh and Uttarakhand. The NRL made 27 assessment visits and also undertook two research projects. It was able to successfully maintain the proficiency of itself and also ensured that all labs under its jurisdiction were certified for proficiency as per norms.

Evaluation of enriched fractions of lead plant extracts for in-vivo anti-tuberculosis and immunomodulatory potentials with first line anti-TB drugs for the development of adjunct phytotherapy

The project is under area of product development to evaluate the efficacy of above two potential *in vitro* leads in mice TB model for the development of adjunct anti-TB phytotherapy.

Characterization and clinical relevance of hypothetical proteins of aminoglycosides resistant isolates of *Mycobacterium tuberculosis*

Aminoglycosides are broad spectrum antibiotics and are an important component of any antituberculosis therapy regimen. As cell wall is the outermost structure of *M.tuberculosis* and resists the diverse stress factors, it is important to identify these entities using 2D and mass spectrometry approaches. In the previous report, thirteen protein spots were found to be overexpressed in aminoglycosides resistant *M.tuberculosis* isolates. Initially five spots were further subjected to LC-MS for identification. Spots were identified as enolase, 3-oxoacyl-[acyl-carrier-protein] synthase 2, diacylglycerol acyl transferase/mycolyl transferase Ag85A, 3-oxoacyl-[acyl-carrier-protein] synthase 1 and inosine-5'-monophosphate dehydrogenase. On analyzing the data of MS, the team observed that there are some proteins which are important for the growth & survival of *M.tuberculosis* and thus can be used as a drug target by performing virtual screening like protein-protein docking simulations.

Study of Toll like receptors SNPs in drug resistant TB with reference to innate immune response

The host immune responses play noteworthy role in resistance/ susceptibility after *M tuberculosis* infection and also in disease severity during the course of disease. This study aims at finding out the role of host innate immune responses (TLRs, TLR2, TLR1 and TLR9) gene polymorphism in drug resistance of Tuberculosis patients. Preliminary findings suggested the association of TLR2 (-196 to -174 del) heterozygous genotype and del allele with severity of TB disease. The study is in progress.

LEPROSY

The department of Immunology of the institute initiated following studies in leprosy for developing immunological and molecular markers for early diagnosis, nerve damage and diagnosis of reactions.

- Validation of Nitric Oxide Synthase 2 (NOS2/ iNOS) gene polymorphism as a molecular marker for diagnosis/prognosis of leprosy reactions (type1 and Type 2)- a prospective cohort study
- To investigate the diagnostic value of Nerve Growth Factors in early case detection and disability prediction in contacts of Leprosy affected Persons- An observational prospective study

Transcriptomic analysis of monocytes and macrophages in leprosy patients, their contacts, and healthy Individuals

The work has been initiated.

Quantitative serum proteomic analysis of contacts of leprosy cases using iTRAQ for early diagnosis of leprosy

Early diagnosis of leprosy has been compromised due to lack of specific markers. Circulating proteins in sera are attractive diagnostic markers of disease. The present study will exploit the proteomics tools for differential expression of novel serum proteins in contacts versus leprosy cases which might serve as potential markers for diagnosis of early leprosy. Subjects for the study were recruited from the OPD of the Institute with written informed consent. Study subjects included healthy persons, leprosy cases and contacts/suspect cases of leprosy. Whole blood of the subjects under study was collected through venipuncture. Total number of participants recruited were eighteen. Following protein

estimation, two-dimensional PAGE was done. A better protein separation was seen on 2DE gel.

Study of profile of deformity in new leprosy cases to analyze predictive risk factors in the development and progression of the disability

Impaired Amplitude in sensory and motor Nerve conduction was seen in 48% cases before presence of Nerve function impairment and restored with clinical improvement. Higher mean level of ND-O-HSA and S-100 antibodies was observed in sera of Leprosy Cases with Grade1 deformity as compared to those with no nerve function impairment.

Immune response to the precautionary third dose of COVISHIELD/COVAXIN among the healthy adult population: an ICMR Cohort study, India

This is an ICMR-initiated study with 25 centers to evaluate the immune responses to a precautionary third dose of COVISHIELD/COVAXIN among healthy adult populations. After approval from the Institute Human ethics Committee, the study was initiated.

HIV/AIDS UNIT (Integrated Counseling and Testing Centre)

This Institute is providing HIV counselling and screening activities/services since HIV screening was initiated in India. the center is to provide Pre-test and Post-test counseling and testing of HIV positivity as per the guidelines laid by Department of AIDS Control, Govt. of India from time to time. It includes DBS sample collection for early infant diagnosis (EID) by PCR, testing of pregnant woman, clients referred by Govt. and Pvt. Health care facilities, target intervention groups, NGOs, Suspected and confirmed TB cases, Leprosy patients who opted for surgery. HIV positive and HIV negative (symptomatic for TB suspects) are screened for Tuberculosis. During this period, a total of 1062 clients were counselled and tested for HIV positivity through rapid testing methods. Among them 24 were detected to be HIV positive which were confirmed by two different rapid tests.

ICMR-NATIONAL INSTITUTE OF CHOLERA AND ENTERIC DISEASES (ICMR-NICED), KOLKATA

COMMUNITY / HOSPITAL BASED STUDIES

Strengthening/promoting evidence-based advocacy for influenza prevention and control in India

This is the first community based multi-site study in India to define the epidemiology and risk factors of influenza and other respiratory viruses associated with ARI among elderly population. A total of 4,082 acute upper respiratory tract infection and 244 acute lower respiratory tract infection were detected from the community cohort. The positivity rate of Influenza was 5.8% in the community and 15.9% in the hospital among enrolled SARI patients.

Fig. 8: Specimen collection from ARI *cases.*

Impact of improved diagnostic tools, practices, training and communication on acute fever case management and antibiotic prescriptions for children and adolescents presenting at outpatient facilities in the Community Clinics of ICMR-NICED, India

This study investigates the benefit of adopting a battery of available diagnostic point of care tests and clinical diagnostic algorithms, coupled with training and communication intervention for both the healthcare providers and patients which can result in improved care of acute febrile illness

and promote rational use of antibiotics among the children and adolescents presenting with fever to outpatient clinics in low- and middle-income countries (LMICs).

Priorities for the Environmental Dimension of Antimicrobial Resistance (AMR) in India

This strategic report, emanating from various dimensions of 'One health', envisages overall cognizance of the policy decision makers about the scope of emerging AMR threat on human health, animal health, and its environmental linkages. The study highlights the importance of effluents containing antibiotic residues from pharmaceuticals and healthcare facilities, expired drugs, excreta from households, manures and litters from livestock being responsible to pollute the environment (water and soil) and transmit Antimicrobial Resistant Bacteria (ARB), Resistance Genes (RGs) and antimicrobial residues. So far, environmental policies did not include components of AMR and health policies did not focus on environmental dimensions of AMR. This gap needs to be addressed on urgent basis for policy/action plan development at the national level.

Validation study of Urinary Tract Infection Rapid diagnostic kit with antibiotic sensitivity (Rapidogram) at health facilities of West Bengal

UTI in the community setting is treated empirically in absence of proper culture & sensitivity result due to inadequate lab set up. Hence, to ensure evidence-based prescription of antibiotics, particularly in peripheral health care facilities, a rapid testing assay (Rapidogram), developed by Sree Chithra Tirunal Institute for Medical Science & Technology is validated at health facilities in this study. The finding of the study may facilitate to make decision in rolling out the said kit at peripheral levels for appropriate evidence-based management of UTI.

Anti-Microbial Resistance Research & Evidence Synthesis for Stewardship implementation and Surveillance program development framework assessment (AMRES)

This is a mission mode project. This study focuses on antimicrobial resistance pattern, prescription practices and community antibiotic consumption behavior through a multitier approach towards developing framework for Antimicrobial Resistance Surveillance Program and assesses preparedness of public health systems for implementing Antimicrobial Stewardship Program through a multidisciplinary consensus network approach.

LABORATORY BASED BASIC STUDIES

BACTERIOLOGY DIVISION

Development of outer membrane vesicles-based vaccine against diarrhoeagenic *Escherichia coli*

Diarrhoeagenic *E. coli* (DEC) strains are divided into six main categories on the basis of distinct epidemiological and clinical features, and specific virulence determinants. This study describes developing a pentavalent OMV-based immunogen formulation from five prevalent DEC pathotypes (ETEC, EPEC, EHEC, EAEC, EIEC) and intends to use this immunogen as next generation candidate vaccine in mice model. Dynamic light scattering analysis of OMVs revealed that different clinical isolates of DEC characteristically secrete different sizes of OMVs. Administration of 10µg dose of OMVs per 100µl of PBS evoked a significant immune response, evident from western blot analysis and ELISA (Fig. 9).

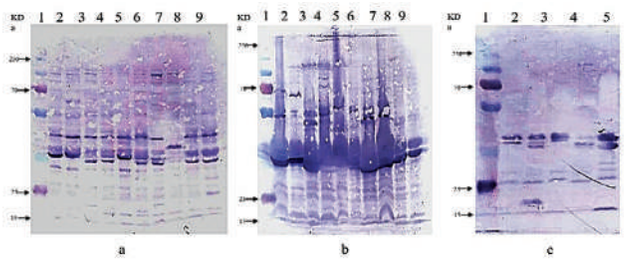


Fig. 9: Study on Carbapenem Resistant Gram-negative Bacilli of Enterobacteriaceae family isolated from blood of sepsis patients admitted in Intensive Care Unit of Tertiary care Hospitals in Kolkata.

Bacterial Sepsis is prevalent in developing countries and mostly caused by Multi Drug Resistant Gram-Negative Bacilli (MDR-GNB).

Currently, Carbapenems, a class of β-lactam antibiotics reserved as "last-line" antibiotic group, are the choice of treatment for sepsis, but resistance to carbapenems is on the rise and is a serious health concern. A total of 682 non-duplicate Carbapenem Resistant- Gram Negative Bacilli (CR-GNB) were included. Among 682 CR-GNB, 569 isolates (83.43%) belonged to *Enterobacteriaceae* family. MIC90 of carbapenem for the CRE isolates were 512µg/ml and MIC90 of colistin was 128 µg/ml. Among CRE isolates, CR *Kleb. pneumoniae* was predominant (531/682, 78.55%) and CR *Esch. coli* was 11.05% (75/682,). Among CR-*Klebsiella*, *oxa*48 like carbapenemase and *tem1* were predominant (74.92% and 85.33% respectively). In CR *E. coli, ndm*1 (46.66%) was predominant along with *blaTEM-1* (86.30%). Through Liquid mating assay, *blaNDM-1* and *blaCTX-M-15* transferred through two different conjugative plasmids. WGS analysis showed the genetic environment of *blaNDM-1* lies between IS91 family transposase and IS 26 family transposases.

Validation of antimicrobial activity of selected herbs against multidrug resistance *Salmonella* Typhi Isolates: development of antityphoid herbal formulation

The crude extract of *Scoparia dulcis* root was fractionated into 13 fractions by column chromatography, of which 5 fractions were selected based on their antibacterial activity against *Salmonella Typhi*. Then 43 compounds were identified from these 5 fractions by LCMS which were computationally screened to state their drug likeness; 35 compounds that followed the Lipinski's rule of five for drug likeness were computationally docked to some of the essential protein of *S.* Typhi viz. The docking result showed folA, murB, murA proteins had highest docking score of -10.9, -8.89, -8.83 respectively with the compound (2R)-7-methoxy-2H-1,4-benzoxazin-3(4H)-one 2-O-β-galactopyranoside. The molecular dynamic (MD) of folA and murA proteins were performed with the top scoring compound in docking study. Both the protein and compound have shown certain level of stability during the 100 nsec stimulation time. The compound had highest interaction with 18th Asparagine amino acid of folA protein in form of H-bond and water bridge and with 329th Glutamic acid amino acid of murA protein in form of Hbond, ionic bond and water bridge.The study is in progress to develop one herbal formulation against typhoid fever.

Loop-mediated isothermal amplification (LAMP) assay for detection of *Vibrio cholerae* O1

Loop mediated isothermal amplification (LAMP) assay has been developed for detection of *Vibrio choleraee* O1. Newly developed assay is working with 100% sensitivity and specificity when tested with pure cultures of *V. cholerae* O1 as positive detection and other *vibrios* and *Escherichia coli* strains as negative detection.

Serosurvey: an estimation of *Vibrio cholerae* O1 infection in India

Serological imprint of *V. cholerae* O1 infection in the previous one year reflects through reciprocal vibriocidal titer ≥320, which was used as a surrogate marker to predict 'Recent Annual Infection' using archived sera collected through nationwide Dengue sero-surveillance conducted during June 2017 to April 2018. Triangulation of vibriocidal data with epidemiological data on cholera cases during that period showed a close match. Therefore, it may be said that sero-surveillance using vibriocidal data can be used to estimate cholera infection status in the preceding year and may be considered as an effective alternative to the disease surveillance.

Regulation of cholera toxin promoter activity based on the number of TTTTGAT heptamer repeats by H-NS and ToxT in *Vibrio cholerae* O1

A complex virulence-regulatory cascade controls expression of the cholera toxin genes (ctxAB) in

V. cholerae, which leads to the production and secretion of choleragen (CT), responsible for rice watery diarrhoea in infected individuals. The cholera toxin promoter (PctxAB) contains a series of heptad repeats (5' -TTTTGAT-3') that plays a crucial role in transcriptional regulation of ctxAB by recruiting the transcriptional activators ToxT, ToxR and the nucleoid-associated protein H-NS along the ctx promoter. The number of these repeats differs not only between the two biotypes of *V. cholerae* O1 strains, but also among the strains belonging to the same biotype. This study examined if regulation of PctxAB is influenced by the number of these repeats. We posit that ctx activation indeed depends on the number of TTTTGAT heptad repeats within PctxAB, and occupation of the distal repeats by H-NS could prevent transcriptional activation of the ctx genes in *V. cholerae* O1 pandemic isolates. The results elaborate on the interplay between ToxT and H-NS and suggest that ToxT-dependent transcriptional activation may not require entire displacement of H-NS and supports a recently described revised model of ToxT and H-NS mediated PctxAB transcriptional regulation.

Exploration of diarrhoeagenic *Escherichia coli* isolated from hospitalized diarrhoeal patients in Kolkata

In India, 30-40% of all diarrheal episodes are generally found to be associated with DEC infection and thus it needs a constant surveillance to understand the disease-causing property and their antimicrobial resistance. Of 8,891 stool samples collected from the Infectious Diseases Hospital, Kolkata, multiplex-PCR identified the presence of DEC in 7.8% of the samples; about 54% cases were due to sole DEC infections. Majority of the mixed DEC infections was caused by the Vibrio spp. (19.1%) followed by Rotavirus (14.1%). AMR profile showed high prevalence of multidrug resistance (MDR) among DEC (56.9%) in which 9% were resistant to antibiotics of six different antimicrobial classes.

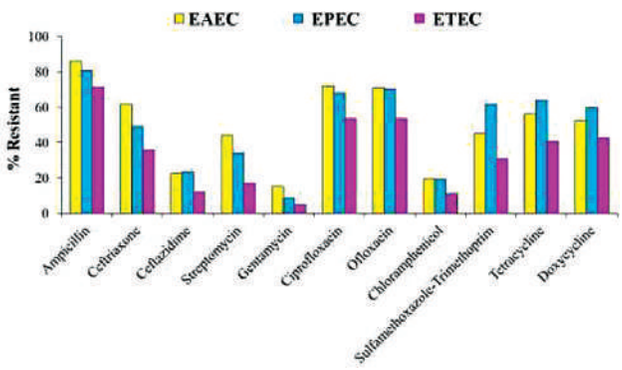


Fig.10: Antimicrobial resistance pattern of DEC *pathotypes.*

Colistin resistance in neonatal septicaemic strains: two-component systems, efflux pumps, lipopolysaccharide modification

Colistin exerts bactericidal activity by destabilizing LPS. Modification of LPS by two-component system (TCS) genes (*phoP/phoQ* and *pmrA/pmrB*), *mgrB*, efflux pumps, their regulators, lipid A biosynthesis and assembly genes - all contribute to colistin resistance. Considering colistin as a 'last resort' antibiotic, this study aimed to decipher the trend of colistin susceptibility among septicaemic neonatal strains and analyse the different mechanisms of colistin resistance among strains with/or without carbapenem resistance. Colistin resistance was found in *K. pneumoniae* (2.8%) only, of all Enterobacterales studied. The transmissible colistin resistance gene, *mcr*, was absent. Colistin resistance both in study and global strains is multifaceted and attributed to mutations in chromosomal genes leading to lipopolysaccharide modification or efflux of colistin through pumps. With no transmissible *mcr*, prevalence of colistin-resistant strains was low in the unit. Colistin-resistant strains with dual carbapenemases causing sepsis are alarming as they are practically untreatable.

Therapeutic intervention of *Shigella flexneri* host pathogen: interaction with a herbal compound

Antibiotics play an essential role in preventing Shigella flexneri infection. However, global rise in antibiotic resistance creates a major challenge

to treat bacterial infection. In this context, this study focuses on determining the role of the herbal compound capsaicin (Caps) in inhibiting S. flexneri growth and evaluating the molecular mechanism behind bacterial clearance. The study showed for the first time that Capsaicin inhibits intracellular *S flexneri* growth by inducing autophagy.

STUDIES ON HIV / AIDS

Development of a Technical Framework for establishing comprehensive surveillance system for HIV/AIDS-related mortality in India

This WHO funded project aimed to provide suitable insights for considering plausible HIV/AIDS associated mortality surveillance in Indian context. The proposed mortality surveillance holds the transformation potential in making HIV associated mortality indicators useful for monitoring PLHIV health and their retention in treatment and care.

A facility based cross sectional study on status of nutrition, immunization and chemoprophylaxis in Children Living with HIV/ AIDS (CLHIV) aged 1- 14 years in a tertiary hospital, Kolkata, India

This study aims to generate evidence on nutritional, immunization and chemoprophylaxis status and adherence gap, if any, in reference to national guidelines for HIV infected children for further policy direction.

STUDIES ON VIRAL DISEASES

Surveillance and molecular characterization of Group-A Rotavirus and other enteric viruses among children reporting with acute gastroenteritis

The surveillance and molecular characterization of enteric viruses aims to assess baseline data prior to and post-introduction of RV vaccine in West Bengal. From April 2021-March 2022, 347 stool samples were collected from the outpatient department of B. C. Roy Children's hospital of which 14.70% were RV positive. Compared to data from 2010-2018, there is significant reduction in RV infection rates in the region.

Host-Rotavirus Interaction Studies: The cross talk between rotavirus and cellular nonsense-mediated mRNA decay (NMD) pathway

Data suggested that rotavirus infection resulted in global inhibition of NMD pathway by down-regulating the expression of UPF1 in a strain in-dependent manner. UPF1 expression was found to be regulated at the post-transcriptional level by ubiquitin-proteasome mediated degradation pathway. Subsequent studies revealed rotaviral non-structural protein 5 (NSP5) associates with UPF1 and promotes its cullin dependent protea-some mediated degradation.

Mutational analysis of circulating SARS-CoV-2 strains in India

The emergence of a novel variant of SARS-CoV-2, named B.1.1.526, in India was identified through this study. This novel variant encompasses 129 SARS-CoV-2 strains which are characterized by the presence of 11 coexisting mutations including D614G, P681H, and V1230L in S glycoprotein. Out of these 129 sequences, 27 sequences also harbored E484K mutation in S glycoprotein.

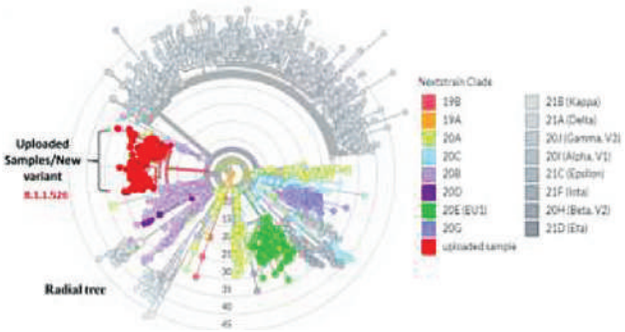


Fig.11: Molecular phylogenetic analysis of the new variant B.1.1.526 by UShER.The phylogenetic tree depicting the position of 129 strains of the new variant (labelled as uploaded sample/ new variant, red color) within the 1127 SARS-CoV-2 strains of different clades or variants.

Assessment of prophylactic and therapeutic role of BCG against SARS CoV2 infection: study in hamster model

Based on epidemiological studies reporting Bacillus Calmette– Guérin (BCG) routine vaccination may protect from COVID-19, several countries like Netherlands and Australia launch clinical trials to test the protective benefit of intracutaneous administration of BCG vaccine in health-care workers. Most of the data, based on ecological study suggesting less COVID-19 in countries with routine BCG immunisation, are prone to be confounded. So, until the trials are complete it is important to evaluate the off target beneficial effect of BCG against COVID 19. To determine the protective effects of BCG against SARS CoV2 infection, innate functions of the macrophages derived from mice and hamsters were studied with BCG stimulation. Although there was a significant decrease in IL-10 production in BCG immunization we did not find any significant decrease in viral load in lung, trachea and nasal swab on either therapeutic or prophylactic treatment of BCG.

Hepatitis C virus drug resistance and the role of host immune factors

This is an ongoing study where till now 160 HCV sero-reactive patients have been recruited of which 82 (51.25%) were HCV RNA positive. Genotyping revealed that majority of hemodialysis patients were infected with HCV genotype 1c (~71%) whereas multi transfused thalassemia patients were infected with genotype 3a (~82%).

Strengthening/ Promoting evidence-based advocacy for influenza prevention and control in India

This is a multi-centric project to understand the status of influenza in elderly populations in Eastern part in India. Out of 666 samples, 10 samples were found positive for InfA/pdm09 H1N1, 22 samples were found positive for InfA/H3N2 virus and 9 samples found positive for InfB/Victoria subtypes.

Genomic and phylogenetic analysis of human respiratory adenovirus circulating in Eastern India

This is an ongoing study which aims to identify the circulating and predominant serotypes of human respiratory adenovirus in Eastern India and find if there is any correlation between HAdV serotype and severity of disease. Based on laboratory analysis, 21 cases of HAdV were confirmed out of 976 patients presenting with respiratory tract infection with a positivity of 2.15% (n=21/976). HAdV infection was highest among the 2-5 years age group followed by ≤ 2 years age group. HAdV infection was lowest among the ≥ 18 age group.

Multi-omics approach towards drug repositioning for Dengue virus infection

Dengue virus, a positive stranded encapsulated RNA virus, is composed of three structural protein genes encoding the nucleocapsid or core (C) protein, a membrane-associated (M) protein, an enveloped (E) glycoprotein and seven non-structural (NS) proteins. So far, no effective antiviral agents have been identified for treating dengue infection and existing treatments are only supportive. Traditional drug discovery takes enormous amounts of time, money and effort to find a new drug. In this approach, the target drugs have already been tested for effectiveness against other diseases and have been proven safe for human use; hence, the success rate in this technique is expected to be high. Here, we applied a computational drug repositioning method by performing omics analyses of publicly available expression profile and protein interaction data. The identified drug candidates are expected to induce a suppressed level of gene expression and disrupt the association of host proteins with dengue virus proteins.

Virus Research and Diagnostic Laboratory (VRDL)

Apart from the diagnosis and research on common viruses and agents of public health importance, this is the first lab in eastern India to start routine testing of SARS-CoV-2. Later, it also became the referral centre in the State for final confirmation of COVID-19 cases. This is an ICMR designated facility responsible for training, quality control, kit validation, and research on COVID-19.

Table .1. The summary of the major findings is presented below.

Investigations Performed	Total No. of Samples Tested in 2021-22	Positive Samples	Positivity Rate (%)
SARS-CoV-2	159065	37298	23.45
Chikungunya PCR	6	0	0
Chikungunya IgM ELISA	68	6	8.82
Hepatitis A IgM ELISA	117	26	22.22
Hepatitis E IgM ELISA	115	11	9.57
Hepatitis B Surface Ag ELISA	51	2	3.92
Hepatitis C Ab ELISA	17	3	17.65
Scrub typhus IgM ELISA	166	31	18.67
Leptospira IgM ELISA	90	5	5.56
Respiratory RSV-A PCR	1112	0	0
Respiratory hmPV-A1A2 PCR	929	302	32.51
Respiratory Adenovirus PCR	929	29	3.12
Respiratory Rhinovirus PCR	929	26	2.80

WGS of SARS-CoV-2 from second wave to study the mutations

The analysis indicated high frequency of the delta variant in the second pandemic wave. In addition to several spike mutations in delta variant, mutually explicit signature constellations of non-spike coappearing mutations were identified driving the symptomatic and asymptomatic infections.

STUDIES ON PARASITIC DISEASES

Identification and molecular characterization of common eneteric parasites in Kolkata

We investigated SNPs associated with coinfection incidence of the parasite, level of genetic diversity and established the genetic structure among the local isolates of *E. moshkovskii* using molecular analysis tool (DnaSPv5 and MEGAX). We observed 10 SNPs in 18S rRNA locus of *Entamoeba moshkovskii* in our study isolates, of which five SNPs potentially associated with specific coinfection incidence**.**

Identification of novel Anti-Parasitic Compound from Natural Medicinal source and their effect on Giardia lamblia

In the current scenario, conventional drug failure and emerging drug resistance of parasites are the major obstacles towards control of the disease. The current treatments either one of a family of metronidazole, nitroimidazole, albendazole, are reported to have life threatening side effects, high toxicity, induction of parasitic resistance, length of treatment and high cost. New plant-based treatments should be less toxic, safe more efficient less expensive and readily available and low-income populations groups. This study indicates that Andrographis paniculata extract may be used as a potential phytotherapeutic agent.

Human pulmonary paragonimiasis in crab eating communities and smear negative suspected TB cases from some states of India

Paragonimiasis disease symptoms can be similar to those observed in patients with tuberculosis or bacterial pneumonia, frequently resulting in misdiagnosis. We screened baseline data of RNTCP to identify individuals with common symptoms and collected serum, sputum and stool samples from them. This work will provide the incidence of Paragonimus spp in crab eating communities in two districts as well as in West Bengal.

Other multicentric studies

1. A Prospective, Multicenter, Randomized, Active-controlled, Observer-blind, Phase II study seamlessly followed by a Phase III study to evaluate the Safety, Tolerability and Immunogenicity of the candidate GEMCOVAC19 (COVID-19 vaccine) in healthy subjects.

2. Immune response to precautionary third dose of COVISHIELD/COVAXIN among healthy adult population: an ICMR Cohort study, India.

NICED is one of the study sites of these multicentric studies coordinated by ICMR.

CAPACITY BUILDING

- 70 PhD students were trained at ICMR-NICED and PhD was awarded to one student.
- 79 summer students from various universities were trained and supported for completion of their dissertation work.
- A total of 143 participants including physicians and health care workers across India were trained through five workshops and training programs on laboratory skill development.

PUBLIC HEALTH

- Adult Zebrafish model development for Shigella pathogenesis, transmission, and vaccine efficacy studies
- Demonstrating that the Haitian variant of *V. cholerae* O1 strain with its altered genomic constitution are more virulent as it produces significantly higher level of cholera toxin.
- Colistin resistance in neonatal septicemia isolates was low, but most colistin resistant strains were also resistant to carbapenems with presence of multiple carbapenemases.
- Analysis of the open and closed conformation of AdeB (efflux pump protein) and its binding with carbapenems helped in visualizing the plausible atomic level causes of pump inhibition driving the discovery of novel inhibitors.
- Sequencing of SARS-CoV-2 from second pandemic wave revealed high frequency of the delta variants and several important mutually explicit signature constellations of non-spike coappearing mutations were identified.
- Lineage analysis in India showed emergence of new SARS-CoV-2 variants, i.e., B.1.617.1 and B.1.617.2, during April-May 2021, which might have caused the sudden upsurge of confirmed cases.
- Generation of evidence on changing pattern of dengue associated spectrum of clinical manifestations and gastrointestinal complications associated with DENV 2 infection
- Identification of kerp2 as genetic marker for disease outcome when infested by Entamoeba Histolytica.
- Generation of evidence on environmental determinants of antimicrobial resistance in India.
- completion of rBCG Vaccine Trial, COVAXIN Phase III Trial, and mRNA based vaccine trial against COVID-19 infection.
- HMGB1 inhibition induces lysosomal degradation to induce antimicrobial activity against *H. pylori*.
- District HCV genomic diversity was observed in two high risk group populations like Thalassemia (3a) and Chronic Kidney Disease (1c), New subtype like Gen-4a is emerging in eastern Part of India
- HCV Gen-6 is outnumbering Gen- 1 and 3 in the north-eastern state of Manipur owing to cross-border transmission.
- Very low percentage of HCV drug resistance is evolved against DAAs treatment and majority of them belong to HCV subtype 3b.
- Genomic diversity of dengue virus serotypes is observed with rapid change in prevalent serotype during dengue outbreak.

ICMR-NATIONAL INSTITUTE OF MALARIA RESEARCH (ICMR-NIMR), NEW DELHI

EPIDEMIOLOGY AND CLINICAL RESEARCH

Strengthening of National Malaria Slide Bank and External Quality Assurance Programme for microscopy at NIMR

NIMR has prepared around 10,000 slides till date, supported training of malaria microscopists for detection and identification and counting of parasites and sent slide panels to various organizations for refresher trainings (Fig. 12). The malaria slide bank has supported to the basic and refresher training course for malaria microscopists by providing malaria slides. ICMR-NIMR malaria slide bank has provided the well characterized blood smear to the organizations for refresher training in states, for training the technicians and for assessing the competency of newly empaneled WHO L1 & L2 technicians.

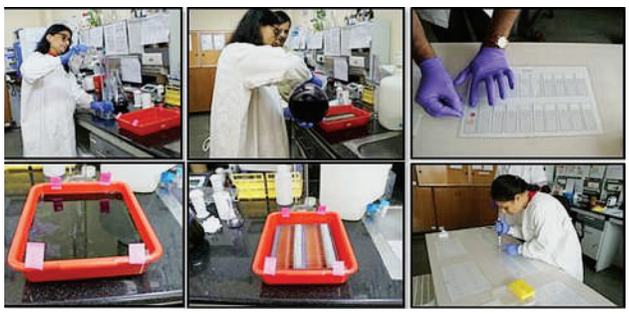


Fig. 12: Blood smear preparations and mass staining of smears at NIMR, Delhi.

Quality Assurance of Malaria Rapid Diagnostic Tests

This laboratory is recognized by WHO to assess the quality of malaria RDTs procured and supplied by NVBDCP in India. *P. vivax* and *P. falciparum* panels were prepared from the samples collected from malaria endemic regions of India. Panels were validated by at least two reference kits, before testing the RDTs every time. The post-dispatch RDTs received from the field were also tested for their quality.ThisI s the only lab of its kind in South East Asia, that performs RDTs lot testing to ensure distribution of quality diagnostics under programme.

FEVER CLINIC

At fever clinic, NIMR HQ, Delhi, 17 malaria cases were diagnosed from April, 2021 to March, 2022. Of which, 76% were males and 24%. All the confirmed malaria cases were given treatment as per the National Malaria treatment guidelines.

A study of low-density malaria parasite infection in the community and its transmission potential in Surendranagar and Dahod districts, Gujarat, India

Total 2600 samples were carried out form both the district. Microscopy and RDT were carried out of 2600 field samples (Fig. 13). In Surendranagar, out of 1300 samples, 3 Pf and 1 Pv positive were found. Treatment was provided by Nearby PHC on the same day as per NVBDCP guidelines. RTPCR results will be generated after getting RTPCR kits from Central Procurement Unit, ICMR-NIMR New Delhi.

Fig. 13: Field Survey by NIMR FU Nadiad staff at tribal area of Dahod district, Gujarat.

Efficacy and safety of ACT for the treatment of uncomplicated *Plasmodium falciparum* malaria in India

The total fever cases screened were 1554. The results were: Total Pv:12, Pf: 69, Mix:3, Follow-up: 53. ACT drugs are found susceptible towards *Plasmodium falciparum* malaria in Gujarat India.

Phase III evaluation of three formulations of Natular (20.6% EC, 2.5% G30 and 7.48% DT) against immature of *Aedes aegypti* and *Anopheles stephensi* and two formulations (20.6% EC, 2.5% G30) against *Culex quinquefasciatus* in three eco-epidemiological settings in India

Larvicide Phase-III Trials were conducted; GR and DT formulation is potent larvicide for the control of *Anopheles* and *Aedes* (Fig. 14).

Fig. 14: Phase-III Natular larvicide trials by NIMR FU Nadiad staff.

Study the change in malaria epidemiology and associated risk factors in low malaria endemic districts of Assam and Meghalaya

The study was conducted in the low malaria endemic districts of Assam and Meghalaya. A case-control approach was used to examine the Individual/ Household Level Risk Factors, epidemiological risk factors (Active case detection/passive case detection/asymptomatic), and vector-related risk factors associated with malaria in low endemic districts of Assam and Meghalaya to explore the association between participants/ household risk factors and malaria infection. The epidemiological data were collected from the low malaria endemic districts of Assam (Kamrup (M), Kamrup (R), Goalpara, Baksa, Chirang, and Nagaon) and two districts of Meghalaya (Rhi-Boi and East Garo Hills) are areas of low seasonal transmission bordering Assam (Fig. 15).

Fig. 15: Epidemiological survey in low malaria endemic districts of Assam and Meghalaya.

A total of 842 subjects have been screened to date, and 71 patients were reported to be positive for malaria. During the entomological investigation, *An. minmus* was collected from the PHCs reporting malaria. Apart from the primary malaria vectors, secondary malaria vectors were also collected from the study sites.

Malaria vector bionomics and transmission patterns in areas with ecotype changes with special reference to re-established vector species, *An. culicifacies* in Assam and Tripura

During the study period, a preliminary investigation was done to identify sites of the prevalence of Anopheline species in the selected villages. During the study period, using CDC trap collection, both culex and Anopheline mosquitoes were collected. *Anopheles culicifacies*, *An.minimus, An. kochi, An. nivipes/phillipiensis, An. baimaii, An. vagus*, *An. maculatus, An.nigerimus*and *An. annularis*were collected. In-plane ecotype, *An. culicifacies*were collected both from cattle shed and Human dwelling. *An. culicifacies*were also collected in the hand catch method. To determine the insecticide susceptibility

status of *An. culicifacies*, adult mosquitoes were collected from different localities of Udaulguri district (Assam). Mosquitoes were collected from stratified ecotypes comprising two selected PHCs of the Udalguri. *An. culicifacies*was reported to be resistant to D.D.T. (4%) and malathion (5%) in Orang PHC, Udalguri (Assam). The per man-hour densities of *An. culicifacies*was 19.05 (95% CI:4 3.14-26.23) and 2.96 (95% CI: 1.43-8.76) in cattle shed and human dwelling, respectively. In the Udalguri district, the percent mortality to DDT and malathion were 68.78% and 89.45%, respectively. It was susceptible to deltamethrin with mortality of 99.75%.

A study of low-density malaria parasite infection in the community and its transmission potential in Bastar and Kanker Districts, Chhattisgarh, India

For the low transmission season, a total of 2600 samples were collected, 1300 from each site. There was no malaria infection detected in district kanker by RDT and Microscopy. In Bastar, malaria prevalence was found to be 4.3%. There were 86 (77%) out of 112 positives were asymptomatic. The average parasite density in the asymptomatic was 2477 and 30676 in the symptomatic infections. Male and females in the infected were in equal proportions.

VECTOR CONTROL

Screening of novel compounds for insecticidal potential

Screening of novel compounds for ant larval activities and development of protocol for large scale screening for their larvicidal potential (Fig.16). Larvicidal protocol was developed for high throughput to screen a large number of compounds. Tests were performed to evaluate the larvicidal potential of their larvicidal potential approx. 40 chemical compounds against Anopheles larvae, Taking this as platform, screening of non-biological synthetic compounds as candidate against mosquito vectors for their efficacy against mosquito immature and adult form is being planned and to estimate lethal concentrations of the candidate compounds so that such compounds which show anti-malarial potential might be useful in either killing mosquito larvae or can clear parasite from mosquitoes or may be targeted for shortening of lifespan of mosquitoes.

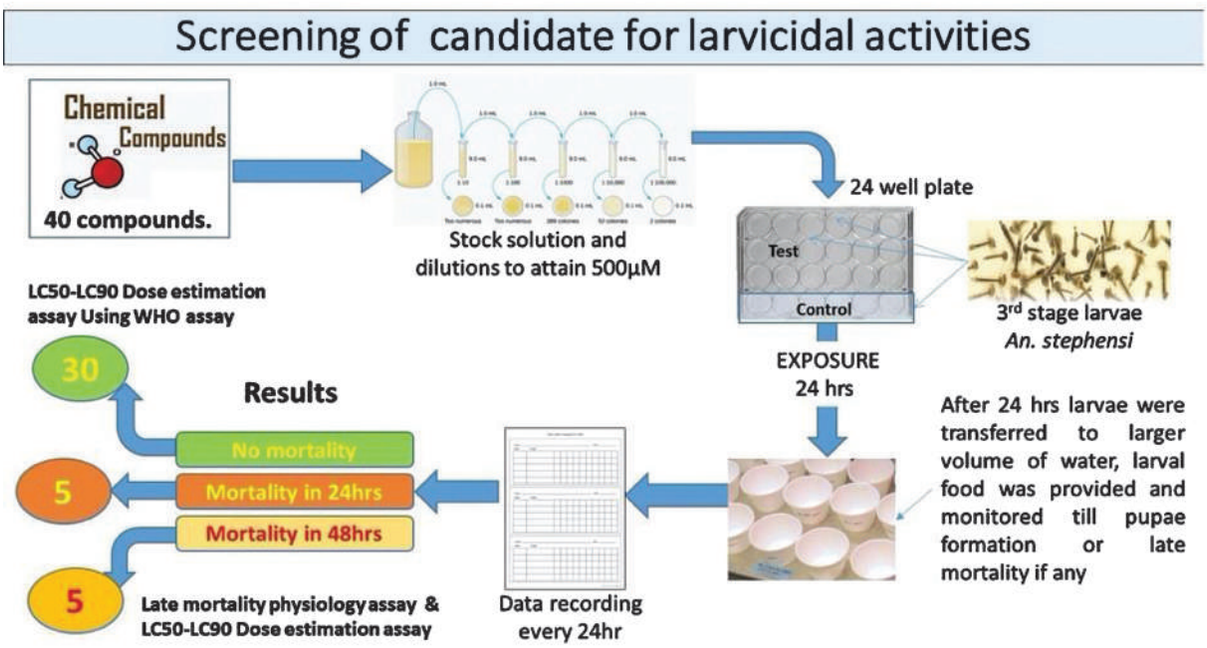


Fig.16: Schematic representation of 40 compounds tested using high throughput bioassay.

PARASITE BIOLOGY AND DRUG DISCOVERY

A novel single step multiplex qPCR assay developed for detection of *Plasmodium knowlesi* (*Pk*) and *P. cynomolgi* (*Pc*)

The qPCR assay was successfully amplified the target 18S rRNA gene segment from *Pk* and *Pc*. The qPCR assay was specific for *Pk* and *Pc* parasites.

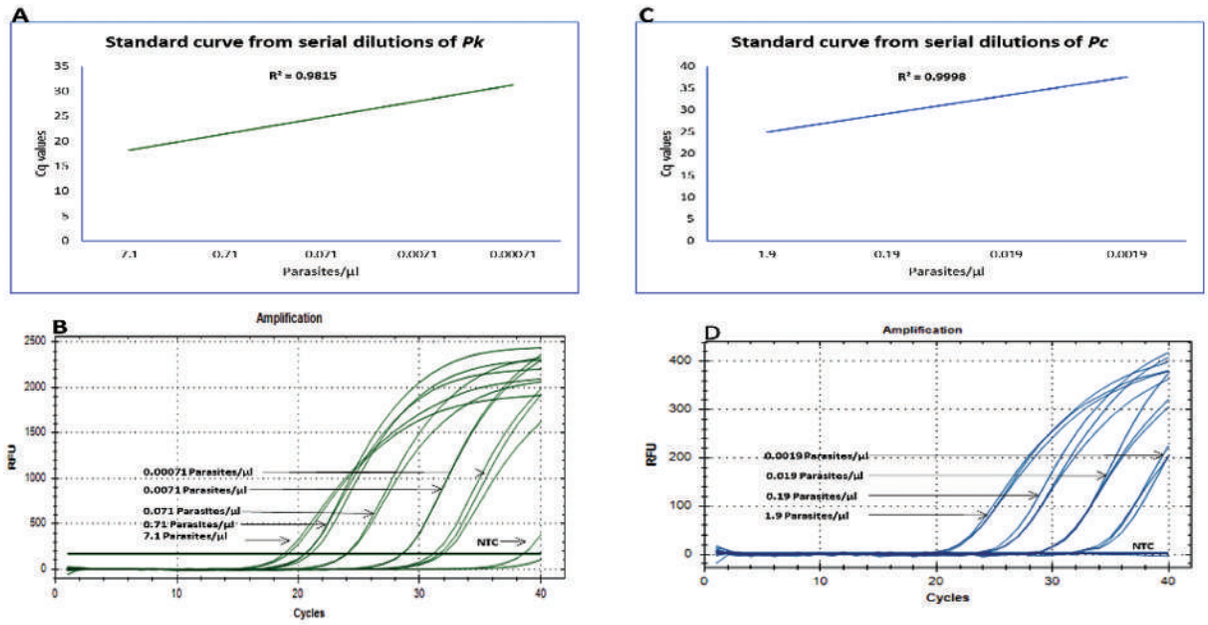


Fig. 17: A. Standard curve generated from 10-fold serial dilutions from known concentrations ofparasites (*Pk*) in the qPCR assay.B. qPCR amplification cycles for *Pk* serial dilutions with fluoroscent probe HEX (green). C.Standard curve generated from 10-fold serial dilutions from known concentrations of parasites (*Pk*) in the qPCR assay. D. qPCR amplification cycles for *Pc* serial dilutions dilutions with fluoroscent probe FAM (blue).

A global joint research program for the defense on high-risk importable infectious diseases (malaria and dengue)

This study using peptide microarray of thirteen amino acid length antigenic proteins of *P. falciparum* identified cyclic constrained peptides, which were further validated by ELISA on field collected *P. falciparum* infected sera samples with high sensitivity and specificity. This study suggested that cyclic constrained immunoreactive peptides can be explored as diagnostic tool for malaria.

Multistage stage malaria vaccine candidate for the prevention of *P. falciparum* infection in mosquito and pre-erythrocyte development in man

The main aim of this study is to evaluate the antibodies for blocking the development of malaria parasites in mosquito vector. To achieve this object, team has established in-vitro *Plasmodium falciparum* gametocyte culture using laboratory strains NF54 and JDP8. The Standard Membrane Feeding Assays (SMFA) were standardized in laboratory-reared *Anopheles stephensi*, a major malaria vector in India. Currently the testing of mosquito infection is going on using SMFA.

Designing, synthesis and screening of potent inhibitors against unusual malarial proteases-metacaspase-2

Plasmodium metacaspase-2 play important role in malaria gametogenesis and sporogony. Deletion of Metacaspase-2 (MCA-2) caused an unregulated stress-mediated apoptosis-like cell death and reduced the formation of gametocytes. A significant reduction in oocysts, ookinete and sporozoites load and delay in hepatocytes invasion in the knockout parasites line.

And MCA-2 inhibitory molecule, C-532 and C-533, inhibits PfMCA-2 activity along with the parasite's asexual and sexual growth in vitro and in vivo. C-532 and C-533 impair *Plasmodium* transmission in *An. stephensi*, possibly by inhibitingMCA-2. These results suggest that this enzyme is important for malaria transmission biology.

NFHS-5

It is an ICMR flagship project named "Establishing a pan-India landscape of human *Plasmodium* infections from dried blood spots collected under National Family Health Survey – 5 (NFHS – 5) for establishing a pan-India landscape of human *Plasmodium* infections from dried blood spots. 83515 DBS samples were received and all DBS are punched: DNA has been isolated from 18,018 (23%) samples and qPCR has been done on 3662 (5%) of samples. The interim positivity rate for *Plasmodium* genus is 18% (674/3662).

Immuno-modulatory role of mesenchymal stem cells in the pathogenesis ofcerebral malaria infection

Using *Plasmodium berghei* ANKA (PbANKA) as a mouse model, it was demonstrated that MSCs attenuate cerebral malaria pathogenesis by diminishing the effect of inflammation, altered organ morphology, reduced parasitemia and increased survival of the mice (Fig. 18). Infusion of MSCs in infected mice decreased hemozoin deposition, preserved the integrity of the blood-brain barrier, oedema and hemorrhagic lesions in vascular organs.

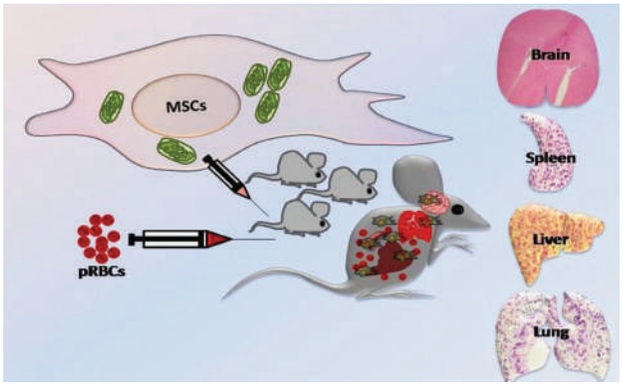


Fig. 18: Overview of the MSCs induced restoration of altered organ morphology.

Regulatory T cells and T helper 17 cells: Their roles in disease susceptibility/resistance in malaria infection

The study revealed that high levels of $CD4^+ICOS^+Foxp3^+$ cells and IL-10 during the course of infection with *P. berghei* and *P. yoelii* 17XL suppresses immune system of host that might help parasite to grow faster, however there is no significant expression of these highly immunosuppressive cells in *P. chabaudi* and *P. yoelii* 17XNL infection. Overall, it is demonstrated that $CD4^+ICOS^+Foxp3^+$ cells play an important role in regulating immune response of host that ultimately determines the outcome of the disease.

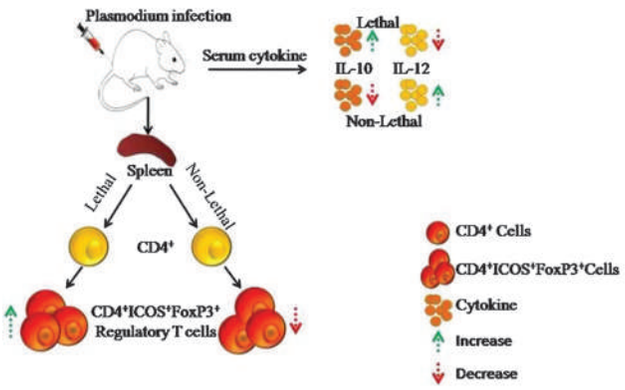


Fig. 19: Upregulation of CD4 + ICOS + Foxp3 + cells in lethal malaria infection.

Elucidation of the role of regulatory B cells during malaria pathogenesis

In this study, a comparable IL-10 competent B-10 cell subset (regulatory B cells) was characterized during lethal and non-lethal infection with malaria parasites using the mouse model (Fig. 8). It was observed that infection of Balb/c mice with *P. yoelii* I 7XL was lethal and a rapid increase in dynamics of IL-10 producing B220+CD5+CD1d+ regulatory B cells with the course of infection was observed. However, animals infected with a less virulent strain of the parasite *P. yoelii* I7XNL attained complete resistance. Adoptive transfer of regulatory B cells to naïve mice followed by infection results in slow parasite growth and enhancement of survival in *P. yoelii* 17XL (lethal) infected animals. Also, there was decreased production of pro-inflammatory

cytokine (IFN-γ) and enhanced production of anti-inflammatory cytokine (IL-10).

VECTOR-PARASITE INTERACTION BIOLOGY

Entomological investigation of Japanese Encephalitis (JE) in district Haridwar

As JE case was reported in Bijoli and Aneki area of district Haridwar. On request of Chief Medical Officer, Entomological investigations of JE were carried out in the two villages. Adults and larval survey of JE vectors were conducted. Larvae were collected from different breeding sites breeding sites such as Pits, ponds and rice fields and reared in the laboratory for adult emergence. In larval collection *Culex quinquefasciatus* and *Cx. vishnui* sub group were recorded. Adult collection was carried out by aspirator and total catch method. In adult collection both species such as *Culex quinquefaciatus* and *Cx. vishnui* sub group of mosquitoes were recorded. A survey report was submitted to the health department.

Entomological investigations were carried out in twelve dengue affected villages and urban areas of Haridwar district, Uttarakhand

ICMR-NIMR field unit, Haridwar on request of the Chief Medical Officer (CMO) of Haridwar, the state health department to conduct entomological investigations were carried out in twelve dengue affected villages and urban areas of Haridwar district, Uttarakhand, during November (Transmission season) 2021 investigate the prevalence, distribution of *Aedes* mosquitoes and identify high risk areas in Haridwar for proposing control in the risk areas. During the Entomological surveys, about 777 houses were screened from dengue affected 12 different villages and municipal areas of Haridwar district. According to Dengue incidences study sites were selected and in each study site about 55–80 houses were surveyed following survey of each fifth house to cover more geographical area, in case of multi-storey houses single house was selected at ground floor for survey. Due to several rounds of fogging and focal sprays, collection of adult mosquitoes could not be collected however, larvae were collected from study sites and reared to adult (F1) mosquitoes. These mosquitoes were subjected to RNA extraction and RT-PCR detection of the Dengue virus for any natural infectivity through the transovarial route.

Entomological investigation of malaria deaths in district Haridwar

As two malaria deaths case were reported in Bhadarabad CHC area of district Haridwar. On request of Chief Medical Officer, Entomological investigations of Malaria deaths were carried out in the two villages. Adults and larval survey for malaria vectors were conducted. Larvae and adults were collected from different breeding sites of Jamaikhera village of Bhadarabad CHC and reared in the laboratory for adult emergence. Adult collection was made with help of aspirator and total catch method. In adult collection both species such as *Anopheles culicifacies* and *Anopheles fluvitalis* mosquitoes were recorded. A survey report was submitted to the health department.

Heme-peroxidase/HPX12 role in the regulation of male fertility

Functional dysregulation of the antioxidant defence system causes a detrimental impact on male fertility and reproductive physiology in vertebrates. But this mechanism is poorly studied in insects, especially mosquitoes. With a combination of functional genomic and cell biology approaches, the protective role of HPX12 was evaluated from oxidative stress, in the maintenance of healthy sperms in the male reproductive system. HPX12 mRNA suppression not only impairs the sperm parameters such as motility, and viability but also causes a significant down-regulation of male -accessory-gland proteins, which constitute a major part of the semen(Fig. 20). Since, high reproductive capacity directly influences the mosquito population, manipulating male mosquito reproductive physiology could be an attractive tool to combat vector-borne diseases.

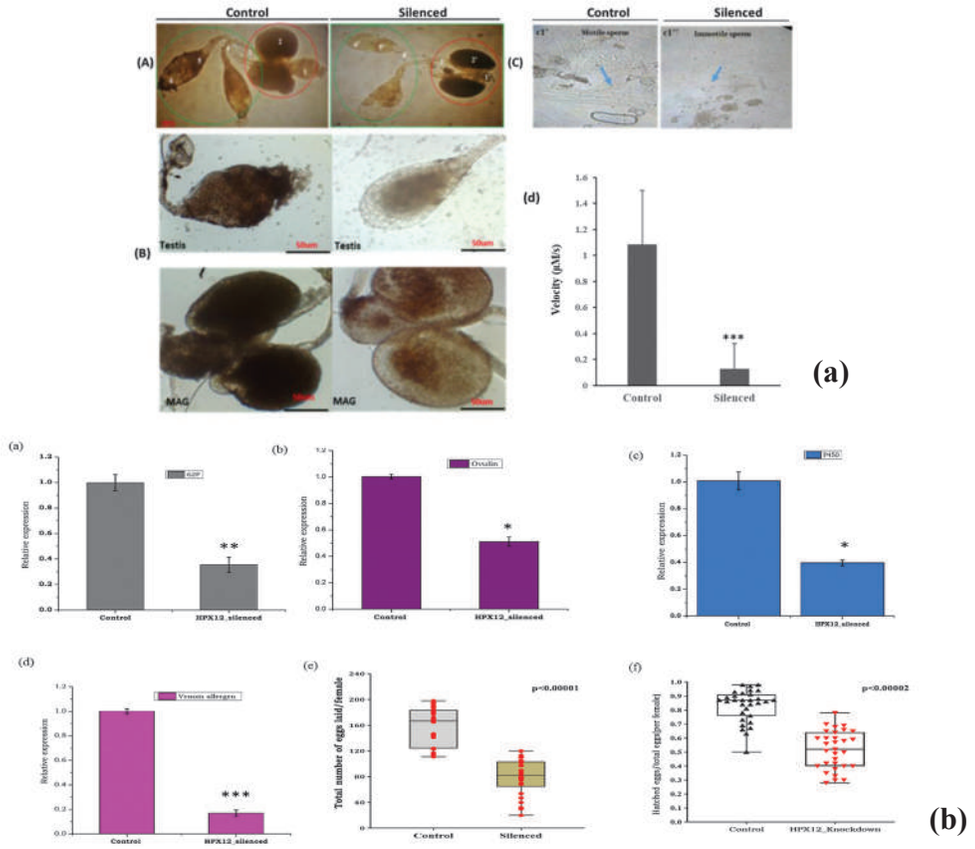


Fig. 20: Impact of KO (silencing) of HPX12 on (a) *MRO* cellular structure and sperm motility; (b) Male fertility (Kumari et al., 2022; Scientific Report).

Studies on bionomics of *An. culicifacies* in relation to transmission of malaria and its control/elimination in western Rajasthan

Training was done for vector bionomics and two entomological surveys were conducted during post monsoon and winter in districts i.e. Barmer and Bikaner for species composition, vector density, Adult resting habitats, biting behaviour, susceptibility to the insecticides. During two entomological surveys a total of 8 species of mosquitoes were collected in the survey of which six were anopheles species i.e., *An. culicifacies, An. stephensi, An. subpictus, An. annularis, An. pulcherrimus,* and *An. tessellatus.*In the Barmer district, MHD of *An. culicifacies* ranged between 0 and 18 in the winter season, whereas ranged between 0 and 3 in summer and between 0 and 18 in the monsoon season (Fig. 21, 22). Parity rates were about 0.71 in Bikaner and 0.93 in Barmer districts. For Blood meal analysisDNA isolation was done for PCR. The insecticide sustainability bioassay of adult *An. culicifacies* shows that resistance for DDT and malathion in Barmer, However, they were found susceptible to Alphacypermethrin and Deltamethrin.

Fig. 21: Light trap collection in Bolasar.

Fig. 22: Human Landing collection Diyatra.

Transmission of Malaria during Pilgrimage Walks in Western Rajasthan

In the first year, the study was initiated during the Mela season only, about 213 pilgrim walkers were screened (48 at Sanchore, 47 at Jahalwar, 62 at Bikaner, and 56 at Ramdevra) due to early called-off of Mela by the Rajasthan Government due COVID-19 (Fig. 23). Among these 213 pilgrims, one pilgrim from Ahmedabad was found positive (Pv) for malaria through RDT at the Sanchore entry point. In enrouted villages, random blood screening for adults was conducted to find malaria cases, if any. The total slides collected were 334 slides in post-monsoon, and 442 in pre-monsoon from these villages and no case was found positive for malaria. *An. stephensi* and *An. culicifacies* were the most prevalent species at all enrouted villages. *An.stephensi* was found to be in high density (PMHD 22.7) in Makhipura Jhalawar enrouted village. The mosquito PCR is under process for infectivity rate estimation. During the mela season, in Sanchore entry point night halting Camp, *An. stephensi* was most abundant species.

Fig. 23: Walking pilgrims of Ramdevra, and collection of blood slides in western Rajasthan.

ICMR-VECTOR CONTROL RESEARCH CENTRE (ICMR-VCRC), PUDUCHERRY

LYMPHATIC FILARIASIS

Development of monitoring and evaluation protocol for accelerated MDA with IDA (Ivermectin, Diethylcarbamazine and Albendazole) for lymphatic filariasis elimination programme

This study was undertaken to develop an appropriate monitoring and evaluation (M&E) protocol to make a decision for stopping mass drug administration (MDA) with Ivermectin, DEC and Albendazole (IDA)by generating evidence base to identify appropriate infection indicator(s) and target population. Following the Phase I study (i.e., baseline survey prior to MDA), follow-up assessment post 2 rounds of MDA in Yadgir (Phase – II) was carried out. While a significant reduction in circulating filarial antigen (CFA) prevalence was

observed among children (48%) and adults (24%), no such reduction was observed in microfilaria (Mf) prevalence. Vector infection also reduced by 49% following 2 rounds of MDA compared to baseline. Currently follow-up survey in Simdega post 3rd round of MDA is in progress.

Fig. 24: School Survey.

Long term changes in filarial infection status among a cohort of individuals treated with IDA in selected villages in Yadgir district of Karnataka

Fig. 25: Night Blood Survey.

In a longitudinal follow-up study carried out in the six villages in Yadgir district of Karnataka, cohorts of individuals with known status of filarial infection detected in a community trial conducted by ICMR-VCRC between 2016-2018 were selected for the follow-up assessment of infection in 2021. Following the trial, these villages received annual rounds of MDA (DA (Diethylcarbamazine and Albendazole) or IDA) under the National Filariasis Elimination Programme between 2019-2021. A total of 763 circulating filarial antigen (CFA) positive individuals and 582 individuals without any evidence of CFA and Ab were retested for CFA, Mf and Ab. Preliminary analysis showed an overall CFA clearance rate of 38.4% irrespective of drug combinations. CFA clearance rate and Mf clearance rate were comparable between DA and IDA irrespective of doses (P>0.05). The overall incidence of infection with CFA was 2.2%.

Application of Artificial Intelligence (AI) for the rapid screening of the blood smears in Lymphatic Filariasis Elimination programme

Currently, though filarial antigens or antibodies are considered markers for the presence of active infection and exposure respectively, blood smear microscopy for the detection of Mf continues to be method for assessing the transmission in the communities by the programme. In order to reduce the burden of slide examination using a microscope, an automated system based on artificial intelligence (AI) algorithm combining image processing and convolution neural networks was developed to pick up the Mf positive slides and tested against the conventional Mf slide examination method as the gold standard. The AI method developed for screening of Mf slides had only a sensitivity of 71% and a specificity of 59% indicating that the AI algorithm needs to be improved to have much higher sensitivity and specificity in screening/ identifying positive slides.

MALARIA

Tracking the elimination of malaria in Odisha State: Evidence to corroborate the decline of malaria to the status of zero transmission

To track malaria elimination by corroborating the entomological, parasitological, sociological and economic indicators over the years, a study is in progress in 11 southern districts of Odisha state. A total of 2143 mosquitoes belonging to *Anophelines* (n= 2077, 96.9%) and*Culicines* (n=66, 3.1%) were collected. Fourteen species of *Anophelines* were

recorded.Per man hour density (PMD) of *An. fluviatilis* in human dwellings was zero in eleven districts. The proportion parous for *An. fluviatilis* was zero in two districts (Bolangir and Nuapada). The overall net usage rate in the 11 districts was 87.3%. The study is in progress.

Phase III evaluation of three formulations of Natular (20.6% EC, 2.5% G30 and 7.48% DT) against larvae of *Aedes aegypti*, *Anopheles stephensi* and two formulations (20.6% EC, 2.5% G30) against *Culexquinquefasciatus* in three eco-epidemiological settings in India

Trials against *Ae. aegypti*, against *An. stephensi and* against *Cx.quinquefasciatus* yielded >80% reduction in larval density in drains for three, two and five weeks respectively. The trial for the summer season to assess the effectiveness of the three formulations against three vector species is in progress.

LEISHMANIASIS

Entomological and epidemiological investigations on leishmaniasis among the tribal populations in the Western Ghats, Kerala

A total of 1720 tribal people from different tribal communities in Malappuram, Thrissur, Palakkad, Ernakulum, Kollam and Thiruvananthapuram districts were surveyed. Active CL (n=9) and VL (n=6) cases were recorded among suspected individuals from the Western Ghats region of Kerala. Entomological investigations revealed that a total of 2734 sandflies constituted more than 20 different species. *Phlebotomus argentipes* (50.65%) was identified to be the most predominant species followed by *Sergentomyia babu and Sergentomyiamonticola*. A total of 63 sandfly specimens were processed for blood meal analysis and found that *P. argentipes* prefers mammalian blood (82.54%)**.** In the xeno monitoring study, 518 specimen of *P. argentipes* (139 pools) were processed for assessment of natural infection with *Leishmania sp., and* none of them tested positive. The high prevalence of the vector species in the region warrants active xeno monitoring to predict the risk of the disease. It will also help to control the vector population.

Mathematical modelling: understanding and controlling the patterns of visceral leishmaniasis (VL) and transmission

Variety of Spatio-temporal models relating monthly VL incidence data at block level from two endemic states Bihar and Jharkhand with environmental and bioclimatic variables as predictors were fitted. The blockwise monthly VL incidence data along with covariates was spilt into two subsets of data covering 2013-2018 and 2019-2020 for training and testing the models. A total of 23 spatial, temporal and spatio-temporal models were fitted to the training data using the Integrated Nested Laplace Approximation (INLA) approach in R-software, flexible for describing the spatial heterogeneity, and temporal variations in VL incidence by selecting appropriate models for the space-time effects and their interactions. The results showed that the best model with lowest DIC (deviance information criterion) was the one that accounted for covariates along with space-time interactions (structured/unstructured) with Leroux CAR (LCAR) priors for the space and RW1 (random walk 1) for time.A model accounting for both spatial and temporal components with their interactions are able to describe block-level VL incidence in the states of Bihar and Jharkhand.

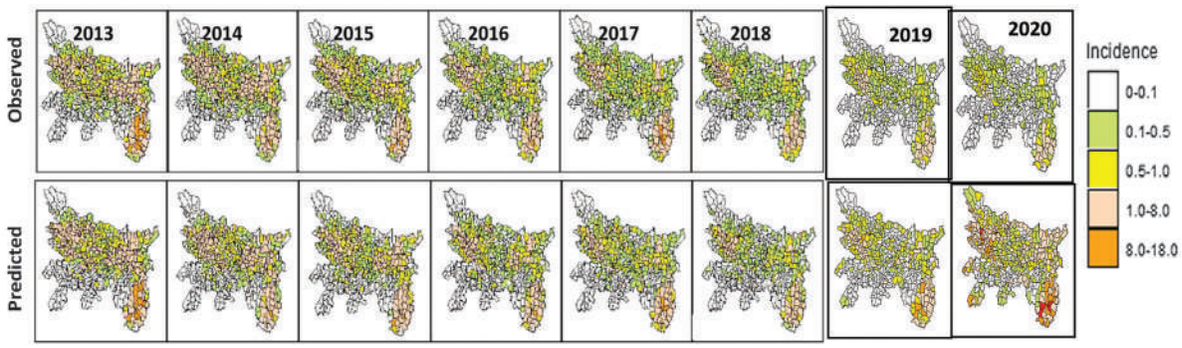


Fig. 26: Block-wise Observed and predicted VL cases in Bihar and Jharkhand.

DENGUE/ ZIKA/ CHIKUNGUNIYA

Prevalence of the natural Wolbachia infections in the wild populations of Aedes aegypti (Linn) mosquitoes from Tamil Nadu, South India

A study was undertaken to confirm the presence of Wolbachia and also estimate their density and prevalence in natural populations of *Aedes aegypti* from 3 different districts with varying endemicity. Screening for the presence of Wolbachia in mosquito samples collected from the Coimbatore district showed that Wolbachia was present in (15.1%) of the *Ae. aegypti* mosquito samples Screening for the presence of Wolbachia in the remaining samples is in progress.

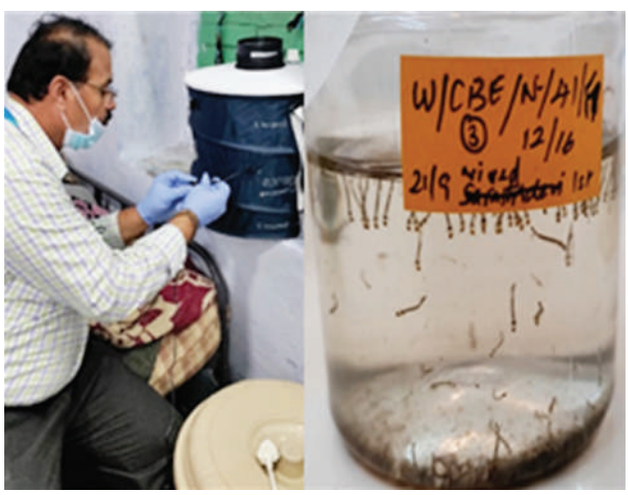


Fig. 27: Aedes mosquito collection.

Exploring potential application of plant lectins for detection of Dengue NS1 antigen

Lectin is a carbohydrate-binding protein or glycoprotein of nonimmune origin that specifically bind to carbohydrates of either mono or oligosaccharide structures. Since DENV-NS1 is a glycoprotein, lectin could be used for the detection of this protein antigen. Therefore, a study was carried out to screen the mannose-binding plant lectins that can specifically bind to DENV-NS1 antigen and for paving the way to use these plant lectins for the diagnosis of dengue virus in the patients' sera. Preliminary experiments show that plant lectins can be used for the detection of recombinant Dengue virus-2 NS1 antigen. However, the lectins will be further screened for detection of dengue NS1 antigen in DENV-infected patients.

Development of an eco-friendly mosquito larvicide for dengue/chikungunya vector control

Environmental risks due to the application of synthetic insecticides have encouraged the exploration of alternative toxicologically safe, eco-friendly larvicides using essential oil formulations. Preliminary results showed that 6 out of 9 essential oils were effective as larvicides in concentration <50ppm and 4 out of 21 binary combinations showed synergistic activity.

KYASANUR FOREST DISEASE (KFD)

Studies on the Spatial Biodiversity of Ixodidae ticks on Domestic animals in Tamil Nadu, India

To explore the spatial biodiversity of Ixodidae ticks, tick survey was completed in 70 villages in Seven

districts of Tamil Nadu (Cuddalore, Peramabalur, Kanyakumari, Tirunelveli, Krishnagiri, Erode and Ooty). A total of 3247 domestic animals were screened for Ticks. Twenty tick species have been reported in domestic animals of Tamil Nadu**.** *Haemaphysalisintermedia* was the predominant tick species. *Haemaphysalisdavisi* is being reported for the first time on the domestic animal in Tamil Nadu.

Mapping and risk assessment on KFD expansion in Western Ghats, India

With the KFD spreading to the newer areas in Western Ghats, with an aim to map the risk areas, locations from two grids out of the seven chosen grids covering the states of Karnataka, Goa, and Maharashtra, were visited and vector ticks were collected with permission from the health and forest departments. Species-wise, identification was made for all the selected samples. The approximate total number of ticks collected in Maharashtra-1591, Karnataka-1988 and Goa- 1164. It has been planned to finish collecting ticks and other parameters in the remaining five grids in Tamil Nadu, Kerala, and Karnataka in 2022.

SCRUB TYPHUS

In-silico prediction and in-vitro evaluation of diagnostic epitopes of outer membrane protein B (ompB) of *O. tsutsugamushi*

The study was planned for the in-silico identification of diagnostic epitopes from outer membrane protein B (ompB) of *Orientia tsutsugamushi* and in-vitro evaluation of the efficacy of the predicted epitopes to detect *Orientia tsutsugamushi* in rodents and vectors. 140 rodents/shrews were trapped, with ectoparasite infestation, observed in 82 animals. 1300 mites were identified based on the morpho-taxonomy. 71 sera samples of animals were positive for antibodies against *O. tsutsugamushi*. Two potential diagnostic epitopes were identified and they were further tested for their utility in developing a diagnostic tool for *O. tsutsugamushi*.

Development of a screening test for *Orientia tsutsugamushi* in rodents using recombinant 56KDa, omp A and Sca4 proteins

The study objectives were PCR amplification, cloning and expression of gene encoding 56KDA outer membrane protein B (ompB), Sca4 and ompA from local isolates of *Orientia tsutsugamushi*, along with in-vitro evaluation of their efficacy in detecting *Orientia tsutsugamushi*. In total 176 animals were trapped since January 2022. Screening of *Orientia tsutsugamushi* in the DNA samples was done by nested PCR targeting the 56KDa gene and by real-time PCR targeting the 47KDa gene. A total of 57 DNA samples extracted from blood were screened by both nested and real-time PCR. Four of them tested positive by nested PCR and three samples tested positive by real-time PCR. The PCR protocol for the amplification of the ompA gene is being standardized in the samples that tested positive for *Orientia tsutsugamushi* by nested PCR.

Study on the risk factors for acquiring Scrub Typhus, in Trivandrum district, in the endemic foci of Kerala

Scrub typhus is a rickettsial disease caused by *O. tsutsugamushi* and is transmitted to humans from the bite of larval trombiculid mite. Many outbreaks in the country have been reported so far. This study explores the association of socio-economic, behavioural and environmental risk factors for acquiring scrub typhus infection in Trivandrum district, Kerala. Results of the study indicate, the presence of domestic animals near the house and people living near thick vegetation & wet agricultural fields, not changing cloths after returning from work and disposal of food waste openly in the yard are found to be the high risk factors for getting Scrub typhus infection.

BIOLOGICAL CONTROL AGENTS

Characterization and evaluation of *Bacillus thuringiensis* (Bt) and *Lysinibacillussphaericus* (Ls) strains maintained in the Microbial Culture Collection Facility of ICMR-VCRC

This present study was carried out to perform a systematic characterization of 169 *Bt* and 108 *Ls* strains available in the MCCF at the ICMR-VCRC by different methods viz. morphological, biochemical, molecular methods, bioassay, etc to select the strains that could be used to develop novel mosquitocidal products. Results of the experiments showed that of the 169 *Bt* strains, 34 showed larvicidal activity comparable to VCRC B17, the Indian standard strain.

New bacterial agents for mosquito control: *Bacillus cereusVCRC 641* and *Bacillus mobilis VCRC-633*

Two indigenous bacterial isolates viz., *B. cereus* VCRC 641 and *B. mobilis* VCRC 633 were studied in the laboratory for their efficacy against larvae of disease transmitting mosquitoes of the genus *Culex, Anopheles and Aedes*. Larvae of *Culex quinquefasciatus*, *Anopheles stephensi* and *Aedes aegypti* are equally susceptible to both the microbial agents. The highly efficacious strains are presently formulated to study their efficacy under simulated field condition and the mosquitocidal effect was found to last for 3 weeks in the treated tanks when challenged with *Anopheles* larva.

OUTBREAK INVESTIGATIONS

Zika Virus outbreak in Thiruvananthapuram

An outbreak of ZIKV occurred in Thiruvananthapuram, the capital city of Kerala with 70 confirmed cases. Vector surveillance in the affected areas showed ZIKV transmission by at least three different species of *Aedes* mosquitoes: *Ae. albopictus, Ae. aegypti* and *Ae. vittatus.*

HUMAN RESOURCE DEVELOPMENT

Higher Education: M.Sc. Public Health Entomology (PHE) course

ICMR-VCRC enrolled 17 students under the M.Sc Public health entomology (PHE)course for the academic year 2021-22 as the eleventh batch and the stipend was also revised to Rs.20,000 from Rs.6000/-. For the meritorious students of M.Sc. Public Health Entomology, an internship programme is offered for a period of one year with a stipend of Rs.12,000/- (+) HRA per month per intern.

Expansion of M.Sc. PHE to other ICMR Institutes

In view of a growing demand of entomologists for effective implementation of global, national and regional programs for the prevention, control and elimination of vector borne diseases (VBDs), the ICMR has introduced the National Public Health Entomology (NPHE) Programme. The ICMR-VCRC, Puducherry has been assigned to take a lead role and facilitate in replicating it's M.Sc. PHE course in four other ICMR institutes, viz., ICMR-RMRCNE, Dibrugarh, ICMR-RMRCGKP, Gorakhpur, ICMR-NIRTH, Jabalpur, and ICMR-RMRIMS, Patna, where vectors and vector borne disease research studies are undertaken.

Ph.D. Programmes

Currently in ICMR-VCRC,31 Scholars are pursuing PhD Programmes in Microbiology, Zoology, Chemistry and Medical Entomology. One research scholar was awarded Ph.D. in Microbiology) in February 2022.

Training on Vector Borne Disease epidemiology and control

Visitors from different Institutes of Tamil Nadu and Puducherry visited (N=268) ICMR-VCRC for orientation and exposure to various ongoing programmes of the Centre. Postgraduate students and Research Scholars from nine Institutions have been offered hands-on/observational training. Students have also been offered guidance and facilities to pursue their Internship/Master's thesis work from other universities/Colleges.

FACILITY PROVIDED

Filariasis clinic

VCRC offers Morbidity Management and Disability Prevention (MMDP) services to 619 lymphoedema

patients from Puducherry and Tamil Nadu. As MMDP services are an exclusive component of the VCRC clinic, other teaching institutes refer cases for clinical evaluation and further management. Video regarding MMDP is displayed on smart TV as an educational tool for the patients. A training program on limb hygiene is organized for patients and their relatives who attend the MMDP clinic for the first time.

Animal House

The laboratory animal house facility is registered with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment, Forests and Climate Change, Government of India (Reg. No. 89/GO/ReBi/S/99/CPCSEA). This facility breeds colonies of BALB/c mice (*Musmusculus*), Swiss Albino mice (*Musmusculus*), Mongolian gerbils (*Merionesunguiculatus*), multimammate rats (*Mastomyscoucha*) and rabbits (*Oryctolagus cuniculus*). These species are used for various research studies with approval from the Institutional Animal Ethics Committee (IAEC).

PATENT

1. A Process for the preparation of a fibrinolytic enzyme. Indian Patent No 391961/2022.

2. Improved process for the production of Cyclosporin-A using the fungus Tolypocladium sp. strain NRRL No: 18950. Indian Patent No. 344829/2021.

Fig. 28: Joint Dengue control activities by State programme and ICMR-VCRC.

Fig. 29: Fit India Freedom Run 2.0 at ICMR-VCRC.

ICMR-NATIONAL AIDS RESEARCH INSTITUTE (ICMR-NARI), PUNE

SIGNIFICANT PROJECTS

- **Clinical trial for COVID-19 treatment**: ICMR NARI served as national coordinating unit for an international multicentric randomized clinical trial of additional treatments for COVID-19 in hospitalized patients (WHO-ICMR-Solidarity Trial) in India. The findings from this trial have been published in New England Journal of Medicine and The Lancet. The trial continues with revised treatment options, the trial is continued at 13 sites from 8 states, however randomization has slowed due to fall in COVID-19 hospitalization.

- **Clinical trial for COVID-19 Vaccine immunogenicity**: A phase 2/3, multicentric study randomized controlled, was implemented to determine the safety and immunogenicity of COVOVAX [SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) with Matrix-M1TM Adjuvant] in Indian adults. An interim clinical study report has been prepared and submitted to DCGI and WHO. Emergency use authorization for vaccination in adults was accorded to COVOVAX by WHO and DCGI in India.

- Testing of NFHS-5 samples to determine the regional prevalence of Diabetes Mellitus and Vitamin D deficiency among adults in the reproductive age group in India is ongoing as part of ICMR-IIPS collaboration. Around 82604 DBS samples were received acrossthe country and are being tested.
- Improved tests for monitoring of response to anti-tuberculosis treatment (ATT) in HIV/ TB co-infected patients were evaluated in collaboration with the Research Institute of Health and Welfare, Kibi International University, Japan. Levels of Matricellular proteins and other inflammatory markers were estimated for their possible use for monitoring response to anti-tuberculosis treatment. The levels of osteopontin and Galactin 9 were found to be significantly reduced at the end of antituberculosis treatment, suggesting their possible role in the overall monitoring of response to ATT.
- Assessment of Air borne Infection Control (AIC) measures and facilitation of Health Care Workers (HCWs) screening for TB was carried out at 95 HIV care settings from 36 districts in 14 states in India. Post-assessment debriefing meetings were conducted with each participating site.
- **India Hypertension Control Initiative (IHCI)**: ICMR NARI is one of the participating sites in a national study for the implementation cum research project in the states of Maharashtra and Goa. In Maharashtra, the project spans to 13 districts and municipal corporations.
- **A state of art biorepository facility** matching international norms has been created at the institute to store the valuable biological samples from different sites across the nation under Cohort of HIV Resistance and Progression in Indian Children and Adults (CoHRPICA) project.The samples are from the different study cohorts such as HIV infected and exposed but uninfected study participants. A well characterized sample repository with all clinical data which may act as valuable resource for future studies in India and will be made accessible to the researcher across the nation.
- Galectin 9 levels were evaluated in HIV infected patients on anti-retroviral treatment (ART) as a surrogate marker of viraemia. Findings showed that testing plasma Galectin level in combination with other markers can be used as a cost effective tool to monitor virologic failures among PLHIV on ART.
- **A case control study to determine factors influencing epigenetic aging in HIV infection** was initiated. Enrolment and sample collection of the aging population could be successfully achieved and the laboratory investigations to determine effect on epigenetic age reversal are ongoing.
- Role of innate immune modulators such as Toll- like receptors (TLR) were examined to reactivate the latently infected cells during HIV infection. Two TLR agonists- TLR-7 and -9 were found to increase the reactivation of latently infected T cells when used in combination with other latency reversing agents such as Bryostatin + Romidepsin.
- Role of microRNAs in liver disease progression in HIV/HCV co-infected individuals was examined. In HIV/HCV co-infected individuals' differential expression of circulatory microRNAs have been identified as novel biomarker of liver fibrosis.
- RNA interference technology has the potential in alleviating HIV replication and the same is investigated against the HIV nef gene. The modulation in the gene expression profile was observed in an *in-vitro* study and found to be useful along with the use of ART.
- **ICMR capacity building project for disease burden estimation and projection (Global burden of Diseases study;GBD)**: Selected scientists and statisticians are undergoing training for GBD methodology and state level disease burden estimation and projection in the form of this research project by Evidence for

Policy Cell at ICMR

EARLY STAGE PROJECTS

- Factors associated with diabetes control and adherence to anti-diabetic medications among people living with HIV and diabetes attending ART centers in Pune, India - a mixed methods study
- Prevalence of selected sexually transmitted infections/reproductive tract infections among subpopulations at high risk of HIV in India: Female Sex Workers (FSW), Men having Sex with Men (MSM), Intravenous Drug Users (IDU) and Migrants
- Anti-retrovirals to prevent HIV acquisition among MSM and transgender (TG) in India: A demonstration project to study the feasibility of Oral tenofovir (TDF)-containing PrEP, administered, once-daily orally to MSM and TG is being implemented in India
- Depression and Anxiety before and after initiation of Dolutegravir based ART regimen among people living with HIV under the national AIDS control programme in Pune
- Social and sexual problems in sexual minority women, and its effect on health: An exploratory study
- Factors Related to COVID-19 Stigma: A mixed methods study mental health and stigma sub group of the ICMR National Task Force on OR/IR in COVID-19
- Role of Network Dynamics among People who inject drugs (PWID) in HIV transmission and access to services in India: a multi-centric study
- Understanding antiretroviral drug resistance and HIV genotypes among HIV infected female sex workers and people who inject drugs in Mizoram
- A phase III, randomized, double-blind controlled trial to evaluate the efficacy and safety of two vaccines VPM1002 and Immuvac(Mw) in preventing tuberculosis (TB) in healthy household contacts (HHC) of newly diagnosed sputum positive pulmonary TB Patients
- Institute is participating in Phase III, multi-country, open labelled, randomized, controlled trials to evaluate efficacy and safety of combinations of new and repurposed drugs against multi-drug resistant (MDR) TB.
- Host-pathogen interactions of HIV and associated common opportunistic infections: identification of important therapeutic targets and their modulators
- Evaluation of antibody-dependent cellular cytotoxicity (ADCC) and antibody dependent enhancement (ADE) responses against SARS CoV-2 infection.
- Study of genetic variation and expression of drug metabolizing enzyme, transporter and Apolipoprotein genes between TDF and TAF -related renal dysfunction among patients of HIV - hepatitis B co-infection
- Comparative analysis of genetic variation and expression of Apo family of lipoprotein, lipid metabolizing enzyme and transporter genes between HIV-associated lipodystrophy patients taking PIs with and without the history of receiving stavudine or zidovudine based regimen.
- Study of genital Human papillomavirus infection in men: type-specific distribution, risk determinants and natural history
- Investigation of the Efficiency of microRNA (miRNA) Loaded Nanoparticles in the Inflammasome-Mediated Extenuation of HSV-2 Pathogenesis
- Exploration of Ayurveda-based Rasayana Botanicals for Biological Synthesis of Nanoparticles and its Application as HIV-1 Inhibitors Through in vitro Studies miRNA Loaded Nanoparticles: Investigation and Validation of Targeted miRNA Delivery as A Prospective Antiviral Approach Against HSV-2 Infection
- Elucidation of the miRNA-mediated Interferon

modulations during early HSV-2 infection

- Investigating the interaction between SARS-CoV-2 Nsp13 and cellular ALIX protein.

PUBLIC HEALTH

- WHO-ICMR-Solidarity trial highlighted little/ no effect of remdesivir, hydroxychloroquine, lopinavir and interferon regimes on hospitalized patients with COVID-19. These findings formed the basis for revised clinical management guidelines for COVID-19.
- ICMR NARI served as national coordinating unit for an international multicentric randomized clinical trial of additional treatments for COVID-19 in hospitalized patients (WHO-ICMR-Solidarity Trial) in India. The findings from this trial have been published in New England Journal of Medicine and The Lancet. The trial continues with revised treatment options, the trial is continued at 13 sites from 8 states, however randomization has slowed due to fall in COVID-19 hospitalization.
- Study for detection of anti-SARS-COV-2 IgG antibodies among unvaccinated HIV-infected individuals (PLHIV) attending ART Centre showed an estimated seroprevalence of 54.6% in unvaccinated, asymptomatic PLHIV. These finding highlight the need of COVID-19 vaccination among this vulnerable group.
- Messages related to COIVD appropriate behavior were given to the clinic attendees through innovative approaches during the period of this study. (Fig. 30)

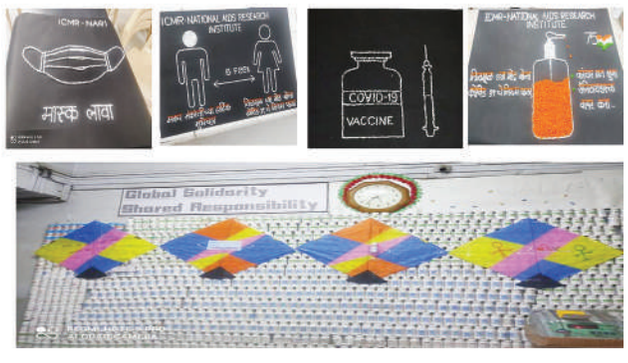


Fig. 30: Dissemination of COVID appropriate behavior messages in local languages on the occasion of 'Makar Sankranti' at ICMR-NARI ART centre.

- The diagnostic utility of self-collected oral swab specimen as an alternative to nasopharyngeal swab specimen for SARS CoV-2 diagnosis was evaluated. Oral swabs were found convenient and useful for SARS-CoV-2 antigen detection among symptomatic individuals residing in remote rural areas and can serve as an initial screening tool during COVID-19 spikes when cases rise exponentially and laboratory capacities for RT-PCR testing become overwhelmed.
- ICMR NARI contributed to the population-based COVID serosurvey crucial to estimate prevalence of SARS-CoV-2 antibodies in India. These estimates were subsequently formed the base for policy decisions for national and local COVID-19 pandemic control and prevention guidelines.
- Impact of Anti-retroviral therapy (ART) under National AIDS Control Programme (NACP) was evaluated and ART programme was found to be cost-effective. Topline findings of the study have been released(Fig. 31).

Fig. 31: Release of key findings of the Impact evaluation study by Secretary DHR, DG ICMR & Additional Secretary & DG, NACO at ICMR.

- Estimating Incremental Cost of treating Antimicrobial Resistant infections in India. The findings from this study have revealed that presence of any of the critical or high priority pathogens leads to increase in the direct medical cost. The incremental cost varies with the type of hospital, Length of Stay (LOS), type of pathogen, comorbidities with underlying pathology and the final diagnosis.

- Finding from RCT to evaluate anti-bacterial activity, pharmacokinetics, safety and tolerability of Metformin suggest that addition of metformin to standard ATT did not hasten sputum culture conversion but diminished excess lung inflammation among newly diagnosed sputum positive pulmonary tuberculosis cases. Hence addition of Met in ATT can be useful in improving post-treatment quality of life of TB patients.
- Findings from 'Social drivers of acceptance and rejection of protective measures against covid-19 infection in the community' indicated that lower knowledge score and having no source of income were independently associated with the risk of not following COVID-19 preventive behaviors among the rural communities.
- Experiential learning-based community engagement tools were developed which will be useful for enhancing the research literacy and participation of rural population in HIV biomedical research in Maharashtra.
- National survey for the state-wise prevalence of microbiologically confirmed pulmonary tuberculosis was conducted in Maharashtra and Goa by ICMR-NARI which provided evidence for effective planning of prevention and control strategies in these states.
- Diagnostic utility of self-collected buccal swab specimen as an alternative to sputum for molecular detection of pulmonary tuberculosis. The final report has been submitted to CTD, New Delhi.
- Seroprevalence of Hepatitis B virus (HBV) and Hepatitis C virus (HCV) among High-Risk Groups and Bridge Population in India was estimated at regional and national level which resulted in evidence-based planning for the National Viral Hepatitis Control Programme (NVHCP) in India.
- ADCC mediating antibodies having an ability to eliminate the reactivated latent HIV reservoirs were successfully generated from the memory B cells of HIV infected Long Term Non Progressors (LTNPs). These antibodies can be used as a potential immune therapeutic strategy for targeting HIV reservoir.
- Reproductive and sexual health needs and access to related healthcare facilities among female sex workers were assessed in selected blocks of rural and urban Maharashtra. Findings highlighted the opportunities to explore how pregnancy prevention and pregnancy testing services and elements of reproductive health services can be integrated within existing HIV Targeted Intervention programs.

SUPPORT TO NATIONAL PROGRAMS

- Integrated and Enhanced Surveillance & Epidemiology (IESE) activities for HIV, STIs and related co-morbidities under the National AIDS and STD control Programme (NACP) Phase-V: ICMR-NARI has developed operational plans for STI surveillance
- ICMR-NARI is a regional institute for HIV sentinel surveillance (HSS) for Western region (Maharashtra (Mumbai), Madhya Pradesh, Rajasthan, Goa, Gujarat, Dadra and Nagar Haveli and Daman and Diu). HSS Plus has covered 203 ANC (tertiary & district hospital) sites, 14 Central Prison sites, 81 HRG and 16 Bridge population targeted intervention sites.
- External quality assurance (EQA) programme for CD4 count estimation and HIV serology: Two rounds of the EQA for HIV serology were provided to all NRLS, SRLs. One round of CD4 EQAS was done and more than 350 centers participated in the round of which 75% centers showed successful performance.
- Consortium for kit quality: The HIV, HBV and HCV diagnostic kits were evaluated through this consortium. This is a self-sustained activity. In the reporting year 48 kits were evaluated by the consortium.
- HIV-1 Viral Load Testing: ICMR-NARI is the Apex Laboratory for Plasma HIV-1 viral load testing support to NACO ART program.

5 ARTCs are linked to the ICMR-NARI VL Laboratory with the patients load of 18995 PLHIV cases. During April 2021 to March 2022, 4425 samples were tested for HIV-1 viral load.

- HIV-1 Viral Load Proficiency Testing: Under the Apex laboratory activities, ICMR-NARI conducts the biannual quality assurance monitoring of 64 NACO public sector laboratories all over India.
- Testing of SARS-CoV-2 samples: in response to COVID-19 pandemic, ICMR NARI served as one of the diagnostic facilities for SARS-CoV-2 testing. The institute also validated various commercial RT-PCR and serological kits.
- The key achievements of ICMR-NARI were communicated through 'Knowledge sharing workshop' to National media health journalists on 31st March 2022.

ICMR-NATIONAL INSTITUTE OF RESEARCH IN TRIBAL HEALTH (ICMR- NIRTH), JABALPUR

A pilot demonstration project for reduction of tuberculosis in Saharia Tribe

Various rounds of IEC activities were conducted and orientation programme were organized for 922 community persons (Sarpanch, ASHA, ANM, CHOs and MPWs). A totalof145campswereorganized at different sub-centers of Sheopur, Karhal, and Vijaypur block which covered 497 villages. During the camp, a total of 2380 presumptive TB cases were screened, out of which a total of 1821 X-rays and1526 sputum (on spot samples) were collected for further diagnosis. Of which a total of 153 patients were microbiologically confirmed for m.*tb*. X-Ray screening for TB resulted in 179 positive cases. Treatment of 144 patients have been initiated as per national guidelines. Contact screening has been done for all the identified cases. X-ray screening of 289 contacts and sputum testing on 149 contacts were performed. No positive *M. Tb* was found in 301 contacts. TPT hasbeenstartedfor217contacts. RUTF has been given to 93 patients who are under BMI of 18.5 kg/m^2.

Fig. 32: IEC Activities.

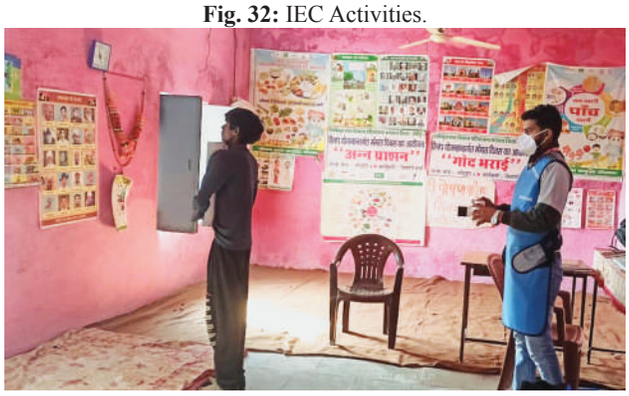


Fig. 33: Chest Xray using Hand-held Xray Device.

Assessment of neonatal screening approaches for sickle cell disease and the effect of early intervention in management of the disease in tribal population

During the report period 3397 new born babies have been tested for various hemoglobinopathies, among them 223 were found to be Sickle Cell carriers, 14 were homozygous for Sickle Cell Disease and 4 were sickle β-thalassemia (SBT) and 2 newborns were identified to be β-thalassemia carrier.

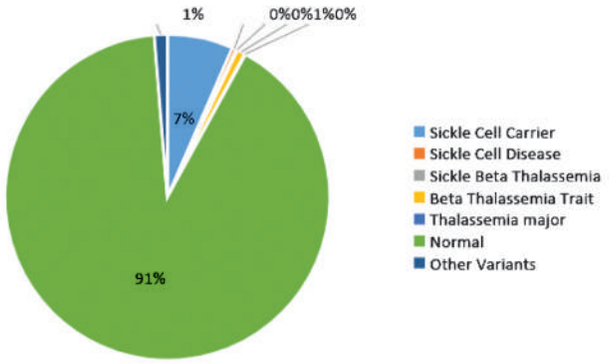


Fig. 34: Overview of hemoglobinopathies status among new born screened in Madhya Pradesh.

Improving the Health Care Access for Achieving Universal Health Coverage (UHC) among Scheduled Tribes: An Implementation Research in Saharias of Sheopur and Shivpuri districts of M.P.

Under Quantitative Household Survey a total of 2040 household of 40 selected villages were surveyed falling under 4-PHC/CHC. In Qualitative survey, 91 outpatients and 48 in-patients were covered under Exit Interview Survey and for Health Facility Survey 21 (4-PHC/CHC,4-SHC and 13 HWC) health centers were covered along with 78-IDIs & 12- FGDs was conducted. The data was analyzed and has identified three potential gaps-increasing institutional delivery, optimizing the services of Health & Wellness Centers and reducing the TB cases. Most (81%) of the child birth was found normal whereas, home delivery (53%) was found higher than hospital delivery (47%). Overall, about 18.7% individuals had at least one episode of hospitalization among the studied population (9,210).

Impact of new, one-minute, sensitive diagnostic with innovative malaria elimination plan

The study was conducted at three different study sites in Sheopur (M.P.), Kotra (Rajasthan) and Jagdalpur (CG). After the screening of about 20,000 fever cases, a total of 3000 volunteers were enrolled for the study at three study sites. A total of 600 samples (Kotra (11%), Sheopur (10%) and Jagdalpur (35.3%)) were found malaria positive by microscopy and RDT. Further, analysis of all 3000 samples by PCR has revealed positive cases of *P.falciparum* (25%), P. *vivax* (5.3%), *P. malarie* (0.1%), Pf+Pv (4.5%), other mixed (0.9%) infections. The performance of the device was found at par with RDT but below PCR. Further, the results of the study show that the differentiation of *P.falciparum* and *P. vivax* are possible on the basis of hemozoin.

Efficacy and safety of ACT for the treatment of uncomplicated Plasmodium falciparum in India in Madhya Pradesh and Rajasthan

A total of about 1600 febrile patients were screened in Udaipur, Rajasthan and Sheopur, Madhya Pradesh. Therapeutic efficacy was determined in 98.7% patients who had completed their 28 days follow-up while one patient withdrew from the study. Adequate clinical and parasitological response (ACPR) was observed in 100% of cases. Neither early treatment failure (ETF) nor late clinical failure (LCF) was observed in this study. Also, in most of the patients (96.3%) parasitaemia was cleared within ≥72hrs.

Tracking antimicrobial resistance and efficiency of malaria diagnostics in tribal areas of India to achieve elimination goals

The aim of the project is to develop a surveillance and intelligence system for antimalarial-drug resistance, diagnostics efficiency, and disease transmission based on molecular/genetic information. Microscopic analysis showed that 88% cases were caused by *P. falciparum*, followed by *P. vivax* (12.8%) and mixed infections (1.4%). The samples have been transported from Jagdalpur to ICMR-NIRTH Jabalpur. The molecular analysis of samples is going on at ICMR-NIRTH Jabalpur. A multimodal stratagem was designed to identify approved drugs with a potential antimalarial activity using computational drug reprofiling. Oxetacaine, Simvastatin, Repaglinide, Aclidinium, Propafenone, and Lovastatin could be repurposed for malaria control and prevention. Moreover, Molecular analysis and mathematical modelling is going on.

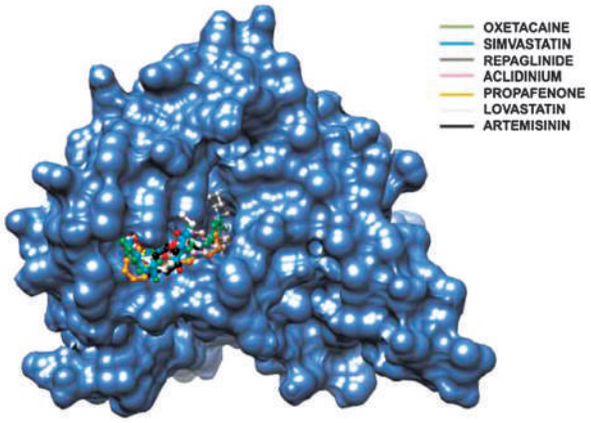


Fig. 35: Docked complex structure of top six compounds in the binding pocket of PfPI3K.

Metabolic syndrome among three PVTGs of Central India

The aim of the study is to estimate the prevalence of metabolic syndrome among adults of three PVTGs populations of Madhya Pradesh and Chhattisgarh of Central India. A total of 726 participants of Baiga PVTG from the Dindori district taken for analysis. Of the total respondents 13.2% were found with Metabolic syndrome according to NCEP ATP III criteria. The individuals with only dyslipidaemia, only diabetes, and with only hypertension, and with diabetes and hypertension simultaneously is a significant number which indicates emerging conditions of non-communicable diseases in Baiga tribes of the Dindori district.

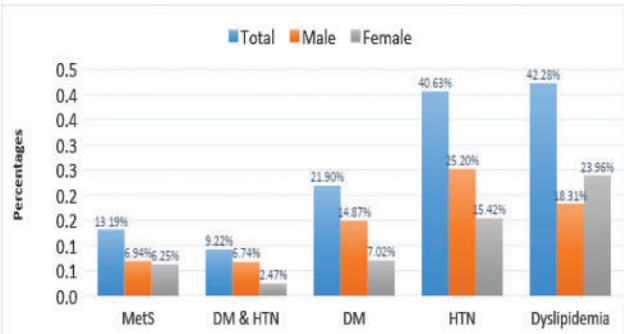


Fig. 36: Prevalence of MetS, DM & HTN, DM, HTN, and Dyslipidemia in Baiga tribe of Dindori District.

Understanding the perspective and coping strategy for recently emerged COVID-19: An exploratory study in tribal population of Himachal Pradesh and Madhya Pradesh

The awareness of COVID-19 was better in Lahaul & Spiti. It was observed that Scheduled tribes (88%) were lesser aware of COVID-19 symptoms compared to other social groups. About 76% of the respondents reported to have knowledge about the place of diagnosis and treatment for COVID-19 infection. Sanitizer was reported by 54% of the respondents. Around 85% of the respondents mentioned that they use face mask regularly. Use of disposable mask was reported by 28% of the respondents. Fifty one percent reported to maintain social distancing. About one-fourth expressed that pandemic has no impact on the employment status. Overall, 47% reported viewing of television, followed by involving in music, dance, and other cultural activities (44%) during lockdown period to cope up with the stress. To cope up with the economic crisis they mainly used their personal savings (62%), borrowing loan from relatives (11%); friends (10%); neighbors (8%) and availing government economic development scheme (18%). Almost all the respondents (95%) were aware of existence of COVID-19 vaccine. Stigma and discrimination related to COVID-19 do exist in these tribal areas. Further, there existed misconception related to ideology of transmission of the infection in the tribal areas.

Development of isothermal amplification-based rapid and sensitive colorimetric diagnostic test for leprosy bacilli

A simple isothermal amplification assay was developed using RPA targeting conserved region of a multicopy repeats in the genome of leprosy bacillus *M. leprae*. This assay can be performed at 39°C in 15-30 min and successful amplification can be visually detected.

PUBLIC HEALTH

- **Control and management of TB among Saharia:** ICMR-NIRTH, Jabalpur continued its intensified tuberculosis control programme among Saharia PVTG of M.P. where there is high prevalence of TB. Total of 8797 cases were detected through active case detection

and put on treatment through the project. The success rate for treatment was more than 90% and the notification of cases increased more than 4 times as compared to NTEP in the area. This year the endline survey for the project was carried out across seven districts. The baseline prevalence for pulmonary TB was 1,357 per 1,00,000 population while the endline prevalence was 752 per 1,00,000 showing a significant decrease in prevalence.

- **Mental Health and Social Stigma Among Healthcare Personnel Involved in The Management of Covid-19 Patients in India:** The study demonstrates the psychological burden of HCWs engaged with COVID-19 care services. The study findings point to need-based psychosocial interventions at the organizational, societal and individual levels. This includes a conducive working environment involving periodic evaluation of the HCW problems, rotation of workforce by engaging more staff, debunking of false information, community and HCW involvement in COVID sensitization to allay fears and prevent stigma associated with COVID-19 infection/transmission and finally need-based psychological support for them and their families.
- **The effect of Hydroxyurea on the clinical profile of Sickle Cell Disease patients in Central India:** A total of 453 SCD patients have received hydroxyurea. Fetal hemoglobin was found to be increased in more than 80% of cases. Severity index of the disease was significantly decreased with continuous usage of Hydroxyurea.
- **India Hypertension Control Initiative:** A total of 2,36,936 patients have been registered under India Hypertension Control Initiative in Madhya Pradesh. The blood pressure control has improved from 25.7% in March 2021 to 49.4% in March 2022. Missed visit also significantly reduced from 45.2% in March 2021 to 16.6% in March 2022.
- **Organised a Webinar on "Sickle Cell Disease: Global Perspective and Indian Scenario":** More than 400 participants have attended the webinar. Various International and National faculties have given lecture in the webinar.
- A **policy brief** for the control of tuberculosis in Saharia tribe.
- The Hon'ble Governor of Madhya Pradesh, Shri Mangu Bahi Patel had visited ICMR-NIRTH on 08 December 2021 for taking overview on the research activities on the Sickle Cell Disease of the institute and inaugurating the Apex laboratory for hemoglobinopathies.

Fig. 37: The Hon'ble Governor of Madhya Pradesh, Shri Mangu Bahi Patel inaugurating the Apex laboratory for hemoglobinopathies.

ICMR- RAJENDRA MEMORIAL RESEARCH INSTITUTE OF MEDICAL SCIENCES (RMRIMS), PATNA

MAJOR PROJECTS

Efficacy and safety of short course combination regimens of Liposmal Amphotericin B and Miltefosine for treatment of PKDL

Under this DNDi sponsored multi-centric study, altogether 126 PKDL confirmed cases were

enrolled and randomized in two arms (63 in each). Treatment regimen for arm-1 was AmBisome monotherapy (5x4 mg/kg IV twice a week at a total dose of 20 mg/kg). Patients in arm-2 were given combination therapy of AmBisome (dose similar to arm-1) followed by allometric oral dose of miltefsoine for three weeks. Post-treatment follow up was made up to 2 years. Overall, treatment was well-tolerated; only one SAE with fatal outcome was observed, which was considered unrelated to the study drug. PK analysis in skin and blood, host immune response and parasite clearance by microscopy and PCR were performed. Followed by complete data analysis, this short course combination therapy for PKDL will be shared to the National Control Program.

A phase 2/3, observer-blind, randomized, controlled study to determine the safety and immunogenicity of COVISHIELD (COVID-19 Vaccine) in healthy Indian Adults

This ICMR-SII sponsored multi-centric vaccine trial was started during the COVID-19 pandemic wherein ICMR-RMRIMS, Patna participated for safety cohort study. Out of 73 subjects screened for eligibility criteria, 48 were blindly randomized through eMedidata software either to COVISHIELD or Placebo arm. Each enrolled subjects were injected 0.5 ml of COVISHIELD/ Placebo (as per arm) at Day 1 and Day 29 and were followed up at scheduled time points D-56, D-90 and D-180. No AE/ SAE were reported at this site. All the data were fed online through EDC for data analysis and interpretation. COVISHIELD was found to be safe and well-tolerated in adults above 18 years of age.

Drug resistant mechanism in clinical isolates of *Leishmania donovani* and its pathogenic implications during visceral leishmaniasis

Drug sensitivity testing with Amphotericin B revealed that 9 out of 55 clinical isolates of *L. donovani* were having more than two folds of IC_{50} in comparison to the reference strain. The IC_{50} value of 6 isolates was even more than 4 fold higher in comparison to that of Ag83. IC_{90} was also correspondingly high. Three of these *L. donovani* isolates were also insusceptible to Miltefosine. The isolates showing cross resistance were also representing up-regulated ABC transporter and the susceptibility was restored upon treatment with Verapamil. Drug sensitivity testing of *L. donovani* may support in the choice of anti-leishmanial therapy.

Safety and efficacy of Fusion Protein Construct of ornithine decarboxylase, Protein di-sulphideisomerise and Cytosolic Trypa-redoxine (ODCYTPD) of *L.donovani* in a pre-clinical vaccine trial against Visceral Leishmaniasis

L. donovani ornithine decarboxylase (Ld-ODC) having vaccine potential also express IL-10, which prompted to explore the potential immunogenic epitopes to drive Th1 immune response. Total 23 peptides were shortlisted using 7 allele based IEDB web server employing 15mer MHC class II restricted epitopes. After BLASTp analysis against *Homo sapiens*, 13 epitopes were considered for further study. Notably, out of these shortlisted peptides, 3 were found potential to induce both humoral as well as cellular immune-response. After HLA diversity analysis, best 10 selected epitopes revealed a moderate to high stability with a good estimated half life. Chimeric vaccine construct was prepared by using EAAAK and GPGPG linker molecule. ***This information is being carried forward in another offshoot project.***

Potential inhibitors against CD-74 and IL-10/ IL-10R to block the host mediated immune suppression against visceral leishmaniasis

In-depth computational analysis revealed that the vital anti IL-10 peptide can partially inhibit the IL-10 activities. The initial observation suggested that use of anti-IL 10 antibody treatment enhances the candidate vaccine potential to trigger the immune cells. However, addition of recombinant IL-10 before vaccination has a minor effect on candidate vaccine potency. Use of anti-IL 10 peptide before

immunization enhanced M1 polarization of macrophages, thereby supporting the immune cell modulation with respect to the vaccine candidate. Further, in-silico analysis demonstrated that the chimeric vaccine construct with anti-IL10 peptide adjuvant can be effective in the development of vaccine candidate against visceral leishmaniasis.

Role of cysteine biosynthetic pathway of *L. donovani* in the parasite survival and drug resistance: A rational drug target

The role of serine-*o*-acetyltransferase (SAT), a cysteine biosynthetic pathway protein of *L. donovani* was demonstrated in parasite survival under oxidative and heavy metal stress conditions and its association with AmpB resistance and parasite infectivity. The heavy metal stress susceptibility of parasites to Arsenic trioxide (As_2O_3) & Cadmium chloride was determined. LdSAT-OE exhibited ~1.8 fold higher IC_{50} for As_2O_3 as compared to LdWT. *In vitro* assessment of J774A.1 macrophage revealed that LdSAT over-expression enhances the parasite infectivity (Fig. 38). Thus, the difference in drug sensitivity, heavy metal susceptibility and percentage infectivity of LdSAT-OE and LdWT indicates that SAT overexpression confers survival advantage in *L. donovani*. Five FDA approved compounds from ZINC database were screened against LdSAT which may provide potent anti-leishmanial compound.

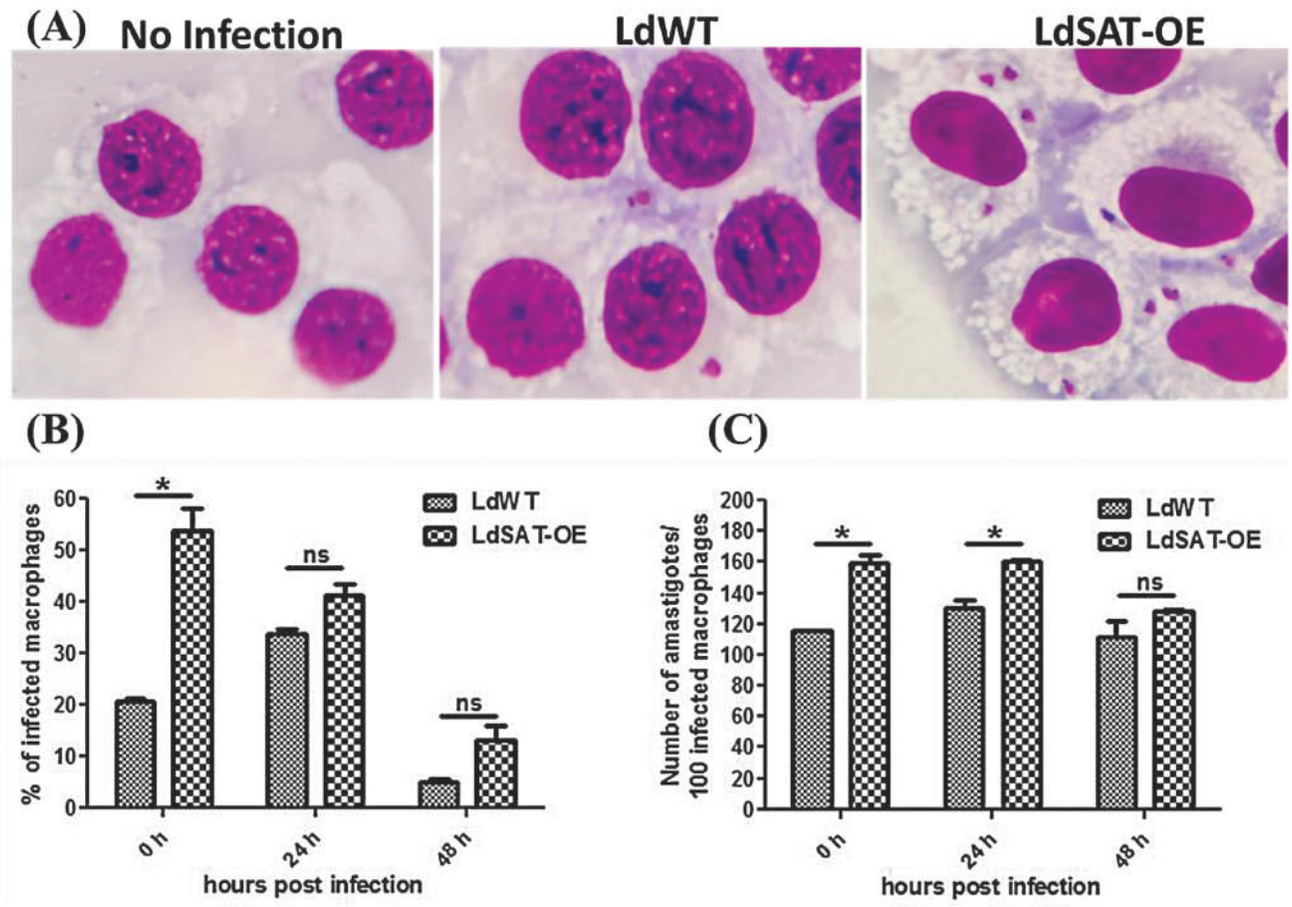


Fig. 38: *In vitro* infectivity assessment. (A) J774A.1 macrophages infected with LdWT and LdSAT-OE promastigotes, (B & C) Post-infection percentage of infected macrophages and amastigotes respectively.

The Role of dithiol glutaredoxin of *Leishmania donovani* (LdGrx1) in drug resistance and parasite survival: a potential drug target

Glutaredoxin (Grx1), a GSH-dependent oxidoreductase was characterized first time in *L. donovani*. The expression of LdGrx1 gene was found to be higher in lab generated Amp-B resistant and clinical isolate as compared to Amp-B sensitive. *L. donovani* overexpressing Grx1 tolerated higher doses of Amp-B, increased enzymatic activity and has an advantage to deal with oxidative stress as compared to wild type. Further, the higher thiol content in overexpressed parasite as compared to wild type also suggested a potential role of LdGrx1 in regulating thiol content. This study suggests that this protein is important in parasite's survival, Amp-B resistance and maintenance of redox homeostasis.

Combining cyclodextrin nanoparticle with IL-10 antagonist peptide and Amphotericin B to enhance chemotherapeutic efficacy and antileishmanial immunity

Emergence of drug-resistant strains of *L. donovani* is a major therapeutic challenge for Visceral leishmaniasis (VL). An antagonist of IL-10, an anti-inflammatory cytokine that promotes parasite survival, may restore host-protective immunity.

A nanoformulation of gamma-cyclodextrin encapsulated amphotericin B and Anti-IL-10 peptide was synthesized. Morphology and structure characterization of nanoparticles was investigated by scanning electron micrographs (SEM), transmission electron microscope (TEM), Fourier transform infrared spectra (FTIR) (Fig. 39). iNOS gene expression was found significantly higher in the synthesized nano formulation (CD-AmB-Anti IL-10 Peptide) as compared to AmB and CD-AmB alone. Polarization of macrophages towards M1 type suggested leishmanicidal efficacy of this nanoparticle. Further, *in-vivo* study is underway to confirm its leishmanicidal effect and possible side effects.

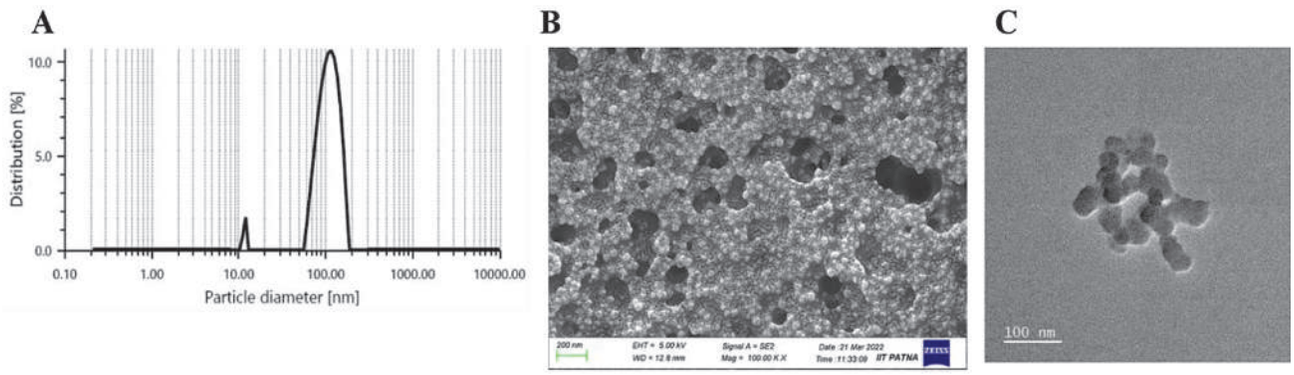


Fig. 39: (A) Dynamic light scattering (DLS) image showing 123.28 nm size of CD-AmB-Peptide nanoparticle. (B) Scanning electron microscope (SEM) image and (C) Transmission electron microscope (TEM) image showing spherical shape and approximately 40nm with uniform size distribution.

Host genetic factors influencing the visceral leishmaniasis relapse in India by NGS-exome analysis

The present study was undertaken to identify and dissect the contribution of disease modifier genes to VL relapse. Altogether, 22 subjects (8 VL relapse, 6 cured VL, 8 healthy controls) were enrolled for exome sequencing analysis. The barplot depicts the combined mutated genes for VL cured and VL relapse cases compared to reference genome (Fig. 40). Variant classification for these groups revealed that most mutations are missense mutations. Other mutations such as frameshift (insertion and deletion), nonsense, translation start site and nonstop mutations are present in smaller numbers. The most common type of mutation in the variants identified is single nucleotide polymorphisms (SNPS). MUC3A, MUC16, MUC4, MUC6, HLA-DRB5, HLA-DRB1, ZNF17, FLG, HLA-B, FCGBP are the top 10 mutated genes in this category.

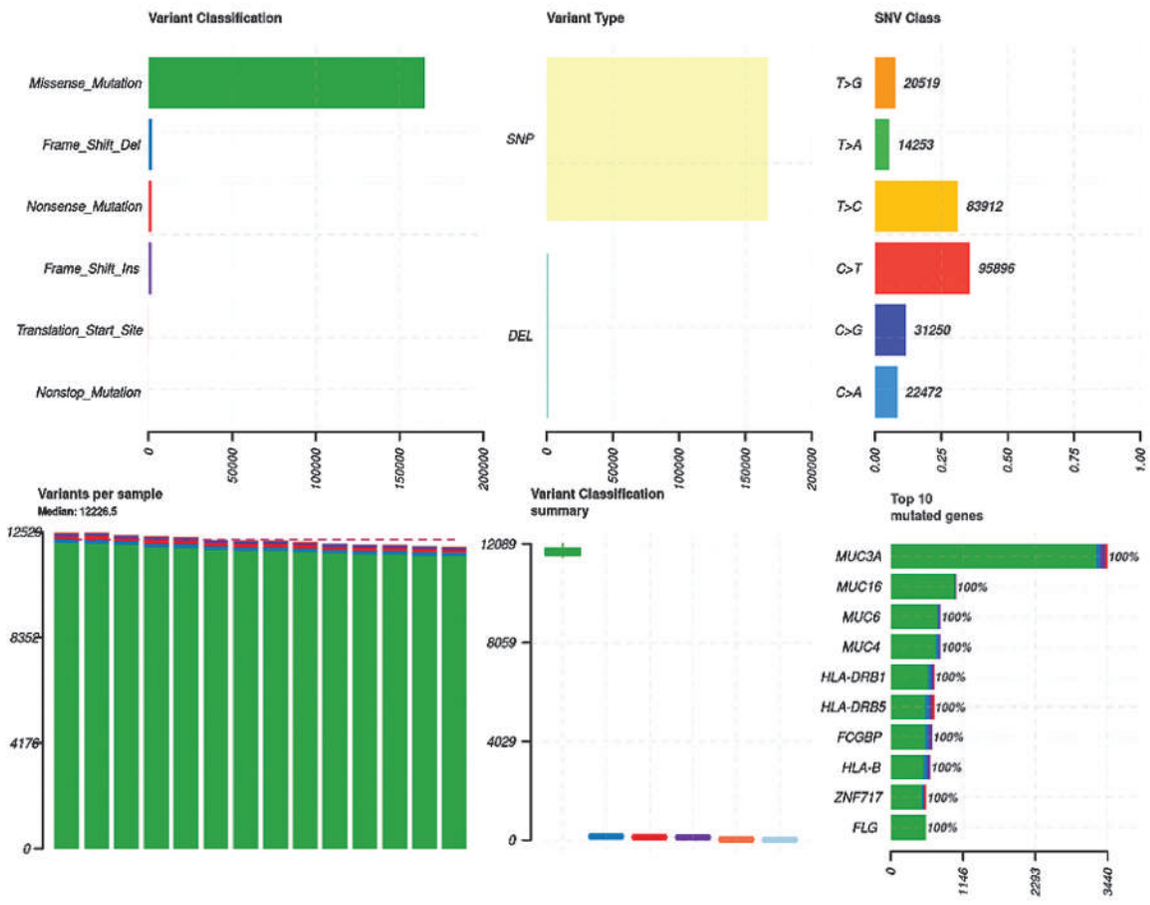


Fig. 40: Barplot of mutated genes for VL relapse and VL Cured.

Genome wide transcriptome analysis of healthy control, VL and PKDL cases to identify PKDL specific disease mechanism

Post kala-azar dermal leishmaniasis (PKDL), a dermal form of the disease, occurs in some of the visceral leishmaniasis (VL) patients following treatment. The present study focussed on role of dermal fibroblasts in VL and PKDL disease mechanism. Dermal fibroblasts were grown from skin biopsy explants collected of VL, PKDL patients and healthy controls; and were subjected to RNA-Seq for analyzing differentially expressed genes (DEGs). Transcriptome analysis of PKDL vs VL identified 516 DEGs (263 were up-regulated and 253 down-regulated in PKDL) (Fig. 41 & 42). The

data demonstrates that PKDL fibroblasts present antigens through MHC I pathway activating CD8+ T-cell mediated response while the VL fibroblasts express NFκB mediated chemokines and cytokines resulting in the recruitment of immune cells to the site of infection leading to the clearance of parasite from skin and visceralization of the disease.

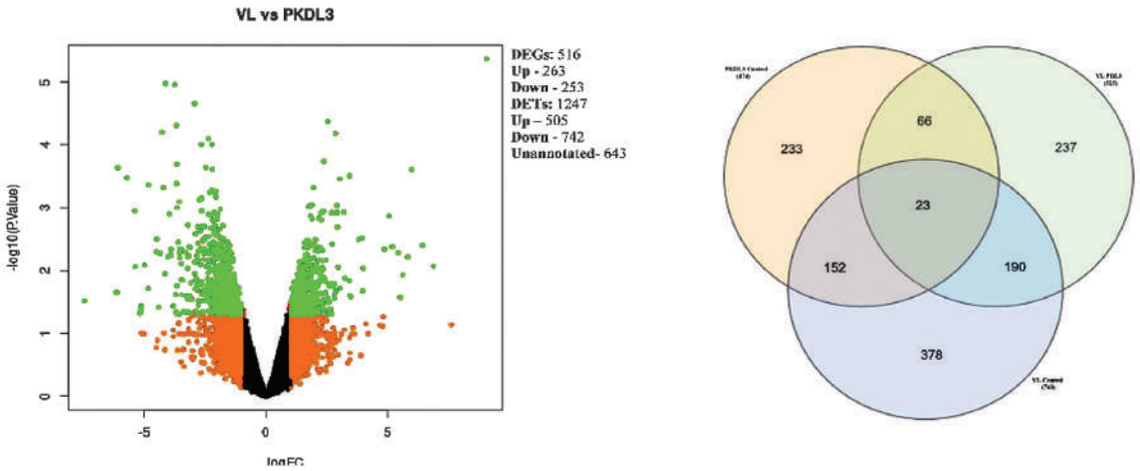


Fig. 41: (a) Volcano diagram of the overlapping differentially expressed genes among PKDL- VL, (b) Venn diagram of the overlapping differentially expressed genes among PKDL- Healthy control, VL-Healthy control and PKDL-VL.

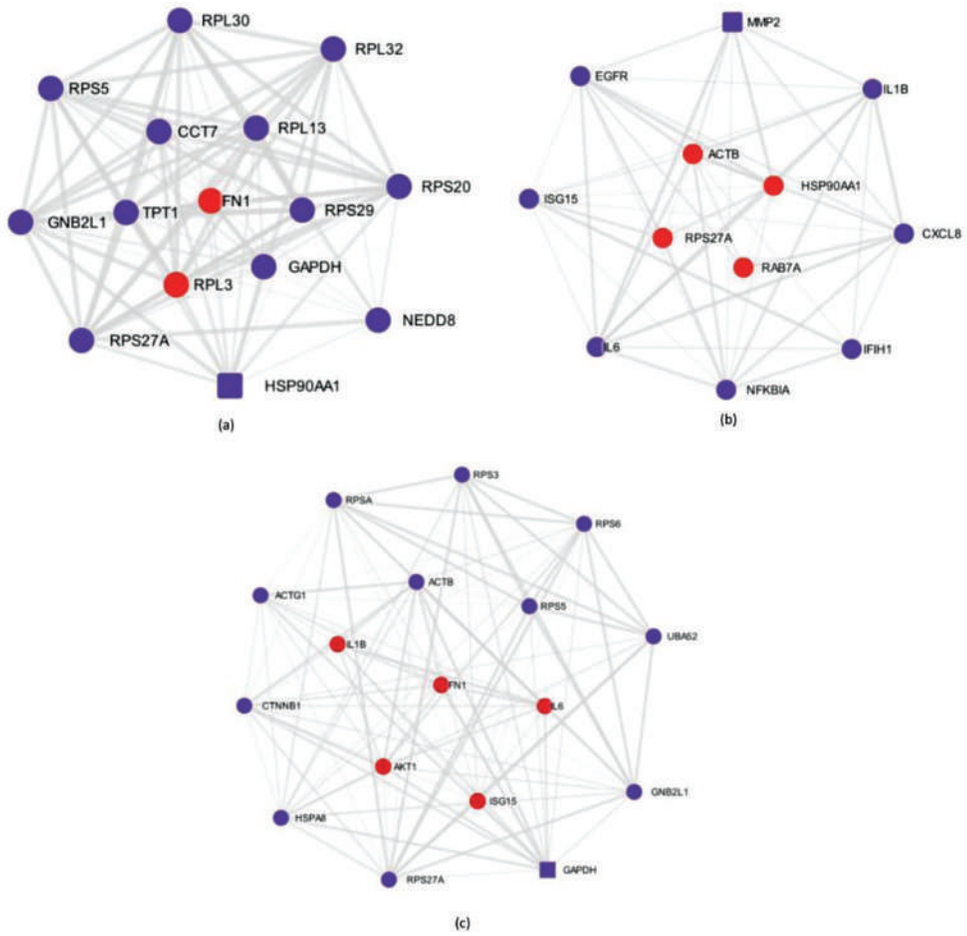


Fig. 42: Hub gene analysis of DEGs in PKDL vs VL: Protein-protein interaction analysis demonstrated that MMP2, IL1β, CXCL8, IFIH1, NFKBA1, IL6, ISG15 and EGFR were down regulated and ACTB, HSP90AA1, RAB7A and RPS27A were up-regulated in PKDL compared to VL.

The role of mammalian target of rapamycin (mTOR) in *Leishmania donovani* infection

It was observed that *L. donovani* infection activates mammalian target of rapamycin of THP1 monocytes derived macrophages. THP1 monocytes derived macrophages were infected with GFP tagged *L. donovani*. The phosphorylation status of m-TOR and S6K was found increased by ~2.5 fold and ~3.5 fold respectively after 12 hrs and 24 hrs of infection as compared to uninfected. Phosphorylation status of 4EBP1 was enhanced by ~5 fold after 24 hrs of infection. m-TOR kinase ELISA assay of PBMC revealed increased expression of p-mTOR (~ 3 fold) in confirmed VL cases as compared to healthy control. Further, increased expression level of cyclin A (~ 2.5 fold) was observed in infected macrophages. These findings showed the role of mTOR in immune-adaptive responses of *Leishmania* survival under stress condition inside the macrophages.

Whole Transcriptome Analysis of Dengue infected patients by Next Generation sequencing

DEN1 and DEN2 genotypes have been found to be more frequently associated with dengue infection than DEN3 in Patna region. Further, Caripill (Papaya leaf extract) treated patients exhibited up-regulated ALOX12 (Arachidonate 12-lipoxygenase) and PTAFR (the Platelet-Activating Factor Receptor) genes and enhanced platelet count. Computational docking study revealed that carpaine, one of the natural alkaloid components found in papaya leaves, has high binding affinity with PTAFR (Fig. 43) suggesting anti-thrombocytopenic potential of Caripill.

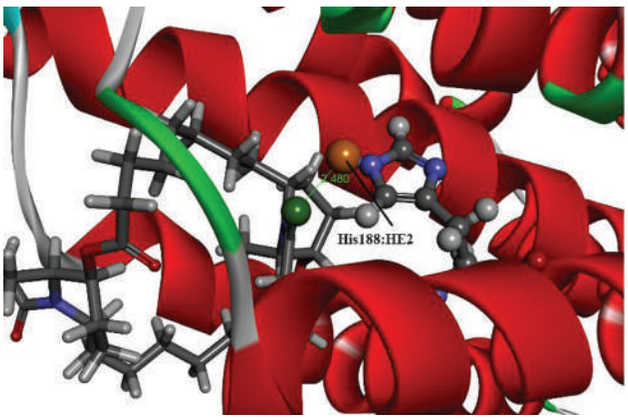


Fig. 43: Docking of PTAFR(PDB ID: 4OIG) with carpaine.

Behaviour study of sand fly in endemic and non-endemic areas under the impact of insecticidal pressure

Pre and Post monsoon entomological survey was conducted in four blocks of two highly kala-azar endemic districts of Bihar. Vector (*P. argentipes*) collection was made through CDC Light trap. Though the vector density in outdoor sites was comparatively lower than indoor sites, vector collection from outdoor sites indicates change in vector behaviour from endophilic to exophilic. It may possibly be attributed to regular insecticidal pressure in the endemic areas of Kala-azar.

Comprehensive knowledge base of immunogenic peptides for *Leishmania donovani* species

A peptide vaccine is preferred over traditional vaccines due to the advancement of immune-informatics, which reduces the exposure of unwanted antigens to the body. The most commonly used screening approaches discard a large number of proteins, making it impossible to detect the key antigen of the pathogen.

An inference system, based on fuzzy logic to classify all proteome peptides as "Low", "Moderate", or "High" depending on their likely epitope status, was developed. It does not discard any peptide, instead categorizes it in a logical way for effective screening. In addition, a searchable and user-friendly *L. donovani* proteome database (https://mhcfisld.biomedinformri.com) was developed based on the proposed method (contains information for 4829904 peptides) (Fig. 44). Results indicate that less than 0.5 % of the peptides have "High" or "Very high" likelihood of being epitopes. The proposed FIS-MHC-I method could potentially streamline the selection of potential MHC-I binding peptide vaccine candidates from a whole proteome of *L. donovani*.

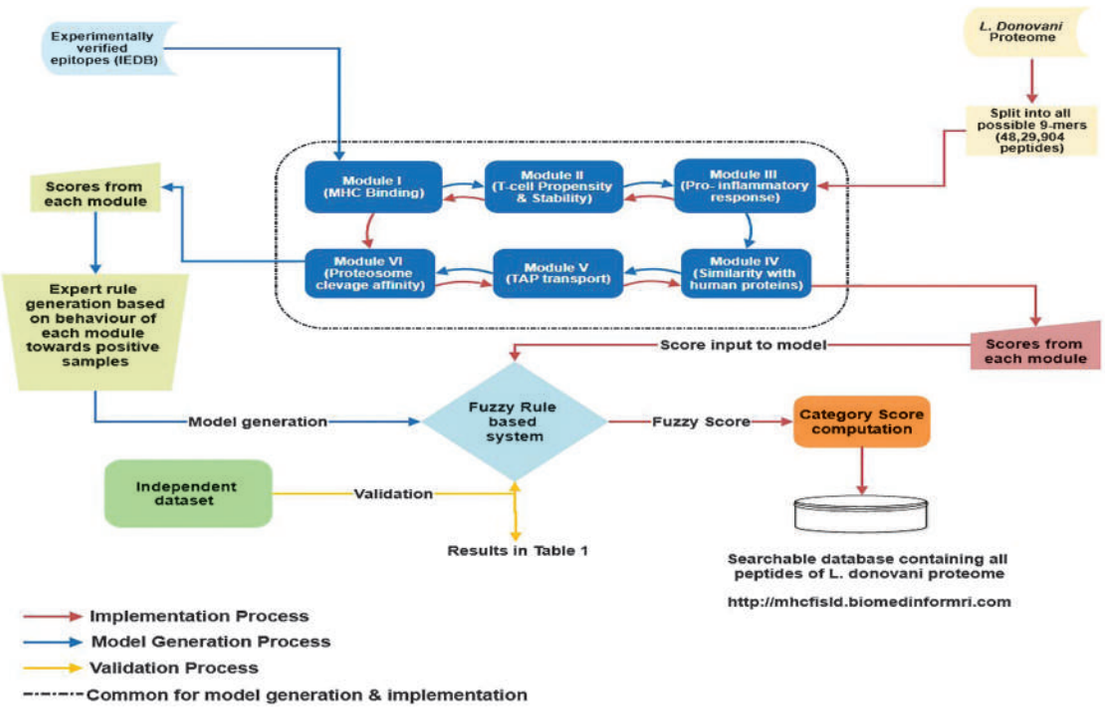


Fig. 44: Schematic representation of the proposed method.

Virus Research and Diagnostic Laboratory (VRDL)

During the period, COVID-19 pandemic continued as a major health problem. VRDL significantly contributed in RT-PCR testing for COVID-19 in Bihar and tested about 9 lakhs sample for COVID-19. This centre also served as zonal QA/QC center for all other RT-PCR centers in Bihar.

Apart from COVID-19, VRDL continued its routine diagnostic support for 24 viruses including JE, Dengue, Chikungunya, Zika, Enterovirus, H1N1, Influenza A&B, HSV-I & II, HAV, HBV, HCV, HEV etc.

Under the National Viral Hepatitis Control Programme (NVHCP), viral load testing and treatment centre for Hepatitis B and C for different districts of Bihar was started in Feb. 2022. Up to March 2022, 113 samples for Hepatitis B and 11 for Hepatitis C were tested.

PUBLIC HEALTH

During the period, COVID-19 continued to be a major health issue at national level. ICMR-RMRIMS, Patna, the first ever RT-PCR testing centre in Bihar, provided round the clock testing facility; about 9 lakhs samples tested during this period. Apart from testing, this institute provided training support to other centres, served as zonal QA/QC centre and conducted SARS-CoV2 sero-surveillance in Bihar. Most importantly, ICMR-SII sponsored Phase 2/3 clinical study on COVISHIELD was successfully conducted as one of the sites for safety cohort and eventually the COVISHIELD was rolled out in national mass vaccination program.

Apart from the substantial contribution towards COVID-19, some of the major achievements in Kala-azar are as below

Limited drug of choice for treatment of PKDL is still a major issue for Kala-azar elimination program. Interim analysis of a clinical trial on short course combination of AmBisome and Miltefosine revealed it as a safe, effective and well-tolerated regimen for treatment of PKDL cases. After final data analysis, the study outcomes will be shared to the National control program for Kala-azar. Further, based on a clinical trial conducted at this

centre, WHO has issued a new treatment guideline for Kala-azar using AmBisome and Miltefosine combination in cases co-infected with HIV, that reduces the treatment time from 38 days to 14 days.

In Kala-azar elimination program, Indoor residual spray (IRS) of insecticides is in the main stay for vector control based on endophilic behavior of sandfly (vector). However, the observed change in vector behavior from endophilic to exophilic might be a major concern for vector control strategies. In a study conducted on correlation of vector density to endemicity level, no significant difference was observed, however rate of natural infection was found higher in high endemic areas as compared to Low and Meso. It was further confirmed that *P. argentipes* (vector) continues to be highly resistant to DDT even after DDT's withdrawal from IRS program, but susceptible to pyrethroid, organophosphate and carbamate insecticides. It warrants regular insecticide resistance monitoring.

Laboratory based safety and efficacy assessment of a Phytopharmaceutical product as topical applicant for Post Kala-azar Dermal Leishmaniasis (PKDL) has been completed successfully. Agreement with a GLP/GMP accredited laboratory for product formulation is in process.

Further, under the National Viral Hepatitis Control Program (NVHCP), viral load testing and treatment centre for Hepatitis B & C for different districts of Bihar was started in Feb. 2022.

ICMR - NATIONAL INSTITUTE OF EPIDEMIOLOGY (ICMR-NIE), CHENNAI

India Hypertension Control Initiative

Around one in three adults in India has hypertension. Still, only about 10% of them have their blood pressure under control. To achieve India's target of a 25% relative reduction in the prevalence of raised blood pressure, approximately 4.5 crore additional people with hypertension need blood pressure control. To support the states in achieving the goal, the India Hypertension Control Initiative (IHCI) was launched in November 2017. The project is coordinated by ICMR-NIE and ICMR HQ. The project has five core strategies, namely standard treatment protocol, uninterrupted drugs supply up to the most peripheral level facilities, task sharing, decentralized care closer to patient's home and cohort-based monitoring system using an app or card based system (Fig 45). Between 2018 and 2022, 130 districts across 23 States enrolled more than 3.4 million patients with hypertension. Nearly half of the facilities where the project was implemented were health and wellness centres. Of the people on treatment, nearly half achieved blood pressure control. The scalable strategies include a simple drug-dose-specific standard treatment protocol, best practices to ensure an adequate quantity of protocol medications, decentralization of care with follow-up and refills at HWCs, task sharing involving all health staff and a digital real-time information system which can track every patient for follow-up and blood pressure control.

Fig. 45: Five core strategies of India hypertension Control Initiative.

The project strategies (Fig 45) are being mainstreamed in the National Programme for Prevention and Control of Diabetes, Cardiovascular Disease and Stroke (NPCDCS). The Ministry of Health and Family Welfare and the Indian Council of Medical Research received the 2022 UN Interagency Task Force Award at the UN General Assembly special event held on 21st September 2022 in New York, USA for IHCI, which was recognized as a highly impactful programme for

hypertension within primary health care system in India.

COVID-19 National Serosurvey, June-July 2021

During the first two years of COVID-19 pandemic, ICMR conducted four nationwide community based serosurveys to measure the extent of SARS-CoV-2 infection and track the progress of pandemic in India (Fig 46).

The fourth serosurvey during June-July 2021 was conducted in 70 randomly selected districts in India. 700 clusters (villages in rural areas and wards in urban areas) were selected from these districts by population proportional to size method. Four random starting points were identified in each cluster and from each random point a minimum of 10 individuals aged >=6 years (6-9 y:1, 10-17: 2, >18: 7) were enrolled. The serum samples were tested for the presence of IgG antibodies against S1-RBD and nucleocapsid protein of SARS-CoV-2 using chemiluminescence immunoassay.

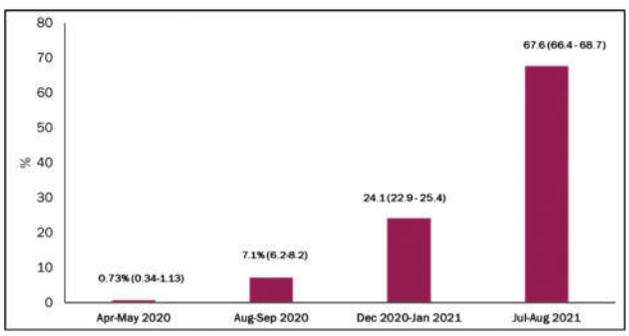


Fig. 46: Seroprevalence of IgG antibodies against SARS-CoV-2 at different time-points in India.

Of the 28,975 individuals who participated in the survey, 10% were aged 6-9 years, 20% were aged 10-17 years, and 70% were aged ≥18 years. 75.2% participants resided in rural areas. The weighted and test-adjusted prevalence of IgG antibodies against S1-RBD and/or nucleocapsid protein among the general population aged ≥6 years was 67.6% (95% CI 66.4% to 68.7%) (Fig 2). Seroprevalence increased with age ($p < 0.001$) and was not different in rural and urban areas ($p = 0.822$). Compared to unvaccinated adults (62.3%, 95% CI 60.9% to 63.7%), seroprevalence was significantly higher among individuals who had received 1 vaccine dose (81.0%, 95% CI 79.6% to 82.3%, $p < 0.001$) and 2 vaccine doses (89.8%, 95% CI 88.4% to 91.1%, $p < 0.001$).

In conclusion, the findings of the fourth serosurvey indicated nearly two-thirds of individuals aged ≥6 years from the general population had antibodies against SARS-CoV-2 by June-July 2021 in India.

Measles and rubella seroprevalence to evaluate the impact of the mass vaccination campaigns in India: Pre-and post- cross-sectional household serosurveys in four Indian districts, 2018-20

India conducted measles-rubella supplementary immunisation activities (MR-SIAs) targeting children aged 9 months to less than 15 years. Measles-rubella seroprevalence was estimated before and after the MR-SIAs to quantify the effect on population immunity and identify remaining immunity gaps. Community-based, cross-sectional serosurveys were conducted in four districts in India before and after MR-SIAs. 30 villages or wards were selected within each district, and one census enumeration block from each was selected as the survey cluster. Households were enumerated and 13 children in the younger age group (9 months to <5 years) and 13 children in the older ager group (5 to <15 years) were randomly selected by use of computer-generated random numbers. Serum samples were tested for IgG antibodies to measles and rubella viruses by enzyme immunoassay.

Specimens were collected from 2570 children before the MR-SIA and from 2619 children afterwards. Before the MR-SIA, district-level measles seroprevalence was between 80·7% and 88·5% among younger children in all districts, and between 63·4% and 84·5% among older children. After the MR-SIA, measles seroprevalence among younger children increased to more than 90% (range 91·5 to 96·0) in all districts except Kanpur Nagar, in which it remained unchanged 80·4%. Among older

children, measles seroprevalence increased to more than 90·0% (range 93·7% to 96·5%) in all districts except Hoshiarpur (88·7%) (Fig 47). A significant increase in rubella seroprevalence was observed in all districts in both age groups, with the largest effect in Dibrugarh, where rubella seroprevalence increased from 10·6% to 96·5% among younger children (Fig 47).

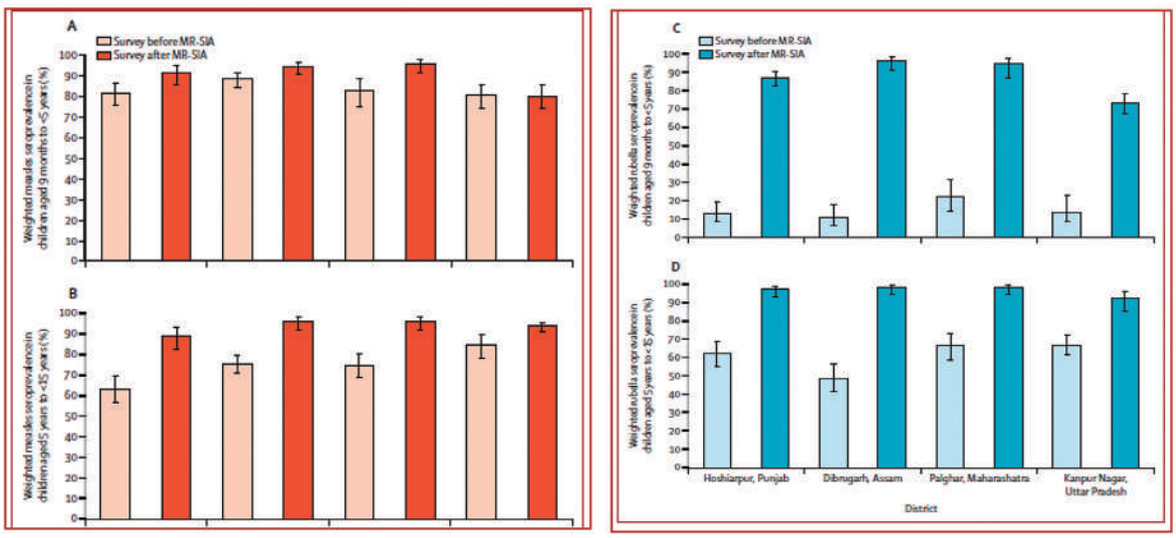


Fig. 47: Seroprevalence of IgG antibodies against measles and rubellaviruses before and after the MR-SIA, by district.

The findings of the study indicated that measles-rubella seroprevalence increased substantially after the MR-SIAs but the serosurvey also identified remaining gaps in population immunity.

Effectiveness of BBV152/Covaxin and AZD1222/Covishield vaccines against severe COVID-19 and B.1.617.2/Delta variant in India, 2021: a multi-centric hospital-based case-control study

India introduced BBV152/Covaxin and AZD1222/Covishield vaccines in January 2021. We estimated the effectiveness of these vaccines against severe COVID-19 among individuals aged ≥45 years. A multi-centric, hospital-based, case-control study was conducted between May and July 2021. Cases were severe COVID-19 patients, and controls were COVID-19 negative individuals from 11 hospitals. Vaccine effectiveness (VE) was estimated for complete (2 doses ≥ 14 days) and partial (1 dose ≥ 21 days) vaccination. The centre enrolled 1143 cases and 2541 control patients. The VE of complete vaccination was 85% (95% CI: 79-89%) with AZD1222/Covishield and 71% (95% CI: 57-81%) with BBV152/Covaxin. The VE was highest for 6-8 weeks between two doses of AZD1222/Covishield (94%, 95% CI: 86-97%) and BBV152/Covaxin (93%, 95% CI: 34-99%). The VE estimates were similar against the Delta strain and sub-lineages.

The study findings indicate that BBV152/Covaxin and AZD1222/Covishield were effective against severe COVID-19 among the Indian population during the period of dominance of the highly transmissible Delta variant in the second wave of the pandemic.

Hyperglycemia and steroid use increase the risk of rhino-orbito-cerebral mucormycosis regardless of COVID-19 hospitalization: Case-control study, India

During COVID-19 pandemic, an increased incidence of rhino-orbito-cerebral mucormycosis (ROCM) was noted in India among those infected with COVID. The team determined risk factors for ROCM post Coronavirus disease 2019 (COVID-19) among those never and ever

hospitalized for COVID-19 separately through a multicentric, hospital-based, unmatched case-control study across India. The study defined cases and controls as those with and without post-COVID ROCM, respectively. The team compared their socio-demographics, co-morbidities, steroid use, glycaemic status, and practices and calculated crude and adjusted odds ratio (AOR) with 95% confidence intervals (CI).

Among hospitalised, the team recruited 267 cases and 256 controls and 116 cases and 231 controls among never hospitalised. Risk factors (AOR; 95% CI) for post-COVID ROCM among the hospitalised were age 45-59 years (2·1; 1·4 to 3·1), having diabetes mellitus (4·9; 3·4 to 7·1), elevated plasma glucose (6·4; 2·4 to 17·2), steroid use (3·2; 2 to 5·2) and frequent nasal washing (4·8; 1·4 to 17). Among those never hospitalised, age ≥ 60 years (6·6; 3·3 to 13·3), having diabetes mellitus (6·7; 3·8 to 11·6), elevated plasma glucose (13·7; 2·2 to 84), steroid use (9·8; 5·8 to 16·6), and cloth facemask use (2·6; 1·5 to 4·5) were associated with increased risk of post-COVID ROCM.

Hyperglycemia, irrespective of having diabetes mellitus and steroid use, was associated with an increased risk of ROCM independent of COVID-19 hospitalisation. Rational steroid usage and glucose monitoring may reduce the risk of post-COVID.

ICMR School of Public Health

The ICMR School of Public Health (ICMR-SPH) at ICMR-National Institute of Epidemiology has been conducting advanced (Master of Public Health and Epidemic Intelligence Services Program) and intermediate (FETP-NCD) field epidemiology training programs in India. These courses are aimed at middle level health managers working with different state health departments. The SPH has trained more than 330 medical officers from 26 Indian states in the last 22 years and thereby contributed to strengthening the health workforce in India.

ICMR-NATIONAL INSTITUTE OF MEDICAL STATISTICS (ICMR-NIMS) , NEW DELHI

PROJECTS

- HIV Surveillance and Estimation–HIV Estimations 2020 under National AIDS Control Programme (NACP).
- Impact Analysis of Behaviour Change Communication (BCC) Intervention for Improving utilization of RCH Services through Male Participation among Saharia Tribes in selected districts of Madhya Pradesh.
- Geo-Spatial Hotspots of Disability and Associated Household Financial Burden in India (Focus on 88 Regions of India).
- Hotspot and Socio Demographic Determinants of TB (Tuberculosis) in North-Eastern States, India: A Spatial Analysis.
- Pre-Project for finalizing multicentric study on all oral shorter treatment regimen with newer drugs for MDR TB.
- Clinical Trials Registry – India (CTRI) www.ctri.nic.in.
- Strengthen Research in Ayurveda by utilizing the CTRI Platform and Impart Capacity Building in Research Methodology.
- Innovations to Improve and Institutionalize Data Quality and Analytics (National Data Quality Forum).
- National Clinical Registry for COVID-19.
- Development and pilot testing of intervention strategies for smokeless tobacco and arecanut cessation among tribal women in Manipur.
- Development of software Task Force Study on prescription research.
- Spatio-temporal variations in malnutrition among children of tribal and non-tribal population of India: level and trends from various rounds of NFHS.

PUBLIC HEALTH

- The National Guidelines for Data Quality in Surveys was released in July 2021 and has the potential to strengthen the data quality of ongoing surveys in the field of health, nutrition and demography. Three regional trainer workshops were conducted for building capacity of researchers engaged in implementing surveys. https://ndqf.in/wp-content/uploads/2021/07/National-Guidelines-for-DATA-QUALITY-in-Surveys.pdf.
- Developed and launched the Customized data set items for Ayurveda studies on the CTRI portal. It was a step towards improving the quality of research in the field of Ayurveda. http://ctri.nic.in/Clinicaltrials/login.php.
- ICMR-NIMS is a nodal Institute for providing burden of HIV estimates since 2003. As per the 2020 estimation, there were 23.19 lakhs people living with HIV with an adult prevalence of 0.22%. There were 57.55 thousand new HIV infections and 31.94 thousand AIDs related deaths. The need of prevention of mother to child transmission was 20.93 thousand.
- Research brief on COVID-19 Stigma: Correlates and Mitigation Strategies were posted on the ICMR website to inform development of appropriate interventions for mitigation of stigma. https://main.icmr.nic.in/sites/default/files/upload_documents/COVID19_Stigma_Reserach_Brief_09_08_21_ICMR_NIMS.pdf.
- The Institute Scientists are providing statistical support and guidance to post graduate and super specialty medical students and many of the ICMR Institutes.

Fig. 48: Release of the 'National Guidelines for Data Quality in Surveys' on 28th July, 2021at ICMR-HQ, New Delhi.

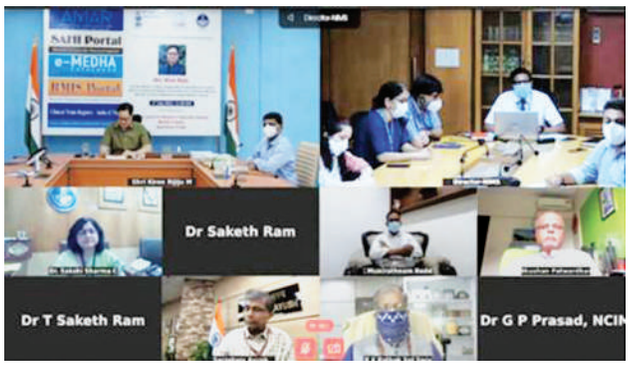


Fig. 49: Hon'ble Minister Sh. Kiren Rijiju launched customized data set for Ayurveda in Clinical Trial Registry-India (CTRI) hosted at ICMR-NIMS, New Delhi on 5th July, 2021. This initiative in collaboration with the Central Council for Research in Ayurvedic Sciences (CCRAS), Ministry of AYUSH and ICMR (HQ) focuses on capturing Ayurveda specific trial details.

EXTRAMURAL RESEARCH

VIROLOGY

The virology unit worked hand-in-hand with ICMR institutes to meet the challenges that arose in the wake of this pandemic.

COVID-19 Testing

Indian Council of Medical Research (ICMR) had established a COVID-19 laboratory surveillance network which is one of India's most extensive networks for communicable diseases. Initially started in January 2020 with a small number of laboratories, the network had grown to include more than 2300 government and private laboratories in March 2021. From March 2021 till March 2022, >1000 laboratories have been added to the network. The capacity for COVID-19 testing was exponentially increased across the country reaching to 3345 laboratories by March, 2022.

To ascertain the quality of *COVID-19* testing by these laboratories, a quarterly Quality Control program and external quality assurance program were implemented for rRTPCR laboratories

SARS-CoV-2 testing by an open system rRTPCR is the gold standard test and is the mainstay of COVID-19 diagnosis in India. Laboratories conducting COVID-19 testing by an open system rRTPCR use a wide range of test kits with different gene targets. Therefore, accuracy, reliability and timeliness of results are of concern. Sustaining this vast laboratory network with good quality testing was accorded utmost priority since the inception of the pandemic. Since Quality Control (QC) of testing was crucial to build trust and confidence in this vast network of laboratories, this component was inbuilt into the expansion plan of the laboratory network. In order to ensure accuracy and reliability of COVID-19 testing in India, where many laboratories were conducting molecular testing for the first time, ICMR implemented a quarterly inter-laboratory quality control (ILQC) program for rRTPCR. Inter-laboratory quality control activity was enrolled in a structured manner in September 2020 on quarterly mode which later on changed to bi-annual mode. To further assess the performance of laboratories conducting COVID-19 testing in India by open system rRTPCR, ICMR was supported by WHO-India and SEARO for conducting External Quality Assurance Program (EQAP) of rRTPCR laboratories through Proficiency Testing (PT) panels prepared by Royal College of Pathologists of Australasia Quality Assurance Programs (RCPAQAP), Australia.

Apart from rRT-PCR technology, other different platforms – TrueNat, CBNAAT, high throughput machines (Cobas 6800 and 8800), Abbott ID NOW, and Accula were also roped in with help of manufacturers of these platforms

Given the need for rapidly implementing large-scale testing for SARS-CoV-2, the field of molecular diagnostics for SARS-CoV-2 rapidly evolved. All these platforms were validated with the open system rRT-PCR test as the gold standard and were approved for use only if they had sensitivity and specificity comparable to the open system rRT-PCR. Various closed system RT-PCR were approved like CBNAAT platforms like TrueNat, GeneXpert, USFDA approved cartridge-based systems like Abbott ID, Accula, and other platforms like RT-LAMP assay, CRISPR-based

tests etc. were considered equivalent to the open system rRT-PCR.

Validation of Home-based testing kits was done and rolled out that helped ease load on rRT-PCR-based testing and provided results in a quick turn-around time

In May, 2021, ICMR issued an advisory on home-based diagnostic kits wherein it was advised to test in symptomatic individuals and contacts of the confirmed positive patients. This platform actually proved to be successful during the third wave when omicron variant of SARS-CoV-2 knocked our doors in January, 2022. This smart "at home" initiative gave rise to many new indigenous products leading India towards "Self-reliance."

Viral Research & Diagnostic Laboratories

In the year, 2021-2022, 11 new Medical colleges were supported to build up the serology and molecular capacity for the diagnosis of viral pathogens. These Medical Colleges were supported for creating the infrastructure and purchasing the equipment required for serology and molecular laboratory. In this support for the staff and consumables were also built in for the smooth functioning of the laboratory.

PAN-India epidemiological, virological, and genomic surveillance for *human influenza* and *COVID-19* through VRDL Network

The ILI/SARI surveillance network is three-tiered, where each site is mapped to a higher-tier laboratory for training, supervision, mentoring, troubleshooting, and quality control. The bottom tier of 15 testing laboratories is mapped to one of the 6 referral laboratories in the middle tier, which in turn is linked with the WHO-NIC & SARS-CoV-2 Reference Center at ICMR-NIV Pune. Each laboratory (NIV Pune, Referral labs, and testing labs) collects and tests 25 samples per week from consenting patients(15 ILI samples from community settings such as Community Health Centers/Primary Health Centers/Urban Health Centers, and 10 SARI samples from hospital settings).

Sewage surveillance for *SARS-CoV-2*

SARS-CoV-2 virus has been found to be excreted in the feces contaminating the sewage water. The standard methodology for the detection of SARS-CoV-2 from sewage water has been established at ICMR-National Institute of Virology, Mumbai Unit (NIVMU). In Mumbai, COVID-19 cases are rising high since its first detection in March 2020. The results obtained since May 2020 in ES of COVID-19 from19 sites in Mumbai correlated well with the trend of COVID-19 cases (unpublished data). With the success of this pilot study ICMR and NPSP/WHO-India had expanded ES in the country in nine sites.

Zika surveillance in the midst of COVID-9 pandemic

During the second wave of the COVID-19 pandemic, outbreaks of Zika were reported from Kerala, Uttar Pradesh, and Maharashtra, India in 2021. The Dengue and Chikungunya negative samples were retrospectively screened to determine the presence of the Zika virus from different geographical regions of India. During May to October 2021, the clinical samples of 1475 patients, across 13 states and a union territory of India were screened and re-tested for Dengue, Chikungunya and Zika by CDC Trioplex Real time RT-PCR. The Zika rRTPCR positive samples were further screened with anti-Zika IgM and Plaque Reduction Neutralization Test. Next generation sequencing was used for further molecular characterization. The positivity was observed for Zika (67), Dengue (121), and Chikungunya (10) amongst screened cases. The co-infections of Dengue/Chikungunya, Dengue/Zika, and Dengue/Chikungunya/Zika were also observed. All Zika cases were symptomatic with fever (84%) and rash (78%) as major presenting symptoms. Of them, four patients had respiratory distress, one presented with seizures, and one with suspected microcephaly at birth. The Asian Lineage of Zika and all four serotypes of Dengue were found in circulation.

Network for the diagnosis of *Viral Hemorrhagic Fever (VHF)*

This study involved capacity building for VHF diagnosis of the existing VRDLs and biomedical laboratories in different geographical areas, thereby strengthening the surveillance and identification of known/unknown/novel agents of epidemic/ outbreak potential at the earliest. Biosafety and Bio-risk mitigation training also strengthened laboratories and health workers across the country for emergency preparedness and response. During 2021-22 three trainings were conducted.

Network of Next-generation Sequencing facility

Whole-genome sequencing (WGS) is a common tool for pathogen identification and tracking, establishing transmission routes and outbreak control. Genetic characterization of SARS-CoV-2 is used to monitor viral evolution and to timely identify potential markers of increased transmissibility, the severity of disease or altered antigenicity. The continued monitoring of global SARS-CoV-2 genomic data have reported a wide range of changes/mutations in its genome. Through global surveillance of SARS-CoV-2 genomes, a number of variants have been identified with evidence of clinical and/or public health significance, termed variants of concern (VOC) e.g. B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.617.2 (Delta), and B.1.1.529 (Omicron). These have been characterized and monitored using whole genome sequencing for genomic surveillance. The evolving nature of SARS-CoV-2 virus may have an impending threat of new VoCs that may cause serious implications over public health in the future. Hence, genomic surveillance is very much required for monitoring the SARS-CoV-2 virus evolution.

ICMR being the nodal agency for the management of COVID-19 pandemic, had mapped its VRDL network laboratories for SARS-CoV-2 genomic surveillance. Next-generation sequencing (NGS) facilities are available 51 sites. These sites are also represented in the Indian SARS-CoV -2 Genomics Consortium (INSACOG).To facilitate these sites, ICMR has placed an order to supply a total of 17824 NGS reactions of different types of available NGS platforms.

Indigenous Mobile BSL-3 laboratory

The mobile laboratory was set up to investigate newly emerging and re-emerging viral infections that are highly infectious and of lethal potential to human beings. This laboratory will be able to access remote and forested areas of the country where specially trained scientists from ICMR can investigate outbreaks using samples from human and animal sources. These activities will ensure timely and on-site diagnosis with a rapid turnaround time for reporting these outbreaks. the mobile lab will help in real-time data collection which will enable us to ensure quick containment and prevent further spread of any emerging viral infections. The laboratory was designed and built by ICMR in collaboration with Mumbai-based bio-safety equipment maker Klenzaids.

Memorandum of Understanding with the International Vaccine Institute (IVI), Seoul for vaccine research

This MoU was signed to host a center at ICMR which will develop projects on vaccine research that will span from the development or identification of vaccine candidates to epidemiological studies to facilitate decision-making for the implementation of new vaccines in India and global health. Another key area of interest for the centre is to assess the impact of recent introduction of newer vaccines like Rotavirus and Pneumococcal Conjugate Vaccines in the Universal Immunization Program of India. Funding for any projects arising out of the joint discussions will be borne by respective partners or appropriate third parties.

ANTIMICROBIAL RESISTANCE

Establishment of Regional Centres for Antimicrobial Research and Surveillance Network

The activities of Antimicrobial Research and Surveillance Network which includes 21 nodal and regional centres were continued during the year 2021-2022. The data emanating from this network enables the compilation of drug resistance data on six pathogenic groups from the country. This data is used to track resistance trends and to better understand the mechanisms of resistance in the key priority pathogens using genomics and whole genome sequencing. Antimicrobial resistance (AMR) data was used by each hospital to devise hospital antibiograms which were necessary to rationalize the prescription of antibiotics in hospitals and to guide infection prevention and control practices.

The AMR surveillance data of the year 2020 emanating from network was published in August 2021 that includes data on six pathogenic groups (i) *Enterobacterales* causing sepsis, (ii) Gram-negative non- fermenters, (iii) Typhoidal *Salmonella,* (iv) Diarrhoeagenic bacterial organisms, (v) Gram-positives: staphylococci and enterococci, and (vi) Fungal pathogens.

Antimicrobial Stewardship (AMS) Activities in Hospitals in India

ICMR supported 20 tertiary care hospitals to set up the structure and framework of Antimicrobial stewardship and created a process of implementation of AMS by providing necessary training and guidance documents. Nearly all hospitals understand the importance of implementing antimicrobial stewardship strategies and embraced this initiative. The progress of this project was monitored by capturing process indicators like establishment of AMSP committees, creation of hospital antibiotic policy, introduction of formulary restriction etc.

Task force on rapid methods for antimicrobial susceptibility testing at point-of-care

This project was initiated to bridge the translational gap between the innovators and the health care system requirements of point of care diagnostics which can be helpful in containment of AMR. The objective of the project is to stimulate the innovations towards development of 'fit-for-use' diagnostics to enable fast diagnosis and better patient outcomes. Guidance for innovators/ developers was provided in the form of a 'draft standard validation protocol for AMR diagnostics' to address challenges in establishing the validity of a new indigenous test. The standard protocol supplement the existing documents and guidelines related to the validation of IVD and act as a reference documents for innovators/developers. It also aims to bridge the gap between developer and regulatory mechanism to limit time delays in the market entry of a validated test. Target Product Profile (TPPs) for the rapid diagnosis of Sepsis, Neonatal sepsis and Typhoid, were developed, which detail the criteria for performance and operational specifications of a 'fit-for-use test as per Indian healthcare needs. These TPPs are a product of diverse set of expert consensus drawing upon in-country knowledge on the respective subjects. The TPPs will guide developers and innovators who are embarking on the initiative of providing indigenous solutions to the problem of AMR in India and other LMICs. This also has a programmatic slant and aligns well with AtmaNirbhar Bharat focus of the Govt of India to give push to in-country innovation and development of diagnostics and devices. Under this taskforce project, field feasibility and cost-effectiveness studies were undertaken to provide recommendations on the use of new indigenously developed rapid diagnostics for AMR in peripheral healthcare settings.

Expansion of antimicrobial stewardship program (AMSP) and infection prevention & control program (IPC) of ICMR in secondary care hospitals

This is an ongoing ICMR-Pfizer collaborative study, where eleven hospitals which are part of the ICMR AMR network were selected to act as mentoring centres for expanding the existing AMR surveillance and stewardship practices along with IPC to secondary healthcare settings (nursing

homes/district hospitals) in different parts of the country. ICMR facilitated all the mentor centres (MC) in identifying their respective Nursing Homes/ District Hospitals to expand AMR activities to small and mid-level hospitals. More than 90 hospitals are part of this initiative. These hospitals are a mix of public/private/missionary/army hospitals catering to diverse patient populations (urban/rural/semi-urban). Training of health personnel from mentor centres (clinicians and microbiologists) involved in the implementation of Antimicrobial Stewardship Program (AMSP) and infection prevention and control (IPC) were conducted by ICMR. Multiple assessment tools (Hospital Assessment, Baseline Assessment and Monthly Assessment) were developed by ICMR for capturing baseline and antibiotic consumption data. This initiative will be helpful in creating awareness and capacity building in smaller healthcare institutions.

ICMR- Global Antibiotic Research and Development Partnership (GARDP) collaboration

Global Antibiotic Research and Development Partnership (GARDP), a new joint initiative by the WHO and DND*i* seeks to develop new antibiotic treatments to address the major public health threat of antimicrobial resistance was announced in on the occasion of the 69th World Health Assembly in Geneva. The mission of the Global Antibiotic Research and Development Partnership (GARDP) is to develop new antibiotic treatments addressing antimicrobial resistance and to promote their responsible use for optimal conservation, while ensuring equitable access for all in need. The priority areas for GARDP are to look at new treatment options for drug resistant Gonorrhoea, Neonatal sepsis, Typhoid fever and *Klebsiella* sps and *Candida auris*. In view of ICMR's initiative on AMR, ICMR and GARDP have signed an MoU to support clinical research related to antibiotics, drug discovery and related challenges and conservation strategies for antibiotics. New treatment options for serious bacterial infections and neonatal sepsis is priority for this collaboration.

ICMR- Foundation for Innovative New Diagnostics (FIND) collaboration

ICMR and Foundation for Innovative New Diagnostics (FIND) joint initiative focus on preventing AMR development and mortality by improving diagnosis and timely initiation of appropriate therapy. A platform 'AMR Diagnostic (Dx) Use Accelerator' was deployed to evaluate a package of social (training and communications) and clinical (diagnostic tools and clinical algorithms) interventions to improve the management of acute febrile illnesses (AFIs) and reduce unnecessary antibiotic use. ICMR-FIND undertook submissions from institutions interested in a demonstration project aimed at improving care of children and adolescents presenting with undiagnosed acute febrile illness in outpatient clinics. The initiative was implemented in four sites; PGIMER, Chandigarh; RD Gardi Medical college, Ujjain; NICED, Kolkata; JSS, Chhattisgarh, to assess changes in antibiotic prescription rates and differences in patient outcomes. The project generated evidence on the impact of diagnostic tools and of the behaviours affecting adherence to prescription that will assist practitioners and policymakers to make informed changes to policies and practices.

VECTOR BORNE DISEASES & ZOONOSES

Malaria Elimination Research Alliance (MERA)-India invited proposals and launched a special call for early career malaria researchers in the second round to promote young investigators to carry out cutting edge malaria research (Operational/ Implementational/Public Health/Translational) on the recommendation of MERA-India Expert Committee. 85 proposals were received under the ad-hoc format and 20 proposals in YMR category. Multiple projects have been articulated under multicentric Task Force format directed towards malaria elimination strategies and accelerating the elimination of malaria using intensified surveillance, mass screening and treatment of

malaria, including asymptomatic and sub-patent infections and vector control in the predominantly tribal population and North Eastern states. In a first of its kind study funded to NIMR, the true burden of malaria in the private sector will be estimated at an overall national and state level using drug sales data. Another multicentric task force study being carried out at 5 institutes will generate data on insecticide resistance in malaria vectors in the endemic states of the country with different history of use of insecticides.

The ICMR Malaria Mission (IMM), a program coordinated by NIMR and Division of ECD, ICMR Hqtrs working towards integrating research efforts and coalescing research expertise available across ICMR Institutes convened an expert committee meeting to decide on the broad themes for First round of Call for Proposals wherein 11 broad areas were decided mostly focused on malarial research.

A call was floated under the theme area 'Impact of climate change on vector-borne diseases' for which 92 (82 ad-hoc + 10 Centre for Advanced Research (CAR)) proposals were received. Pre-screening was conducted to shortlist the proposals relevant to the thematic area. A PRC meeting was convened to discuss the shortlisted projects wherein 17 ad-hoc proposals and one CAR proposal were selected for further discussion.

A call for research proposals on Kala-azar was announced to encourage interdisciplinary, innovative, close to practice research in the field of Leishmaniasis. 20 ad-hoc proposals were approved for strengthening the elimination program against VL.ICMR Task Force study entitled "Analytics and field evaluation of identified immunological markers for diagnostic performance to detect Bancroftian filariasis and their potential as Surveillance tools for stopping decision of MDA and post MDA surveillance" funded to VCRC Puducherry to work on to validate Point of Care diagnostics for Lymphatic Filariasis for use in monitoring and evaluation of the National programme. A prototype Lateral Flow Point-of-Care test based on the rec antigen, viz, RMRC-BLG1, has also been developed. This indigenously developed kit by ICMR will be of great national significance in public health and in LF elimination programme and its monitoring and evaluation in current and the post elimination scenario as well. Another study is being carried out at RMRC Bhubaneswar to assess filarial infection in human and vector in selected non-MDA districts in Odisha and develop an appropriate strategy for mapping LF in districts with uncertain filarial endemicity/ transmission for inclusion under MDA in India. This study will facilitate the ongoing national programme to accelerate LF elimination by 2030.

ZOONOSES

ICMR has been working in areas of zoonoses to strengthen its footprint and taken initiatives to take forward research focused on One Health. It has supported extramural ad-hoc and task force studies which have been carried out on diseases like Lyme disease, rabies, scrub typhus and anthrax which have been carried out at various key institutes of human and animal research. A task force study involving 8 institutes was funded to determine the presence of Lyme disease causing agents and status of controversial Tick-borne LD in India. A nationwide multi-centric representative community survey has been carried out by ICMR-NIE Chennai to estimate the incidence of human rabies deaths and animal bite burden, a first of its kind in India. Another multicentric study funded to NIE is aimed at determining the immunogenicity of the intradermal abridged Cambodia regimen and updated intradermal Thai red cross regimen for shortening the course to improve patient compliance thereby reducing direct/indirect cost to patients as well as National Rabies Control Programme of India. An ICMR ICAR collaborative study involving 4 sites have been carried out in Northeast region to investigate the prevalence of selected zoonotic pathogens in livestock and the status of intermingled ecological niche including environment and farm workers.

A project is being carried out at RMRC Bhubaneswar to help strengthen community members and key stakeholders capacity by bringing together public health professionals, epidemiologists, microbiologists, veterinarians, entomologists, and socio-behavioral scientists to effectively establish a peri-urban cohort to address zoonotic diseases with a one-health focus.

PUBLIC HEALTH

- The collaborative IDDO-ICMR project for capacity building of young researchers aimed at honing the scientific capability of Junior Indian Researchers to design and conduct robust research using available secondary data on key diseases of interest to the Indian population is being carried out with specific work packages targeting three diseases of mutual interest-Malaria, Visceral Leishmaniasis (VL) and Lymphatic Filariasis (LF).
- The white paper entitled "India's Road to Independence in Manufacturing Active Pharmaceutical Ingredients (API): Focus on Essential Medicines" was published in *Focus on Essential Medicines. MDPI-Economies Journal* highlights the various steps to be taken by the government in moving towards domestic manufacturing of APIs and provides certain short-, medium- and long-term recommendations in the policy, fiscal and technology domains, to promote API independence. Another white paper on "Diethylcarbamazine citrate fortified salt as an adjunct to mass drug administration will accelerate lymphatic filariasis elimination in India" has been accepted in IJMR. This white paper has been shared and discussed in the ministry and has been proposed for a policy change as an alternative strategy to accelerate the elimination of lymphatic filariasis (LF) in the country.
- The ICMR scientists and professionals have revised/amended the 'Common Protocol for Uniform Evaluation of Public Health Pesticides Including Biolarvicides for Use in Vector Control' considering the recent advancements and changes in methodology.

TRIBAL HEALTH

Since, sporadic outbreaks of measles cases are being reported even with two doses of vaccination, an observational study to measure measles IgG antibody titre by quantitative ELISA following two doses of measles vaccine, was conducted to estimate the proportion and level of protective immunity developed following vaccination and factors for non-response. The immunization coverage records indicated more than 99.62% children receiving measles vaccine. Quantitative measles IgG assay showed 44.89% having absence of seroconversion. The results indicated that since non-response is high, it may be required to think of additional dose of measles vaccination (3rd dose) & strengthening nutritional supplementation along with immunization programme.

An operational feasibility approach of double fortified salt as a supplementary measure to the ongoing MDA for eliminating a persistent foci of diurnally sub-periodic *Wuchereria bancrofti* towards accomplishing elimination in two islands of Nancowry group with *DspWb* prevalence, showed that supplementing MDA with mass consumption of DEC fortified salt, enhanced the reduction in parasitaemia, and the infection levels were below the threshold. Hence, these two islands (Kamorta and Chowra), which were under MDA alone arm earlier, were targeted for implementing DEC fortified salt strategy. After one year of implementation of salt strategy, the community microfilaraemia prevalence reduced from 0.74% to 0.07%, demonstrating a reduction of 91%, while geometric mean intensity (*Mf*) showed a reduction of 92.6%. During post intervention period, the antigenaemia prevalence in children of 2-3 and 6-7 years was nil. It was observed that the DEC double fortified salt was easily deliverable and acceptable to the tribal community of Nancowry islands, suggesting that DEC double fortified salt strategy can be implemented in other LF endemic

areas with effective monitoring, thus facilitating the elimination of LF at national level, much before the target period 2030.

In order to develop an online geo-referenced database on malnutrition among children comparing tribal and non-tribal populations for each state and district of India, a study was undertaken involving spatial and temporal variations of under-nutrition using various rounds of National Family Health Survey (NFHS-2, NFHS-3, NFHS-4). Spatial Hotspots of under-nutrition were identified using the spatio-temporal techniques. The study suggests that the burden of childhood under nutrition varied significantly across social, economic, demographic and contextual factors in India. The multi-level modelling analysis indicated that village/community (PSU) level nutritional interventions could help address the issue of childhood undernutrition, rather than treating districts as a homogenous unit for nutritional programme implementation.

A community based cross-sectional study was carried out among the Nicobarese residing in Car Nicobar Islands ≥18 years to assess the prevalence of oral premalignant & malignant lesions as well as to find out the sociodemographic, nutritional, habitual risk factors and viral pathogens associated with oral malignant/ premalignant lesions among the Nicobarese. This study provided useful information on the prevalence of oral cancer and the risk factors in this particular indigenous population. The study also helped in creating awareness of the harmful effects tobacco & other risk factors and sensitized on the role of screening in their early detection. The findings of the study and the details of the subjects identified with lesions were conveyed to the District hospital at Car Nicobar for timely treatment, management and follow-up of these cases. The information gained from this study was also communicated to the Directorate of Health Services for planning of public health strategies for reducing disease burden significantly in the future.

A cross-sectional study targeting Irula tribes in the Kancheepuram, Chengalpattu and Dharmapuri districts of Tamil Nadu assessed the knowledge, attitudes, and behaviour / practices (KAB) toward Hepatitis B Virus (HBV) Infection among 1171 adults of Irula tribes, by using a systematic random sampling technique. This study found that overall, 38.9% of them had moderate knowledge, 25.9% poor attitude, and 23.4% had moderate behaviour / practice towards HBV.

In view of the increasing cases of severe anaemia among the subjects attending the District Hospital at Gadag, a study assessed the prevalence and types of anaemia among 305 pregnant women belonging to the Lambani tribe to develop appropriate strategies to mitigate the problem of anaemia, of which 198 (68%) were anaemic. The results revealed the prevalence of anaemia among Lambani pregnant subjects to be much higher than global (40.1%, WHO) and Indian (50%, NFHS-4) averages. The socio-demographic data indicated that majority of the subjects are either have primary education (173) or are illiterates (86) and therefore the awareness about anaemia and its complications is very low in the subjects. The result of detailed haematological investigations of 158 anaemic cases indicated different types and degrees of anaemia in the subjects. The results of KAP showed that almost all (99.7%) subjects are aware about anaemia and its complications. Still, about 1/4th of them are unaware about the precautions for preventing/treating anaemia. The data on the pregnancy outcomes (n=37) reported no mortality either in new-borns or in mothers. It was further noted that most of the babies (89.2%) are in the normal body weight category (> 2.5 kg body weight at birth; WHO). The outcomes from this study will help the health authorities to address the problem of anaemia among pregnant women in Lambani tribe by designing suitable interventional strategies to mitigate the problem and for better health in the Lambani tribe at large.

An exploratory study involving both qualitative and quantitative techniques was adopted in four geo-cultural tribal dominated areas in Himachal Pradesh and Madhya Pradesh to understand the perspective

and coping strategy COVID-19. The survey analysis revealed that there is paucity of trained service providers including health infrastructure in all the four tribal areas, with overall awareness of COVID-19 found to be better in Lahaul & Spiti. It was observed that STs (88%) were lesser aware of COVID-19 symptoms compared to other social groups. Almost all the respondents (95%) were aware of existence of COVID-19 vaccine. However, stigma and discrimination related to COVID-19 also existed in these tribal areas, apart from misconception related to ideology of transmission of the infection in the tribal areas.

North East Region (NER)

A hospital based study involving anti-HEV IgM and HEV mRNA positive cases belonging to HEV genotype 1 from northeast India and healthy term delivery as control subjects, aimed to evaluate the role of oxidative stress in HEV related pregnancy complications and its cross-talk molecular endocrinological factors/signalling specific to pregnancy using biochemical and molecular tools. The study has helped to generate novel consolidated data on specific or combination of oxidative stress biomarkers along with specific molecular endocrinological factors, which will have specificity with the issue in question, prognostic significance, correlation with pregnancy outcome and gestation period; and hence may prove vital in allowing treatment efficacy in a targeted manner, which till now has been a far cry during HEV related pregnancy complications. The data also indicates the prognostic significance of progesterone and especially progesterone induced blocking factor (PIBF) as well as their inverse correlation with oxidative stress & HEV infected pregnancy complications.

In continuation of a recently concluded study funded in the Division, another study has been initiated by the same investigator from ICMR-RMRC, Dibrugarh during 2021-22, based on the evaluation of effectiveness of single dose of *Japanese encephalitis* vaccine SA 14-14-2 among adults over a period of seven years in two highly endemic areas of Assam and that rendered ample protection of six years post-vaccination. In the seventh-year, effectiveness of the vaccine was seen to reduce to statistically insignificant levels and there has been an appreciable reduction in number of JE cases. In this newly initiated study, long term effectiveness of JE vaccine will be studied to further monitor the change in effectiveness of the vaccine for 3 more years to generate a conclusive and continuous data on the effectiveness of the vaccine, which will help to decide whether a booster dose will be required. The study will further compare HLA polymorphisms within the vaccine non-responders and vaccines responders and also try to elucidate if HLA polymorphisms plays a role in vaccine non-responders.

TUBERCULOSIS

I*ndi*a TB Research Consortium

ICMR initiated India TB Research Consortium (ITRC), a flagship programme of ICMR and DHR to tackle TB in a mission mode. The significant achievements are as below.

DIAGNOSTICS

- TrueNat (M.TB& Rif.) validated for detection of TB/MDR-TB paediatric TB and Extrapulmonary TB (in addition to pulmonary TB) and recommendations sent to CTD
- C-Tb (New Skin test for Latent TB): ICMR completed multicentric validation of the new skin test C-Tb in 6 states and the sensitivity of C-TB is higher in General population, high risk population in adults and Children above 6 yrs. (although the number of children were less) as compared to TST while the specificity is comparable. The safety of C-Tb and TST at 48 hrs and at 28 days is comparable. The C-TB can be used for detection of latent TB in adult population more than 18 yrs under the NTEP. The report was launched on world TB day on 24th March 2022.

Three new kits validated:

- TB Detect for improved smear microscopy at peripheral level,
- Sputum transportation kit for bio-safe sputum transportation of sputum at room temperature from peripheral areas
- DNA extraction kit for extracting DNA for testing drug resistance through Line probe assay (LPA) from the transport kit. (Recommendations sent to CTD)

The feasibility study for using kit under NTEP is ongoing.

Standard Treatment workflow for *T*uberculosis

Standard Treatment workflow for paediatric pulmonary TB and Extra-pulmonary TB have *b*een prepared for use at all levels of health care to facilitate management of paediatric TB in the country under NTEP (Till date no such thoroughly prepared document for peripheral health setup is available on TB). The document, posters and the App was launched on World TB day on March 24th 2022.

Quality Management System

A study on introduction of quality management system with well-defined modules and processes under National programme laboratories has shown significant improvement in TB diagnosis at these facilities in programme labs both in Govt and private sectors. The introduction of quality management system will have a larger impact on TB diagnosis under the National Programme

THERAPEUTICS

- For Drug sensitive TB: ICMR recommended use of high dose rifampicin (25mg/kg BW) for Drug sensitive TB in the current standard treatment used under NTEP for improved treatment outcomes
- For XDR-TB: The all oral 6-9 months shorter regimen with 4 drugs i.e Bedaquiline, Delamanid, Clofazimine and Linezolid were also found to be effective for treatment of XDR-TB and has been recommended to National Programme.
- For DS-TB: A clinical trial to evaluate safety and efficacy of Piperine 225 mg with standard anti tubercular treatment in newly diagnosed sputum positive drug sensitive pulmonary tuberculosis adult patients revealed that there was early culture conversion at 2nd and 3rd weeks with addition of piperine. The data on AE was comparable between control and intervention arms.
- A study with drug Sertalin (SRT), an antidepressant, as an adjunct for enhancing effect of ATT intervention (SINERG) showed that SRT in combination with standard TB drugs was more effective in early control of infection. Analysis suggests that combination of SRT to TB drugs prevents reactivation of infection upto 1 year. The animals with TB treatment alone show increased bacterial burdens in one year. Findings reflectsthat the combination therapy leads to betterment of lung pathology and protects against spontaneous reactivation.

VACCINES

A Phase III regulatory clinical trial for evaluating the safety and efficacy of two TB vaccines: VPM1002 and MIP (indigenous vaccine), as against Placebo is ongoing at 8 main sites with 10 sub-sites. The trial completed enrolment of 12717 participants in December 2020, who are under different stages of follow-up, however the efficacy was inconclusive in view of the limited FU duration. The safety analysis by DSMB has shown that both the vaccines are safe and acceptable. The follow-up for efficacy is ongoing as per recommendations of the DSMB.

Implementation Research

- National TB Prevalence Survey: National TB prevalence survey for prevalence of national and state-wise data on TB and latent TB along with health seeking behaviour has been concluded by ICMR and the report shared

with CTD. This mega survey is a significant contribution and will help immensely in tackling TB elimination of India.

- Active case finding in severely malnourished children admitted to Nutritional Rehabilitation Centers (NRC) has shown very high (5%) incidence of TB and case detection improved with proper training and providing point of care diagnostic tests under National Programme.
- Intensified case finding in High-risk groups in secondary care hospitals: Based on recently concluded study by ICMR, the experts recommended :
    - Routine screening for symptoms (cough/ fever, hemoptysis, weight loss, night sweats) & Chest X-testing for following high risk groups visiting health care facilities for any reason (all patients aged 60 years or more, all diabetics, and all people living with HIV, all patients admitted to medical wards)
    - One spot sputum in case of symptomatics and X-ray positives. The study showed that current diagnostic algorithm (2 spot and one overnight sputum sample) can be simplified by limiting sputum collection to a single spot sample only.

The strategy is likely to help in identifying additional new pulmonary tuberculosis patients across these high-risk patient categories.

- A pilot demonstration project for demonstration of reduction of tuberculosis in Sheopur district (MP) - with predominant Saharia Tribe is ongoing. It contains approximately 6% Saharia tribes. The study includes screening of all TB suspects in a camp approach using handheld X-rays and sputum testing. The intervention near the doorstep of patients showed increased acceptance, increase in the case detection rate and better compliance to ATT. The intervention also helped in initiation of preventive therapy in contacts of TB cases.

Central TB Division – Global Fund Grant – Phase - II

To strengthen the TB research in India, the Central TB Division, New Delhi has funded the implementation studies in collaboration of ICMR under Global Fund Grant – Phase – II. There were four projects undertaken by ICMR Institutes, NIRT Chennai and JALMA, Agra. The achievements of the studies are given below.

- The cross-sectional observational study involving 12 states in 6 geographical regions of the country found association of NTM infection with AIDS and is encountered with increasing frequency in the general population. The method for diagnosis is limited for NTMs and usually requires high resource settings. The NTM infections are diagnosed very late and, therefore, the probability of saving the patients reduces significantly. The study will help to develop diagnostic algorithm for early detection of NTM. The developed NTM algorithm can be placed within the integrated DR-TB Diagnosis and Treatment Algorithm.
- In another study, a TB Verbal Autopsy (VA) Tool has been developed and validated in another study. The VA tool demonstrated an accuracy of 85%, which is satisfactory and can be implemented under the National TB Elimination Programme for conducting surveillance to estimate the TB deaths occurring in the community.
- Another study reported very high occurrence of TB among the household contacts (HHC) as compared to general population. This implies that the contacts contribute significantly to the pool of TB cases. Targeting the contacts will prove to be an important strategy towards elimination of TB.
- Another study on National Hospital Based Sentinel Surveillance to examine trends and patterns of TB attributable to selected high risk groups/clinically vulnerable population attending tertiary care hospitals in India

including immunosuppressive group and patients with kidney disease revealed that the proportion of patients with TB notified by the medical colleges was high underlining the importance of these institutions in diagnosing and treating cases which may have missed from the primary care level.

LEPROSY

- **Development of field based diagnostic test for early diagnosis of leprosy**: A multiplex PCR for *M.leprae* detection in Paucibacillary (PB) cases was developed which showed 93 % sensitivity and 100 % positivity. A PCR based early detection kit was developed for use in screening PB cases and contacts which can be applied in the field for immediate treatment with multidrug therapy to stop transmission.
- A prospective study to evaluate the bacteriological and antigen specific immunological responses induced by MIP and/ BCG vaccines as adjunctive treatment (immunotherapy) in multibacillary leprosy patients treated with multidrug therapy is being conducted to assess vaccine associated immune responses induced by the *Mycobacterium indicum pranii* (MIP) vaccine.

MYCOLOGY

Advanced Mycology Diagnosis and Research Centre (AMDRC)

- This is a new initiative of Division of ECD, ICMR Hqrs. A separate 'Mycology unit' developed under division of ECD to support the establishment of Advanced Mycology Diagnostic and Research Centers (AMDRCs) in different geographical region of the country.
- Mycology is one of the neglected areas in our country. Although India has the largest burden of fungal diseases per capita in the world, it remains as a challenging problem with increasing incidence rates. In recent time during COVID -19 pandemic we have witnessed huge number of COVID-19-associated pulmonary aspergillosis (CAPA) and post COVID mucormycosis or secondary systemic mycoses which leads to serious complications and even death. On the other hand, Invasive fungal diseases (IFD) are silent ICU killers. It is thought that after COVID -19 pandemic, the major cause of mortality in coming years would be drug resistant fungi.
- In order to be prepared it is necessary to set up of Advanced Mycology Laboratories in phased manner. These laboratories will provide a quality and range of services to public health not only in their hospitals but will cover the complete region.
- Thus, ICMR has initiated Eight (08) Advanced Mycology Diagnosis and Research Centers (AMDRCs) in different geographical region of the country to provide diagnostic facility for patient care, create awareness and to establish a strong platform for fungal research to map the fungal infections in the country. PGI, Chandigarh is identified and funded for Staff training and External Quality Control for all AMDRCs.
- AIIMS Bhopal inaugurated 'ICMR Mycology Advanced Resource Center" (iMARC) in presence of Honorable Health and Union minister Dr. Harsha Vardhan and DG, ICMR on 13.3.2021.

Mycology Clinical Registry

- A Mycology Clinical Registry entitled "ICMR MYCONET Inpatient Clinical Registry: Establishment of an analytics platform" approved as additional component of ICMR Myconet TF program. The objectives are to develop a PAN India digital mycology clinical registry to collect data regarding epidemiological, socio-demographical, clinical and laboratory features, treatments, and outcomes of hospitalized patients with Invasive fungal infections (IFI).
- ICMR-NIMS is identified as data management and software partner for development of online data platform, data compilation data cleaning

and data analysis etc. Protocol, Case report form (CRF) and informed Consent form (ICF), parental assent form has been developed. CRF training and field test has been done.

COVID -19 associated Mucormycosis

- During the 2nd wave of COVID -19 pandemic, there was sudden upsurge of post COVID Mucormycosis, commonly known as black fungus disease. It had huge impact on total mortality and morbidity. ICMR conducted a case control study to identify factors responsible for the development of the disease entitled "Risk factors for Covid Associated Mucormycosis in India: a case control investigation." Total 12 centres participated in the project from different geographical zone of the country.
- An evidence based advisory on screening, diagnosis and management of COVID 19 associated mucormycosis was published on ICMR website (09.05.21) during the 2nd wave of COVID 19 pandemic.

PUBLIC HEALTH

- During the 1st and 2nd wave of COVID -19 pandemic, there was sudden rise of COVID associated Aspergillosis (CAPA) and CAM causing huge number of deaths. Thus, ICMR initiated six AMDRCs in different states of the country, which will fulfill the gap and a big step for the country to face the future outbreaks.
- During second wave of COVID -19 outbreak, there was sudden rise of COVID associated Mucormycosis and related deaths. At that crucial moment, ICMR released an evidence based advisory on screening, diagnosis and management of COVID 19 associated mucormycosis, which was published on ICMR website (09.05.21) during the 2nd wave of COVID 19 pandemic.
- ICMR also initiated a TF project to collect systematic data on the demographic profile, clinical, and therapeutic factors related to COVID associated mucormycosis (CAM). Data generated from the will help to identify unknown risk factors for COVID-19 associated Mucormycosis and in framing a better clinical and public health response to CAM.

DIARRHEAL DISEASE & FOOD-BORNE INFECTIONS

Surveillance of food-borne pathogens from North-East India

- A Task force project entitled "surveillance of foodborne pathogens from North-East India" was initiated from North-East India to estimate the burden of food borne diseases so that risk of acquisition of infection from food can be assessed, which may provide a foundation for food safety policy and prevention efforts.
- ICMR-NICED Kolkata site has been identified for External quality control and laboratory training and Centre for Development of Advanced Computing (CDAC). The project consists of market survey, Hospital and community survey and outbreak investigations. Hands on Laboratory training (at ICMR-NICED Kolkata) and data management training (at CADC, Kolkata) were organized. Web based Data Repository, Retrieval and Analytics Platform for Foodborne Diseases for North-East India was developed.
- ICMR Foodnet website /dashboard was inaugurated on 3rd of August 2022. Web based Data Collection Module for Food Sample Survey Data has been completed and tested. Mobile App for Clinical Survey Module has been completed and FoodNet App Version 2.0 has been released.
- Standardized all laboratory tests and SOP were developed. Guidelines of outbreak investigation was developed and circulated.

Estimation of *Vibrio cholerae* O1 infection in India: a step towards identification of cholera hotspots

The Project was initiated from ICMR-NICED Kolkata to achieve significant cholera reductions globally. To estimate incidence of *V. cholerae* O1

infections across 5 regions of India using sero-epidemiological methods along with triangulation of data on cholera from available multiple sources (a) published literature and grey literature archives (b) program data like Integrated Disease Surveillance Program (IDSP), Field Epidemiology Training Program (FETP) reports, National Health Profile (NHP) maintained by Central Bureau of Health Intelligence (CBHI) and data on Swacch Bharat initiated sanitation drive (c) information from annual reports and (d) serological testing for cholera markers on stored samples collected during Dengue National serosurvey. Study results generated robust estimates on risk-prone areas vulnerable to cholera outbreaks in India. Highest sero-incidence was seen in Tamil Nadu (16.7%) followed by Madhya Pradesh (13.4%), Rajasthan (12.6%), Uttar Pradesh (12.6%), and West Bengal (12.1%).

PUBLIC HEALTH

- Data generated from the 'food borne pathogens surveillance' may provide a foundation for food safety policy and prevention in India.
- Identification of cholera hotspot, followed by active cholera surveillance, may provide a concrete estimation of cholera burden, which may help to drive national policy to implementation of OCV during outbreak.

Drone related studies

- Feasibility study on vaccine delivery by drone at IIT, Kanpur (Limited efficacy trial)
- Conducted *i*-DRONE feasibility study for drone-based vaccine and medical supply delivery in hard-to-reach terrains of Manipur and Nagaland
- Developed i-DRONE portal for storing data of the medical supplies delivered during the drone study.

HIV

- ICMR has been supporting several international collaborative projects such as Indo-US, Newton-Bhabha funds and Indo-Japan Collaborative calls.
- Currently, 14 projects under Joint Call with NACO are under progress.
- Seven projects are ongoing in the Indo-US HIV/STI prevention collaborative call with ICMR.

Sexually Transmitted Infections

ICMR developed a task force for research on priority areas related to STIs under which 173 proposals were received in the call for Ad-Hoc concept proposals. Out of which 40 studies have been recommended for submitting full proposals of the study and 27 studies have been considered for pooled pan-India multicentric study as the aims and objectives are similar but study sites are different.

Innovation and Operational Research related to COVID-19

- Validated X-ray based AI tool for COVID-19 diagnosis
- Developed Indian Novel Claim Portal: *inovecop*
- Six Ad-Hoc projects were conducted pan-India to assess the socio-behavioral aspects such as, stigma experienced by COVID-19 recovered people, mental health of healthcare workers, operational challenges in implementation of COVID-19 mitigations in North-East India, and impact of COVID-19 on maternal child healthcare schemes.

CAPACITY BUILDING

Capacity building for disease burden estimation and projection: Under this project, a cohort consisting of 27 scientists from 14 ICMR institutes have been developed to enhance their leadership capacities to carry forward the assessment of global burden of disease research in India.

PUBLIC HEALTH

i-DRONE study

The *i*-DRONE study was first of its kind in the South Asian region where drones were used for delivering

of COVID-19 vaccines from land to island. In this study, drones delivered 21,000 units of medical supplies including multivitamin tablets, syrups, COVID-19 vaccines and routine vaccines from district health centres to 13 primary health centres and two Community Health centres in districts Bishnupur, Imphal West and Churachandpur of Manipur and districts Mokokchung and Tuensang of Nagaland in more than 80 sorties. Additionally, training to more than 70 healthcare workers was imparted for packaging of the consignments for drone-based deliveries.

For the i-DRONE project, the first drone sortie between Bishnupur District Hospital to Karang Primary Health Centre was inaugurated and launched by Hon'ble Minister of Health and Family Welfare, Dr.Mansukh Mandaviya.

Fig. 50: Helicopter drone used for delivery of COVID-19 vaccines from District Hospital in Bishnupur to Primary Health Centre, Karang.

Fig. 51: Drone landing at Longsa village near Primary health Centre, Longsa (Mokokchung, Nagaland).

Additionally, the launch of drone sortie from Mokokchung district health centre to Longsa Primary Healthcare centre was inaugurated by District Collector, Mokokchung and Superintendent of Police, Mokokchung. Based on the findings and experiences of the *i*-DRONE activities, the Ministry of Civil Aviation proposed ICMR to develop a guidance document on use of drone which was launched in Bharat Drone Mahotsav 2022.

The acceptability and adaptability of the stakeholders and healthcare providers regarding the novel technology of drones for healthcare deliveries was also assessed through in-depth interviews. The study highlighted that the distance covered and time taken by drones was 735 kms in 11.5 hours which was much lesser in comparison to use of conventional mode for transportation which revealed that the distance was approximately 2000 kms (by road) and time taken was 56.4 hours.

Operational research in COVID-19

A set of stigma scales were developed to assess experienced stigma among COVID-19 recovered and perceived stigma of the community towards COVID-19 patients in collaboration with scientists from ICMR-NIMS.

Four guidance documents related to CVID-19 were drafted and released on the ICMR website which were of public health importance, such as:

- Guidance document for Psychosocial Counselling for COVID-19 Positive Patients and their Family members.
- Standard Guidelines for Autopsy in COVID 19 deaths.
- Manual for "Health Care Professionals" in providing "Psychosocial Support" to family members in bereavement in the time of COVID-19.
- Guidance document for Psychosocial Counselling for Healthcare providers and their family members during COVID-19 pandemic.

Two guidance documents related to i-DRONE project were drafted and released in Bharat drone Mahotsav 2022, and available on ICMR website:

- Guidance document on Use of Drones in Healthcare.
- Training module for drone-based delivery of medical supplies.

REPRODUCTIVE, CHILD & NUTRITION HEALTH

ICMR is undertaking research in the field of reproductive, child and Nutrition health through its research institutes viz. National Institute of Research in Reproductive Health, Mumbai, National Institute of Nutrition, Hyderabad as well as extramural research projects. These studies are aimed to protect and enhance the reproductive and nutritional health of people through research and development of technologies and programmes for field applications which can be incorporated into National Programmes.

INTRAMURAL RESEARCH

ICMR - NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE HEALTH (ICMR-NIRRH), MUMBAI

FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Deciphering the Putative Epigenetic Mechanisms Pertaining to Polycystic Ovary Syndrome

Peripheral and tissue-specific alterations in the global DNA methylation (5mC) and hydroxymethylation (5hmC) profiles have been charted as biomarkers for disease prediction. Global and gene-specific epigenetic alterations in the 5mC profiles have shown widespread implications in the etio-pathogenesis of polycystic ovary syndrome (PCOS). However, no attempts have been made to explore correlation between 5mC and 5hmC signatures and the levels of DNA methylating and demethylating enzymes in PCOS. Therefore, study assessed the global 5hmC levels in peripheral blood leukocytes and granulosa cells (GCs) in women with and without PCOS and found that 5hmC content is increased in PCOS women. The transcript and protein levels of DNA demethylating enzymes i.e. TET1, TET2, TET3 and DNA methyltransferases (DNMT1, DNMT3A and DNMT3B) were assessed in GCs. Relative transcript and protein levels of all three TETs were higher in PCOS and were positively correlated with 5hmC levels in GCs. Further, all three DNMTs at transcript level showed altered expression in PCOS although only the downregulated DNMT3A positively correlated with decreasing 5mC levels. These results indicate that DNA demethylation observed in the GCs of PCOS women may arise due to intrinsic alterations in transcriptional regulation of TETs and DNMT3A.DNA methylation and demethylation in an animal model of PCOS is being investigated.

Follicular Microenvironment and its Relationship with Oocyte and Embryo Quality in Women with Polycystic Ovary Syndrome

Oocyte quality is suboptimal in women with PCOS. This can be attributed to altered microenvironment (follicular fluid-FF and granulosa cells-GCs). Oocyte depends on GCs for supply of metabolites for its nourishing, as it cannot metabolize glucose. It is known that around 50-60% women with

PCOS have insulin resistance, which can influence glucose metabolism in GCs, lead to increased glycation and cell damage. Study measured the levels of advanced glycation end products (AGE) and its decoy receptor (soluble RAGE-protective in nature) in FF; and found higher AGE and lower RAGE levels in PCOS than controls. AGE levels negatively correlated with pregnancy rate and outcome in both groups. The transcript levels of SORD1 and AKR1B1 (rate limiting enzymes of polyol pathway) in GCs were upregulated in PCOS. Polyol pathway usually accounts for low activity but gets hyper-activated under metabolic stress. The study data indicates altered glucose metabolism and increase in metabolic stress in the follicles of PCOS women.

Understanding Follicular Angiogenesis in Women with Polycystic Ovary Syndrome

Angiogenesis is crucial for ovarian folliculogenesis. Study reported altered expression of several angiogenesis-associated genes/proteins in the GCs and FF of women with PCOS, which may contribute to follicular growth arrest and corpus luteum (CL) insufficiency in these women. The study reanalyzed the available microarray datasets and enlisted additional angiogenesis-related genes, which are dysregulated in PCOS. To predict miRNAs regulating dysregulated angiogenesis-related genes in the ovary of women with PCOS, we used *in-silico* approach by querying miRNA databases. The study also identified miRNA-mRNA interactions and signaling pathways involved in impaired follicular angiogenesis in PCOS. Further, analysis showed that PI3K/Akt signaling was the most enriched pathway in the ovary of PCOS. Upon validation, study found expression of some of the miRNAs associated with the PI3K/Akt pathway up-regulated in the GCs of women with PCOS. This work provides a novel insight into the mechanism of aberrant ovarian angiogenesis contributing to PCOS pathophysiology.

Unraveling Pathogenetic Mechanisms of Polycystic Ovary Syndrome by Genetic Approach

The genetic underpinning of PCOS has been studied by a variety of approaches including case-control and genome-wide association studies, however, a conclusive genetic marker for PCOS is yet to be determined. Genetic loci identified in one ethnic population do not necessarily reflect similar association in other ethnically and geographically different populations. For this, team carried out replication studies for polymorphisms previously identified in GWAS in Han Chinese women, of which rs2479106 polymorphism of DENND1A and rs1894116 of YAP1 showed significant association with increased PCOS susceptibility. The study also completed genotyping for polymorphisms in LHCGR, c9orf3 and RAB5B genes, which failed to show association with PCOS risk in our population. Additionally, the team initiated genotyping for rs853854 of MAPRE and rs1784692 of ZBTB16 genes. Consequently, the findings show that delineating the genetic predisposition of Indian women with PCOS is essential. For that reason, the team initiated a study on exome sequencing in well-characterized Indian women with PCOS. Initial analysis shows association of known and novel genetic loci with PCOS susceptibility.

Analysis of Mitochondrial DNA Sequence Variants in Polycystic Ovarian Syndrome Women with Insulin Resistance

Polycystic ovary syndrome is a common cause of infertility among women of reproductive age. Earlier the team reported altered mitochondrial DNA copy number and variants in mitochondrial DNA (mtDNA) in women with PCOS. mtDNA copy number was found to be negatively correlated with insulin resistance. In the reporting year, the team studied correlation of 60 PCOS women and 45 healthy control women and identified that mtDNA copy number is significantly negatively correlated with AMH, a novel diagnostic marker in PCOS and a marker of ovarian reserve ($p=0.049$). Investigation of mitochondrial ROS in PCOS women ($n=16$) and healthy control women ($n=6$) using a fluorescent probe MitoSOX, a red mitochondrial superoxide indicator, suggest

that mitochondrial ROS production is increased significantly in women with PCOS compared to healthy control women (p=0.022). This implies the mitochondrial dysfunction in PCOS women plays a crucial role in ROS production thereby causing oxidative stress.

ICMR Task Force Study on Estimating Prevalence, Phenotypes, Comorbidities and Risk Factors of PCOS - A Multicentric Study

This is an ongoing task force study by ICMR to estimate community based prevalence in India. NIRRCH study site recruited a total of 1086 eligible women. Out of which 145 were probable, 18 known cases and 923 controls. Clinical and lab Investigations were completed among 91 probable, 13 known and 144 controls. USG was completed among 90 probable, 12 known and 136 controls. COVID-19 pandemic resulted in large dropouts. Repeated follow-upswere done and many enrolled participants (59 probable/known) wereunwilling to come forth for further investigations or became ineligible to continue in the study or migrated and no longer in contact. The study is ongoing.

Development and Validation of Multi-Scale Dynamic and Steady State Metabolic Network Models for PCOS using Computational and Wet-Lab Methods

To accomplish the aim of developing a dynamic and steady state model for PCOS, a mathematical model of human menstrual cycle was adopted from literature and simulated to study development of PCOS phenotype. The model consisted of 71 parameters of which 28 parameters were found to be associated with PCOS phenotype. These parameters were related to hormone secretion, release, and clearance along with various stages of oocyte development. In addition, using a combination of system biology and qRT-PCR approach, it was demonstrated that FSHR antagonism might lead to PCOS-like state. Further, meta-analysis of microarray datasets associated with PCOS provided novel mechanistic insights into pathophysiology of lean and obese PCOS.

Studies to Evaluate the Effect of Metformin on Endometrial Functions

Metformin, an antidiabetic drug, has been repositioned in the treatment of several nondiabetic disorders including reproductive disorders such as polycystic ovarian syndrome. It is known to have beneficial effects on reproductive outcomes in PCOS women. However, studies addressing direct effects of metformin on endometrium are still limited and hence, this study was proposed to evaluate the direct effect of metformin on endometrium. The team previously conducted studies to profile metformin treated HEC-1A (endometrial cells) at molecular level. In the reporting year, validation experiments were carried out for certain differentially expressed genes. Of the 8 genes chosen for validation, 5 genes (MRPS34, EGR1, GDF15, ODC1 and DDIT4) showed a similar pattern of up or downregulation as revealed by microarray. While 3 genes (CYCS, EDF1 and TP53) showed a similar trend as that of the microarray analysis, but were not statistically significant. Further, higher SDHD expression in metformin treated cells corroborated with higher mitochondria number in lower concentration of metformin treated endometrial cells. *In-vivo* studies have been initiated in rat model of thin endometrium to investigate the effects of metformin on endometrial functions.

Pathways to Oncogenesis in the Pathophysiology of Endometriosis

Endometriosis is a benign condition characterized by the presence of endometrium-like tissue at extra-uterine sites. Several theories of endometriosis pathogenesis have been proposed but the exact mechanism remains elusive. Few studies demonstrate differential abundance of miRNAs in plasma and/or sera from women with endometriosis. However, there exists a lack of consensus on the identity of a non-invasive marker for endometriosis diagnosis. An integration of transcriptome and miRNome may serve as a novel approach to address this issue. In the reporting year, we searched the existing literature for microarray

and high throughput sequencing studies on mRNA and/or miRNA expression profiles of either eutopic endometrial tissues or plasma/sera of women with and without endometriosis. Since a majority of the studies focused on the secretory phase samples, these studies were selected for the reanalysis. Data submitted to GEO database were reanalyzed to identify mRNAs and miRNAs significantly ($p<0.05$) dysregulated in different studies. Cumulative scores were calculated depending upon the consistency in the expression pattern of various mRNA/miRNA across the selected studies. miRNAs known to target the differentially expressed genes in the eutopic endometrium were compared with the differentially abundant miRNAs in plasma/sera of women with endometriosis. A total of 26 miRNAs (one upregulated and 25 downregulated) emerged as a miRNA panel displaying dysregulation in women with endometriosis. Validation experiments are warranted to explore the potential of these miRNAs in endometriosis diagnosis.

Investigating the Contribution of DNA Damage, Repair and Demethylation in the Pathogenesis of Endometriosis

Endometriosis is a condition in which endometrium like cells are found outside the uterus. Our previous studies demonstrated that the eutopic endometrium from women with endometriosis encounters higher DNA damage than its control counterpart. The present study was initiated to explore if higher DNA damage observed in the eutopic endometrium of women with endometriosis is associated with alterations in the DNA methylation machinery. DNA repair protein GADD45 (Growth Arrest and DNA Damage Inducible), also involved in DNA demethylation, was found to be upregulated in the eutopic endometrium of women with endometriosis. During the reporting year, studies were conducted to investigate if the expression of MBD4 (Methyl-CpG Binding Domain 4), a DNA repair protein known for its glycosylase activity, is altered in eutopic endometrium of women with endometriosis. Initial data revealed that MBD4 is significantly increased in proliferative phase eutopic endometrium from women with endometriosis. Further, our in-vitro studies revealed increased expression of GADD45a and MBD4 in response to H_2O_2 induced oxidative DNA damage in tHESC cell line. These investigations collectively revealed that DNA damage is associated with higher expression of MBD4 in endometrial cells. Studies are being conducted to assess whether higher DNA damage is associated with alterations in the DNA methylation status in endometrial cells. The study is anticipated to provide insights into mechanisms by which the endometrium acquires differential gene expression signature in women with endometriosis.

Role of Homeobox Gene HOXA10 in the Pathogenesis of Endometriosis

The study was aimed to understand the role of the transcription factor HOXA10 in the pathogenesis of endometriosis. Endometriosis was induced in mice that were hypomorphic for HOXA10. The study observed that loss ofHOXA10 leads to epithelial to mesenchymal cell transition by activating the transcription factors like Twist2. These cells underwent fibrosis only in the ectopic but not the eutopic endometrium of HOXA10 hypomorphs.

Pregnancy Outcomes in Indian Women with Endometriosis and Biomarker Correlation: A Cohort Study

In a cohort of 204 women with endometriosis-associated infertility, we observed deep infiltrating endometriosis (DIE) as the most common lesion (40%), followed by ovarian endometrioma (OMA) [31%] and superficial peritoneal endometriosis (SUP) [29%]. Women recruited in eastern India had the highest proportion of SUP (41%). OMA was most commonly seen in the southern Indian population (40%), followed by the north Indian population (33%). The highest proportion of DIE was observed in the northern region of India (83%). The study demonstrated that women with SUP and only one type of endometriotic lesion were more likely to conceive post-surgery. Therefore, the study recommends that infertile women with endometriosis, younger than 35 years of age

with SUP or with only one lesion type should be encouraged towards natural conception or assisted reproductive technology within 6 months after surgery.

Clinical Phenotypes and Genetic Regulation of Endometriosis in Indian Women

ECGRI is a large-scale, multi-site, case-control study covering representative Indian populations of eastern/north-eastern, northern, central, western and southern geographical zones of India. Endometriosis was classified as minimal, mild, moderate and severe disease [rASRM stages: I (n=153/476, 32.1%), II (n=53/476, 11.1%), III (n=93/476, 19.5%) and IV (n=177/476, 37.2%)]. The highest proportion of endometriosis cases in all the geographic zones was diagnosed with one subtype (range 46%-83%). The proportion of women diagnosed with two subtypes of endometriosis was highest in the north zone (39%) while lowest in the south zone (10%). All three subtypes of endometriosis were reported in 18% of patients in northeast and east zone, 12% in central zone, 9% in west zone, 7% in south zone and 2% in north zone. Pain symptoms such as dysmenorrhea, dyspareunia and chronic pelvic pain were significantly higher in endometriosis cases as compared to controls.

Damage Associated Molecular Patterns (DAMPs) and their Receptors in Endometrial Repair

Endometrium is an extremely dynamic hormone responsive tissue that continuously undergoes cyclical shedding and repair during a woman's reproductive life. Endometrial repair post menstruation is highly efficient and scar-free process. Impairment in the endometrial repair may lead to heavy menstrual bleeding or menorrhagia. Initial repair of endometrium is sex steroid-independent. The team hypothesized that Damage-Associated Molecular Patterns (DAMPs) released during the menstruation may give cues to the immune cells to initiate the repair of endometrium. The team developed a rat model of endometrium breakdown and repair to understand the role of DAMPs in the endometrial repair. The preliminary analysis showed increased expression of alarmin HMGB1 and its receptor RAGE during the endometrial breakdown and repair in endometrium and uterine fluid. Studies are ongoing to identify the molecular signatures activated in response to DAMPs during endometrial repair.

Uterine Alarmins and their Relevance in Implantation

The project has been designed to understand the role of alarmins HMGB1 and S100A8 on implantation and to determine whether altered levels or loss of function of alarmins can cause immune modulation at the time of implantation. The team created an excess of HMGB1 in the uterine fluid by intrauterine administration of recombinant HMGB1 (rHMGB1) in the uterine horns of pregnant rats on day 2.5 post coitum (p.c.) to determine whether excess of rHMGB1 in the uterine milieu alters the uterine immune cell repertoire during implantation, regulatory T cells (Tregs) from the uterine draining para-aortic lymph nodes (PALN). A trend ($p = 0.0592$) towards higher frequency of Treg cells (ratio of $CD4^+FOXP3^+CD25^+$ to total $CD4^+$ cells) was observed in the PALN of rHMGB1-treated animals as compared to that of sham control. Furthermore, a higher frequency of pan macrophage marker $CD68^+$ cells at the implantation site was observed in HMGB1-treated animals. However, the number of anti-inflammatory M2 macrophages (cells co-expressing CD68 and CD163) were found to be lower at the implantation sites of HMGB1-treated animals as compared to sham control animals. Flow cytometric analyses of uterine macrophages revealed reduced number of activated M2 macrophages ($CD163^+CD86^+MHCII^+$) in the endometrium of HMGB1-treated animals. Thus, these results suggest that excess of HMGB1 in the uterine microenvironment leads to altered immune profile during implantation, which may contribute to implantation failure. Experiments will be performed to determine whether reduced levels of HMGB1 also affect implantation and alter immune profile. These studies may help us understand the

role of alarmins in implantation and implantation failure.

Identification and Preparation of Radiolabeled Modulator of hFSHR for Therapeutic Applications

Systematic review and data extraction of 161 experimentally validated FSHR LMW modulators from published literature. Using molecular docking experiments, the potential FSHR binding sites of these modulators were identified and these sites were then mapped to the FSHR modulating activity documented for the binders. Six novel peptidomimetics with potential FSHR modulating activity were identified and validated by measuring cAMP levels in HEK-rFSHR cells. Structural analysis of docked complexes revealed that all six peptidomimetics displayed H-bond interactions with Asp521 of FSHR.

MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Functional Significance of Testis Specific Histone H2B Variant (TH2B) in Spermatozoa and Early Embryonic Development

Sperm retained histones and their variants are some of the significant epigenomic contributions of the father to the embryo. Two such histone variants, TH2A and TH2B, escape spermiogenic nuclear remodeling and are retained in the mature sperm. Importance of TH2A and TH2B in histone eviction during spermiogenesis is well acknowledged. However, their significance post spermatogenesis is not clear. The team previously identified the genomic loci associated with TH2B in human sperm. In the reporting year, the study analyzed the genes associated with TH2A(TAAGs) and TH2B(TBAGs) in mature mouse sperm. The team observed a degree of conservation between human and mouse TBAGs that included genes crucial for embryo development. Additionally, it was found that although TH2A and TH2B share the same bidirectional promoter, their genomic distributions are very diverse. TH2B is enriched at genomic coordinates important for spindle assembly and meiosis specific genes and embryo development was the most significant term amongst TBAGs. TH2A was highly enriched with mitochondrial function or mitochondrial encoded genes.

Microtubule (Mt) Dynamics and Sperm Function: Involvement of Tubulin Acetylation/ Deacetylation

This study highlights the role of Microtubule (MT) acetylation-deacetylation and microtubule associated proteins (MAPs) in sperm motility. The team investigated α-tubulin polymerization in rat- and human sperm flagella and its influence on sperm motility, using HDAC6 inhibitor- Tubastatin A and a depolymerizing agent, Nocodazole. The study observed that Tubastatin A neutralized motility debilitating/depolymerizing effect of Nocodazole when incubated in combination. The team also observed that HDAC6 demonstrated MAP-like behavior. In asthenozoospermic men, the levels of polymerized axoneme, MT stabilizing protein – SAXO1 and expression as well as activity ofHDAC6, were reduced. Mass spectrometry analysis of MAP fractions - and HDAC6 interacting protein in human sperm, revealed 'Tubulin complex' and sperm anomalies like 'Asthenozoospermia', respectively, as significant terms by Gene Ontology (GO). In addition to MAPs, human homologs of a few MT inner proteins were identified. LFQ quantification identified the proteins differentially expressed in sperm of normozoospermic and asthenozoospermic men.

Unravelling Sperm Epigenetic Landscape Regulated by Estrogen Receptors in Adult Male Rats

Since several endocrine-disrupting compounds encountered in the environment are estrogenic in nature and are known to cause adverse effects on the reproductive health, it is important to understand the role of estrogen receptors in modulating the sperm epigenome and subsequently male fertility. The project aimed to elucidate changes in the sperm DNA methylation patterns after selective estrogen

receptor agonist treatments in adult male rats, which could contribute towards decrease in fertility observed after these treatments. Whole genome bisulfite sequencing was initiated to decipher the DNA methylation changes in the sperm epigenome. Genomic feature distribution revealed that majority of the differentially methylated CpG sites lie within the intergenic regions, followed by intronic regions. Small percentage of these sites were also located in the -10kb upstream region from the TSS, promoter regions, exon and 3' end regions of the genes. Further data analysis is ongoing.

Unravelling the Sperm Epigenetic Landscape in Infertile Men with Clinical Varicocele

Varicocele is one of the leading causes of male infertility. Elevated oxidative stress has been implicated as a key factor in varicocele associated male infertility. High oxidative stress during spermatogenesis may affect sperm mitochondrial functions and lead to epigenetic modifications in spermatozoa. The study suggests that infertile men with varicocele have significantly lower sperm count, motility, intact morphology and viability compared to healthy fertile control. Varicocele group shows a significantly lower mitochondrial membrane potential (MMP), high mitochondria copy number and higher intracellular reactive oxygen species than healthy fertile controls. Increased Sperm DNA fragmentation and low testosterone level were also detected in varicocele group. The methylation level of genes involved in mitochondrial functions such as UQCR2, MIC60 and LETM1 was found to be altered in men with varicocele. Therefore, decreased MMP, high mitochondria copy number, increased iROS and altered methylation levels of mitochondrial genes indicate sperm mitochondrial dysfunction in men with varicocele. Further studies are underway to investigate the methylation landscape in spermatozoa of men with varicocele.

Development and Validation of a PCR Based Technology for Detection of Yq Microdeletions in the Diagnosis of Male Infertility

Herein, the team aims to develop and validate an assay for the detection of Yq microdeletions, as a major genetic cause of male infertility. Using previous datasets, the team developed a multiplex PCR using 16 STS markers that can detect Yq microdeletions. Reproducibility, sensitivity and specificity were tested. The technology was transferred to the industry partner through ICMR. The assay will be validated at different centers across the country for its sensitivity and specificity.

Understanding the Molecular Mechanisms of Gonadal Development in the Mouse

The present study aims to understand the involvement of Lim homeobox gene Lhx2 in the XX and XY gonads. For the first time, study reported that Lhx2 is expressed by the germ cells in the developing ovaries. Using mice that lack Lhx2, team identified that in the developing XX gonads there is ectopic vascularization in the XX gonads. This was due to a disruption in the expression of angiogenesis-related genes. The study highlights the role of germ cell suppression of vascularization of developing ovaries. Currently, the roles of Lhx2 in the developing male gonads are being explored.

RTI/ STIS/HIV/ MICROBICIDES

Development of a Multistrain Probiotic Lactobacillus Formulation Effective against Reproductive Tract Infections

The team investigated 100 vaginal Lactobacillus isolates for their ability to produce exopolysaccharides. Two lactobacillus isolates were shortlisted based on their ability to produce exopolysaccharides and biofilms. These two lactobacillus isolates, identified as *L. salivarius* and *L.reuteri*, inhibited the growth of urogenital pathogens including Candida. The purified exopolysaccharides also exhibited anti-bacterial, anti-fungal and anti-cancer activities *in vitro*.

In-vitro Evaluation of Vaginal Lactobacilli Isolated from Indian Women for Potential Anti-Cervical Cancer Activity and Elucidating its Possible Mechanism of Action

Four Lactobacillus isolates among 327 vaginal isolates were identified to have potent anti-proliferative activities on HPV 16 and 18. The inhibitory effect of their metabolites on *in vitro* migratory ability of the cervical cancer cells (HeLa and SiHa cell lines) was observed. Further, antimicrobial susceptibility testing of the lactobacillus isolates revealed that they were resistant to eight antifungals and seven antibiotics mainly comprising of quinolones and aminoglycosides. A few lactobacillus isolates were subjected to whole-genome sequencing analysis which indicated differences in genome size, GC%, SNPs, INDELs, CRISPR cas genes, exopolysaccharide biosynthesis genes, presence of plasmids and phages. Comparative genomics analyses provided an insight into the characteristics of the Lactobacillus species which may help them adapt to the vaginal environment. The results revealed inter-species differences in numerous protein families suggesting that each species has experienced lineage-specific gene gain and loss to develop unique repertoire of protein families.

Role of *Gardnerella vaginalis* Membrane Vesicles in Pathogenesis of Bacterial Vaginosis

Gardnerella vaginalis is the predominant anaerobe associated with bacterial vaginosis. Our previous work demonstrated the cytotoxic potential of membrane vesicles (MVs) produced by *G. vaginalis*, towards vaginal epithelial cells. In continuation with these observations, studies on the effect of *G. vaginalis* MVs on epithelial cells lining other regions of the female reproductive tract such as the cervix (HeLa) and endometrium (HEC-1A) revealed significant variations. The extent of MV induced cytotoxicity was maximum in HEC-1A cells and least in HeLa cells. Likewise, induction of the pro-inflammatory cytokine, IL-8 was highest in HEC-1A and least in HeLa cells. The results thus suggest the possibility of *G. vaginalis* MVs induced pathogenesis in a distal location such as the endometrium, which is also the site of occurrence of polymicrobial biofilms containing *G. vaginalis.*

Molecular Characterization and Antifungal Resistance of *Candida glabrata*

A total of 19 *Candida glabrata* strains were retrieved from previously obtained vaginal isolates. Antifungal susceptibility testing was performed for four azole and two echinocandin drugs. Selective PCR amplification of six *Candida glabrata* housekeeping genes (FKS, LEU2, NMT1, TRP1, UGP1 and UR) was carried out followed by sequencing of the amplicons. Multi-locus sequence typing (MLST) of the isolates and characterization of the azole resistance genes is in progress to examine the correlation with the observed phenotypic resistance.

Three Dimensions of *Mycoplasma genitalium* Infection - Detection, Cure Rate and Co-Infections in Women Attending STI Clinics

This project is joint collaboration with Brihanmumbai Municipal Corporation, MDACS and Regional RTI/STI centre, Nair Hospital, Mumbai. The project focused on emerging STI pathogen *Mycoplasma genitalium*, its detection rate and coinfections among women clinically diagnosed with lower genital tract infections and attending STI Clinic, Nagpada. Total 193 women have been recruited and the prevalence of *Mycoplasma genitalium*was 7.2%. The mean age of the recruited women was 32.9±5.7 years, 84.8% have multiple sexual partners, 91.7% belong to the upper lower strata of socioeconomic class and 53.9% were using public or common toilet facility. Among coinfections, *Neisseria gonorrhea* was detected in 3.5% (n=8), *Chlamydia trachomatis* in 2.2% (n=5) and *Trichomonas vaginalis* in 1.31% (n=3).

Longitudinal Cohort Study to Evaluate the Effect of Various Contraception Methods on the Composition and Diversity of the Vaginal Microbiota

This project is a joint collaboration with Nowrosjee Wadia Maternity Hospital to map the baseline vaginal microbial (VMB) composition of women

attending a community clinic in Mumbai and to map the changes in vaginal health status before and after using various contraception methods by diverse methods. Healthy sexually active women in the age group of 18-45 years visiting a community clinic in Mumbai for their contraceptive needs are being recruited as a part of a longitudinal contraception cohort study. A cohort of 79 women using various contraceptive methods: barrier, intrauterine devices, injectable contraception, LNG IUCD and control group have been formed and followed up. Evaluation of vaginal microbiome profile showed that the most abundant at phylum and class level were *Firmicutes* (60.8%) and *Bacilli* (55%). The predominant genus was *Lactobacillus* (51.10%) and at species level maximum were *Lactobacillus iners* (34.3%). Women with bacterial vaginosis had significantly higher abundance of *anaerococcus*, *peptoniphillus* and *Dialister*. There is evidence of restoration of VMB after 12 months of childbirth with significant decrease in *Bifidobacterium*. No specific genus showed up statistically with respect to age, menstrual cycle and sexual and hygienic practices.

Highly Dampened HIV-specific Cytolytic T cell Responses Define Viremic Nonprogression

The study aims to identify gut trafficking potential and virus specific functional attributes that could underlie the paradoxical virus-host equilibrium observed in Viremic Non Progressors (VNPs), a distinct group of HIV-1 infected individuals who remain asymptomatic for several years (>7 years) and have good preservation of CD4 count without ART treatment but display high viral replication. The study revealed that Gag-specific IFN-γ response in CD4+ central memory (CM) compartment associates with viremic control while dampened Env-specific CD107a response in CD4+ effector memory (EM) characterizes VNPs. In CD8 compartment, VNPs tend to maintain lower proportion of Env-specific CD107a response while keeping higher proportion of MIP-1β response similar to putative progressors (PuPs). Cytolytic activity is primarily limited to polyfunctional cells in Viremic Non-Progressors. Reduced frequency of α4β7 expressing (gut homing) CD8 memory subsets suggested a reduced gut pathology in VNPs. HIV-specific T cell responses in Viremic Non-progressors are modulated towards a dominant non-cytotoxic response enriched for MIP-1β production with concomitantly dampened degranulation ability. Understanding the complex mechanism underlying protection in VNPs may allow immunotherapeutic interventions to achieve functional cures in the context of ART resistance.

Immune and Microbiome Correlates of TB Reactivation in PLHIV and a NHP Model

India bears a high burden of cases of TB/HIV coinfections. The present study seeks to elucidate both innate as well as adaptive immune correlates for their utility as prognostic markers for TB reactivation following HIV infection in tertiary health care setting based in Mumbai, India. Immunophenotyping of 101 participants was completed by flowcytometry. For 87 participants, IGRA reports were generated and shared with the clinical collaborators. Frequency of type 3 innate lymphoid cells (ILC3) was found to be significantly decreased in HIV+ LTBI+ and HIV+ LTBI - groups compared to both HIV-LTBI+ and HIV-LTBI- groups. A rebound in ILC3 frequency was observed in 6 months post ART follow up samples of HIV+LTBI+ individuals. ILC3 frequencies showed a significant positive correlation with absolute CD4 count in all study groups, though no significant correlation was observed with the viral load. Reduction of circulating ILC3s frequency in LTBI+ individuals with HIV may alter maintenance of protective lymphoid follicles within granulomas leading to an increased risk for latent TB reactivation. Increase in ILC3 frequency after 6 months of ART is indicative of restoration of gut barrier integrity and thereby reducing possibility of latent TB reactivation.

Harnessing T Cell Exhaustion for the Treatment of Immunopathology Associated with Excessive Immune Response to Inflammatory Agents

Infection with emerging or re-emerging pathogens results in self-injury and immunopathology due to excessive immune reaction. Available immunosuppressive drugs have undesired side effects and are unsafe during pregnancy. Team investigated the effect of different exhaustion marker agonists (rTIM-3, rCTLA-4 and rPD-1) in reducing the expression of activation markers (CD25 and HLADR) on the surface of T cell subsets (CD4+, CD8+ and γδ+ T cells. A549 lung epithelial cell line was stimulated with synthetic viral mimic-Poly I:C and subsequently co-cultured with peripheral blood mononuclear cells (PBMCs). Treatment of PBMCs with combination of rTIM-3 and rCTLA-4 significantly decreases the expression of activation marker-HLA-DR on the surface of CD3+CD4+, CD3+CD8+ and CD3+γδ+ T cells. In the same group, a significant upregulated expression of exhaustion marker-Tim-3 on the surface of these T cell subsets was also observed. The study also found poly I:C induced IFN-γ production from A549 cells.

Identification and Validation of Potential Drug and Drug-Targets for Infectious Diseases Using *in Silico* and Wet Lab Methods

Validation was done of two novel aspartyl protease inhibitor peptidomimetics that demonstrated higher inhibitory effects against *Candida* spp. in combination with fluconazole as compared to fluconazole alone. By *in vitro* assays identification and validation of two repurposed drugs showing potent antifungal activity was done. Screening and identification of novel peptidomimetics was carried out against *Candida* SAP2, an important virulent factor, using docking and MD simulation studies.

MATERNAL AND CHILD HEALTH

Enhancing Male Participation in Interventions to Prevent Unintended Pregnancy

Gender equity in family planning interventions is posited to be an important means of supporting women's reproductive decision well as to improve modern contraceptive use. There is a need to educate males too on family planning methods, marital communication and joint decision making in family building. The CHARM2 intervention involves five sessions of family planning and gender equity counseling, two gender synchronized sessions delivered separately to husbands and wives by sex-matched health providers and a final session for the couple provided by either the male or female provider who delivers the individual sessions for the couple, whomever is available. Overall, the findings suggest that the intervention supports joint contraceptive decision-making, contraceptive use, marital communication over time in short-term effect and increased male engagement.

Understanding the Molecular Basis of Embryo Implantation

In this project, the team aims to investigate the fundamental mechanisms by which embryos breach the endometrial epithelium and the control of decidualization of stromal cells. The study observed that at the site of implantation, in the luminal epithelial cells there is a switch in the expression of markers associated with epithelial to mesenchymal transition (EMT). The team observed that this EMT occurred due to the loss of HOXA10 and the activation of NLRP3. Mice treated with NLRP3 inhibitor had implantation failure and the luminal epithelial cells did not undergo EMT. Further, decidualization was also compromised in mice treated with NLRP3 inhibitor. We are currently dissecting the molecular targets of HOXA10 in endometrium and investigating how NLRP3 mediated inflammasomes control decidualization.

Genetic and Epigenetic Changes in Imprinted Genes in Male Partners of Women Experiencing Recurrent Spontaneous Abortions

The project aimed to elucidate the paternal epigenetic factors that could contribute to idiopathic recurrent spontaneous abortions (RSA). It was found that aberrant DNA methylation patterns in several imprinted genes involved in embryo development in spermatozoa of male partners in couples experiencing unexplained RSA. In order to

determine whether the methylation levels of these imprinted genes can be used as a diagnostic marker to identify epigenetically abnormal spermatozoa, the team used multiple logistic regression and combined the average methylation levels of five differentially methylated genes into a probability score (between 0-1). A threshold of 0.61 was set for the probability score with a specificity of 91.78% and sensitivity of 65%. This was further experimentally validated in an independent cohort of 38 control and 45 RSA spermatozoa samples. The validation results revealed that 97.36% of control samples were correctly classified below the threshold and a subset of RSA cases (40%) had abnormal methylation levels. The study proposed that the combined DNA methylation levels of these imprinted genes can be used as a diagnostic tool to identify spermatozoa samples with epigenetic defects, which could contribute to the pathophysiology of RSA.

Idiopathic Recurrent Pregnancy Loss: Possible Association of Paternal Exposure to Endocrine Disruptors and Epigenetic Modifications in Sperm

Endocrine disruptors are known to affect sperm epigenome. Investigations are underway to explore the possible association between paternal exposure to endocrine disruptors and sperm epigenetic modifications of iRPL couples. Whole Genome Bisulfite Sequencing of sperm DNA samples was used to identify differentially methylated CpG (DMC) sites in sperm of iRPL cases compared to fertile control sperm. A total of 9497 DMCs with highest enrichment in intronic regions were obtained and 2087 differentially methylated genes were noted. DMCs within genes relevant to embryo and placenta development were selected to further validate their methylation levels in the study population by pyrosequencing. DMCs within genes *PPARG*, *KCNQ1*, *SETD2* and *MAP3K4* showed hypomethylated sub-populations within iRPL study population. The study highlights the altered methylation landscape of iRPL sperm and their possible implications in embryo and placental development. The CpG sites that are hypomethylated specifically in the sperm of iRPL sub-population can be further assessed as predictive biomarkers.

Understanding the Role of Cannabinoid Receptors in Placental Calcium Transport

Placental calcification commonly increases with gestational age and becomes apparent after 36 weeks' gestation. The preterm placental calcification may hinder the uteroplacental blood flow and adverse fetal outcome. The gestation day 18.5 placentae were collected from gravid C57BL/6 females for explant culture and treated with cannabinoid receptor 1 (Cnr1) agonist N-arachidonyldopamine (NADA) or antagonist (AM251). To study the calcium deposition, the placentae were cultured with or without $CaCl_2$ in the presence of NADA or AM251. The expression of cannabinoid receptors and calcium transporters was upregulated. Alizarin Red S staining in placental tissues done to assess calcium deposit was found increased in Cnr1 agonist treated placental tissues. The findings suggest that Cnr1 may contribute towards placental calcification.

Detection of Infections Associated with Preterm Births

The aim of this study is to develop and validate a multiplex PCR assay for the detection of common bacterial species that are associated with preterm births. The team shortlisted eight bacteria that are commonly found in the vagina of women with preterm delivery and a multiplex PCR is optimized. The team is currently prospectively testing high vagina swabs of women who delivered preterm and term for validating the assay.

Maternal Near Miss Review and Corrective Measures at District and Women's Hospitals in Maharashtra

Government of India released operational guidelines for Maternal Near Miss - Review (MNM-R) in December 2014 designed for use

by program managers at different levels of public health system. This information is used to bring health system improvement aimed at reduction of maternal morbidity and mortality. MNM-R is complementary to Maternal Death Review. The objective was to implement these MNM-R guidelines developed by Government of India and take corrective measures at the District and Women's hospitals (Nasik, Parbhani, Ratnagiri, Akola and Nanded) in Maharashtra. The total number of MNM cases identified and forms filled in software at all District/Women's Hospital during April 2018-March 2022 were 460. Out of these, hemorrhage (64.6%) was the most common adverse event followed by hypertension (23%). MNM meetings were conducted at all the selected district/women's hospitals. After meeting, minutes were prepared, corrective measures were recommended based on three-delay model by the MNM Committee and corrective measures were taken by these hospitals accordingly. The findings of the District MNM study suggest that it is feasible to implement MNM-R guidelines at the district hospitals. However, there is need to revise the guidelines with respect to MNM facility based form and critical review of the criteria. Challenges at this level are lack of dedicated staff for this activity, inadequately filled case sheets leading to difficulty in identifying MNM cases, lower case load of MNM as many cases are referred out leading to lack of a separate committee for MNM. The study findings have been communicated to district and state government. These will be useful for implementation of the MNM-R guidelines of Government of India at the district hospitals in the country.

Implementation of Dakshata Program to Improve Quality of Institutional Deliveries in a Tribal Block of Maharashtra

Dakshata program aims to reduce maternal deaths resulting due to sub-optimal care provided during labour and delivery by providing competency based training to health providers. Despite a rise in institutional deliveries, districts with substantial tribal population still record higher maternal mortality. Objective of the present study was to document the enabling factors and challenges affecting implementation of Dakshata program at four government facilities with high delivery load - Dahanu, Jawhar, Kasa and Wada in Palghar district of Maharashtra. Assessment was carried out using checklists from program guidelines. Status of human and material resource, availability of supplies, adherence of staff to critical practices and compliance to standard protocols was recorded. To understand system bottlenecks, 17 key informant interviews were conducted. Shortage of staff and unavailability of specialist doctors makes management of obstetric complications difficult. Majority of the staff was untrained. Utilization of Safe Childbirth Checklist was poor. Supply of essentials was affected by poor coordination between district and state. Support and handholding from health authorities was required and maintaining records and data was deemed a secondary priority. Findings were disseminated to state health and maternal health care providers by a dissemination meeting. Strategies encouraging coherence between various levels of healthcare must be promoted for effective implementation of the Dakshata program to improve quality of care in the underserved tribal areas. A larger implementation study to address the gaps identified in the formative research is planned in the selected tribal area.

Population Based Birth Defect (BD) Surveillance in Linkage with Rashtriya Bal Swasthya Karyakram (RBSK) Programme in Rural Blocks of Palghar District in Maharashtra

This ongoing surveillance project is being implemented at MRHRU Dahanuto to estimate prevalence of Birth Defects (BDs) in children upto 6 weeks age in seven rural blocks of Palghar district. At present, there is no database on BD except for data collected from screening done through RBSK Mobile Health teams. Therefore, the project has been linked with RBSK to utilize existing resources and in turn strengthen the BD component

of RBSK. Through this project, a BD registry will be developed and maintained at PHC, RH and SDH. To avoid missed diagnosis at community level, trainings are being conducted for ASHAs to identify BDs during home based neonatal care (HBNC) visits. For training purpose, IEC materials like information booklet, flyer and video have been developed. A total of 1905 ASHAs were trained in total 38 PHCs of Palghar district. A total of 117 birth defects were registered at facility level. Thirty nine cases of birth defects were reported by ASHAs through Block Facilitators till March 2022. Birth defects were also verified through RBSK compiled data. From April 2021 to March 2022 - 67 birth defects were reported through RBSK. Total birth defect cases (facility, ASHAs, RBSK) from April 2021 to March 2022 after removing of duplicates was 155. Data analysis was conducted for the first quarter of data collection to measure prevalence, types, age and sex wise distribution of birth defects. Among the visible birth defects, cleft lip/ palate followed by club foot were commonly reported.

Development of a Non-Invasive Evaluation Protocol for Detection of Congenital Cytomegalovirus Infection in Newborns

Newborn screening is important for early diagnosis and management of congenital infections such as cytomegalovirus (CMV) infection, a leading cause of childhood mortality and morbidity. A hospital-based study was conducted for detection of CMV infection in 500 neonates by PCR, using a non-invasive sampling strategy. The results revealed that use of multiple, non-invasive samples such as saliva, urine and stool resulted in higher birth prevalence (16%) compared to that with only saliva samples (1.6%). Validation of this approach in studies with larger sample size will aid its eventual implementation in national programs aimed at comprehensive newborn healthcare management.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and the Effect of Early Intervention in Management of the Disease in Tribal Populations: Research cum Intervention Study

This ICMR Task Force study is implemented through seven centers across the country and NIRRCH is one of the centres. The study is being conducted at Dahanu block of Palghar District (SDH-Subdistrict Hospital, Dahanu and Kasa, PHCs). Sickle cell disease has the highest prevalence amongst tribal ethnic groups with an increased risk for severe morbidity during first 3 years of life. Currently, there is no national neonatal screening programme in India and children are identified only when they become symptomatic. The present study is undertaken to understand the magnitude of the sickle cell disease and to understand the barriers for undertaking such programme and to measure the benefit of early comprehensive care of affected babies. It also aims to evaluate the genotypic and phenotypic correlation to understand role of genetic modifiers for disease severity. From April 1, 2021 to March 31, 2022, 3438 deliveries were conducted at both sites, out of which 2087 samples were screened by HPLC. A total of 172(8.24%) heterozygous babies were detected. Ten (0.48%) babies were detected to have disease. Out of these, seven were found to have Sickle Cell disease and three were HbS - Beta Thal Compound heterozygous. The babies are being followed up at 6 weeks for confirmation of diagnosis and for screening of family members as per the protocol followed by genetic counselling. Sickle cell homozygous babies were started on pneumococcal vaccinations and prophylactic antibiotics from 3 months age as per the standard of care and are being followed up to 3 years of life.

Community-based Screening and Management of Latent TB among Under-Five Children from Urban Slums in Mumbai

The diagnosis and treatment of Latent TB infection (LTBI) forms an important aspect of WHO's End TB Strategy. The present study is a community based study in urban slums in collaboration with a tertiary hospital and health post (MCGM), aiming to screen under-five children at risk for LTBI as per WHO guidelines. The study also aims to assess acceptability of testing and adherence to treatment

of LTBI among parents. Total 369 eligible children have been enrolled and screened for LTBI using Tuberculin Skin Test (TST), CBC and IGRA by QuantiFERON-TB Gold Plus. It was observed that total number of IGRA positives was 46 (12.46%), out of which 39 (10.56%) were TST positives and 7 (1.89%) were TST negative. Total TST positives accounted to 79 (21.40%) and 39 (10.56%) were TST negative. IGRA results were indeterminate among 26 (7.04%) children. Active tuberculosis was ruled out amongst children suspected for LTBI. Children with LTBI completed their INH prophylaxis at BJ Wadia Hospital-TB Clinic as per the guidelines. Children with LTBI are being followed up at the Clinic as per the protocol.

Exploring Clinical and Therapeutic Relevance of Novel Biomarkers among the Children Presenting with Idiopathic and Incomplete Precocious Puberty at Tertiary Hospital, Mumbai

Precocious Puberty (PP) comprises of central, peripheral or incomplete variants. Central PP is most common and idiopathic central precocious puberty (ICPP) contributes to almost 90% in girls. Precocious Puberty is mainly associated with adverse outcomes such as risk of short stature, PCOS, Diabetes mellitus-1, metabolic disorders in later life and most detrimental effect is psychosocial stress. Currently ICPP poses significant diagnostic and therapeutic challenge. Few studies have shown that Kisspeptin, Neurokinin B, Neuropeptide Y and MKRN3 are involved in the PP pathophysiology. This project seeks to explore the clinical and therapeutic relevance of these potential novel biomarkers. The study will evaluate whether altered levels of these markers contribute to ICPP and incomplete PP. So far, 153 girls have been screened, out of which 36 girls have been enrolled as controls, four cases as ICPP and four as early puberty (PT). Circulating serum/plasma levels of Kisspeptin, Neurokinin B, Neuropeptide Y and MKRN3 have been evaluated from these study participants. Kisspeptin and Neuropeptide Y levels were marginally higher in ICPP as compared to controls. There was no difference in the circulating levels of Neuropeptide Y in ICPP and in PT cases. Validation and standardization of kits for the estimation of Neurokinin B and MKRN3 is ongoing.

Role of Kisspeptin Mediated Signaling in Onset of Puberty

Inactivating mutations in the neuropeptide kisspeptin-1 (KISS1) or its cognate G-protein coupled receptor, the kisspeptin-1 receptor (KISS1R) can lead to hypogonadotropic hypogonadism (HH) or delayed puberty whereas activating mutations can cause precocious or early puberty. Identification and characterization of mutations in KISS1/KISS1R is therefore important in order to gain insights into the pathophysiology of pubertal disorders. Four naturally occurring heterozygous mutations $R^{38}P$, $P^{46}Q$, $S^{125}L$ and $R^{198}G$ in KISS1R, reported in HH, were generated *in vitro* using site directed mutagenesis. As compared to Wild type (WT) KISS1R, all the four mutant receptors exhibited low cell surface receptor expression. Consequently, KISS1 stimulated inositol phosphate production was also lower in cells expressing the mutant receptors as compared to those expressing WT KISS1R. Thus, these mutations caused an impairment in receptor function.

A Study on Depressive symptoms in Lower and Middle Socio-Economic Status Urban Post-Menopausal women with Osteoporosis and its Effect on Quality of Life

A pilot study was conducted to study the association of depressive symptoms among lower and middle-income urban post-menopausal osteoporotic women (50-75 years) and their quality of life. Women (n=100) were screened for depressive symptoms by Patient Health Questionnaire-9 (PHQ-9) and Quality of Life by using WHO-QOL BREF-26 questionnaire was undertaken. The preliminary analysis revealed depressive symptoms as follows - mild depressive symptoms (17%), moderate depressive symptoms (4%) and moderately severe depression (1%) with 78% of women having no

symptoms of depression. Significant association of depressive symptoms with physical domain (61±13 SD v/s 86±11 SD), psychological domain (74±16 SD v/s 85±10 SD) was observed. Association of depressive symptoms with physical domain can be explained as 78% women had various musculoskeletal problems, which can affect the quality of life among the menopausal osteoporotic women.

GENETIC RESEARCH CENTRE

Building and Analyzing Gene Network associated with Polycystic Ovary Syndrome

PCOS is one of the most common causes of anovulatory infertility. While several genes have been reported to be associated with PCOS, the genetic etiology is incomplete and not well understood. Network analysis and gene prioritization are powerful insilico approaches for the identification of novel candidate genes. Approximately, 2000 probable candidate genes expressed in the ovary were predicted to be associated with PCOS. The study also found ~ 300 genes encoding secretory proteins among the 2000 predicted candidates. Coagulation and complement cascade was identified as the most prominent pathway among the predicted secretory proteins to be associated with PCOS. These predicted candidates are a useful resource that can be explored experimentally for their association with PCOS.

Identification and Characterization of Genetic Factors Associated with Multiple Morphological Abnormalities of Sperm Flagella

Male infertility can result either due to quantitative or qualitative defects of spermatogenesis. In recent years, morphological (motility and flagellar defects) are more commonly defined as a new syndromic phenotype characterized by multiple morphological abnormalities of the sperm flagella (MMAF). Individuals with MMAF show sperm morphology abnormalities, aberrant flagellar phenotypes (no flagella, short flagella, coiled flagella, bent flagella and/or irregular flagella) and seriously impaired sperm motility. Standards for the evaluation of MMAF differs from other conditions of teratozoospermia and asthenozoospermia (such as primary mitochondrial sheath defects and primary ciliary dyskinesia) and is primarily characterized by axonemal defects. Genomic studies of the MMAF phenotype in the past five years had shown that MMAF is a genetically heterogenous condition and ~18 genes were identified to induce MMAF and thus male infertility. However, the frequency of MMAF phenotype and the underlying genetic cause of MMAF among Indian infertile men is unknown. Hence, this study is primarily aimed at the identification and characterization of genetic causes associated with MMAF in infertile men from India. Three patients have been recruited till date.

Comprehensive Genetic Evaluation of Fetus in Antenatally Detected Abnormal Pregnancies with Fetal Malformations: Outcomes, Benefits and Limitations - a Pilot Study

Fetal malformations are the major causes of recurrent spontaneous abortions. Chromosomal abnormalities, microdeletion/duplication and single gene defects are the major causal agents. Hence, genetic evaluation of abortus material/ fetus is very important. The study aims to identify genetic mutations associated with fetal malformations in an Indian cohort, evaluate the efficacy of the available genetic platforms and use the data generated for effective genetic diagnosis and possible management options. Karyotype analysis of the POC samples of twelve malformed fetuses identified Downs Syndrome (Trisomy 21) as one of the causes of fetal malformation.

Identification and Evaluation of Novel Metabolites with the Potential of Prenatal Diagnosis of Fetal Congenital Heart Diseases

This project proposes to perform untargeted metabolomics using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and nuclear magnetic resonance (NMR)-mass spectroscopy (MS) to measure all detectable metabolites present

in different biological samples collected from women with congenital heart diseases (CHD) fetus (n-75) and age-matched healthy pregnant women with healthy fetus (n-75) in 11-24 weeks of gestation. The study may provide novel insights into the metabolomics of CHD, as the Indian context varies with unique dietary habits and geo ethnic risk factors. The study is translatable and has therapeutic potential in the diagnosis and treatment of CHD. This may also help in conducting prenatal counseling, timely obstetric management and postpartum diagnosis. The ethical approvals, recruitment of staff and design of the work plan are in process.

STEM CELL BIOLOGY

Functional Study of Voltage-Gated Calcium Channel Gene Mutations in Schizophrenia using Induced Pluripotent Stem Cells (iPSCs): A New Approach for Developing a Cellular Model

Schizophrenia is a complex neuropsychiatry disorder in which patients loses touch with reality. Genetic etiology of this disorder is not well established, however, the heritability as high as 80% makes it most heritable among common neuropsychiatric disorders. The aim of the project is to find to identify candidate genes to elucidate the genetics of Schizophrenia and further modelling it through iPSCs. Whole exome sequencing analysis revealed involvement of 6 coding variants in 5 genes. Among these variants, PIGQ gene has two pathogenic variants, one nonsense NP_683721.1:p.W634X and the other in-frame deletion NP_683721.1:p.E74_F80del. Four variants are found to be missense and their pathogenicity have been analysed using in-silico approach. Two missense variants (NP_065743.2:p.E377G in GALNT16 and NP_055383.1:p.P641S in GALNT5) have variable damaging score, however, the other two variants namely NP_891550.1:p.T957P in ADAMTS9 and NP_001036009.1:p.Y1500C in LTBP4 have highest damaging score. Further analysis has showed that the variant NP_891550.1:p.T957P in ADAMTS9 gene was found to be significant and was present in the thrombospondin repeat motif, one of the important motif of ADAMTS9 protein. Detailed molecular dynamics (MD) simulation study on this variant showed damaging effect on structural stability of the ADAMTS9 protein.

Genetic and Biochemical Characterization of Mitochondrial Oxidative Phosphorylation (OXPHOS) Disorders in Children

Oxidative phosphorylation (OXPHOS) disorder also known as mitochondrial disorders are a complex family of disorders with a vast array of clinical manifestations. OXPHOS mutations produce disease that affects a variety tissues, organs or organ systems, having more energy demands like muscles, nervous system, brain etc. Due to its clinical heterogeneity, large number of children remained undiagnosed. Moreover, lack of diagnostic facility is also a major limiting factor for confirmatory diagnosis in India. This research study is an attempt to develop a diagnostic method using a combinatorial approach of biochemical and genetic analysis. Muscle biopsy samples were collected for 30 controls and 2 patients. Biochemical enzymatic assays for complex I-IV and citrate synthase (CS) have been carried out in muscle homogenates of control samples; average activities would be used for determining enzyme deficiencies in patient's samples. Upon analysis of two patient samples, one sample found to have complex II deficiencies.

Investigating the Effects of Neonatal Exposure to Estrogen and DES on Mouse Testicular Stem Cells

It was previously demonstrated that testicular dysgenesis syndrome has a stem cell basis and that various pathologies can be reversed by transplanting mesenchymal stromal cells and by treating with XAR (nano-formulation of resveratrol). In the reporting year, detailed studies were undertaken to understand how testicular cancer initiates upon DES treatment. Sixty five percent of DES treated mice developed testicular cancer-like changes

associated with increased expression of OCT-4, PCNA, Ki-67 and cancer stem cell marker CD166 along with minimal expression of PTEN, MVH, c-KIT and SOX-9. Excessive expression of OCT-4 in the VSELs initiated testicular cancer. Reduced 5-methyl cytosine expression suggested global hypomethylation and led to increased expression of *Igf-2 and Dlk-1* along with reduced expression of *H19* and *Meg-3,* which pushed VSELs out of their quiescence and initiate cancer. Transcriptome analysis of FACS sorted SSEA-1 positive VSELs was undertaken by low-input RNAseq and showed dysregulation of transcripts and pathways associated with cancer and stemness after DES treatment.

Studies on Ovarian Stem Cells (OSCs)

The study team was able to track various events during oogenesis from very small embryonic like cells (VSELs) across estrus cycle, which leads to oocytes formation and primordial follicle assembly in adult mice ovaries under normal physiological conditions. Further evidence was accumulated in the reporting year to support this by BrdU uptake studies. BrdU positive stem cells differentiated into oocytes and BrdU incorporation was detected in the oocytes present in the primary, secondary and pre-antral follicles within 15 days of BrdU injection. This suggests that follicles form and mature on regular basis in adult ovaries. This data is suggestive of a possibility that ovarian senescence/menopause occurs because of stem cells dysfunction. VSELs and OSCs exist along with increased numbers of germ cell nest (GCNs) arrested in pre-meiotic or early meiotic stage in aged ovaries and primordial follicle assembly is blocked possibly due to age-related changes in their microenvironment.

Investigating the Effects of Follicle Stimulating and Steroid Hormones on Uterine Stem Cells

Further evidence to suggest that VSELs are indeed the most primitive and yet elusive stem cells in the uterus was provided in the reporting year. VSELs enriched from GFP mice, upon transplantation in wild type mice showed their differentiation into epithelial cells lining both the lumen and the glands within the same estrus cycle. In addition, upon mechanical scratching, OCT-4 positive stem cells get activated and regenerate the endometrium. Further experiments were undertaken to delineate a possible role of VSELs in the initiation of endometrial cancer. Various 'uteropathies' including non-receptive uterus, hyperplasia, adenomyosis, endometriosis, endometrial cancer and *leiomyomata* are caused due to the dysfunctions of VSELs. The team showed that dysfunctional VSELs and epithelial progenitors migrate to the myometrium / perimetrium (adenomyosis) or ectopic sites in mice neonatally exposed to endocrine disruption to expand and differentiate into endometriotic tissue.

Neonatal Exposure to Estrogen and its Effects on Adult Mouse Prostate Stem Cell Biology

Studies have been undertaken to show the presence of VSELs and their characterization in adult mouse prostate. VSELs were found to express follicle stimulating hormone receptor (FSHR). Androgen deprivation by bilateral castration resulted in prostate atrophy, but VSELs survived and increased in numbers. FSH treatment (5 IU/day for 2 days) resulted in increased numbers of VSELs along with up-regulation of alternately spliced FSHR isoform *Fshr-3* whereas canonical *Fshr-1* was not detected. On the other hand, DHT (50 µg/kg for 7 days) exerted a moderate effect compared to FSH. Prostate differentiation and function as well as prostate cancer growth are believed to be androgen-dependent. The results presenting VSEL driven regeneration of atrophied prostate by FSH are surprising and question the current clinical practice of orchidectomy to manage prostate cancer patients. Although, androgen deprivation results in prostate cancer atrophy but concomitant increased FSH levels are possibly responsible for resurgence and death of patients due to the highly aggressive castration-resistant prostate cancer.

Evaluating the Role of Hypoxia in Human Embryonic Stem Cells (KIND1) Differentiation towards Trophoblast Lineage

Fetal growth is supported by placenta and failure of proper placental development can compromise embryonic development and lead to complications like miscarriages, stillbirth, pre-term labour, pre-eclampsia and intra-uterine growth restriction. Early development of placental trophoblast cells is poorly studied due to limited sample availability and ethical concerns. Availability of a proper human model is highly warranted to investigate early trophoblast development. The study differentiated in-house derived human embryonic stem cell line (KIND1) into trophectoderm lineage. The differentiated cells were characterized by expression of trophoblast specific markers namely, Gata3, Tfap2a, Tfap2c, Cga and Cgb. Further studies are underway to optimize this protocol to obtain detectable levels of hCG in spent media. The team has also planned to develop placental organoids to study the effects of hypoxia during differentiation.

NATIONAL CENTRE FOR PRECLINICAL REPRODUCTIVE AND GENETIC TOXICOLOGY

An Endocrine Disrupter- Atrazine Induced Epigenetic Regulations in the Male Germ Line Following Perinatal Exposure

Atrazine (ATR), an endocrine disruptor, has been associated with altered endocrine and reproductive functioning in-vivo in animals exposed during the critical window of development. Thus, the present study investigates the effect of ATR exposure on F1–F2 male progeny exposed through gestation and lactation. F0 dams were administered with ATR at 2, 10, 70 and 100 mg/kg b. wt/day from gestation day 6 to postnatal day 21. The F1 male rats were assessed for sexual maturation and fertility on PND75. Delayed testicular descent was observed in 10, 70 and 100 mg/kg b. wt/day ATR dose with significantly lower serum testosterone, sperm count and motility with testicular defects. Expression of Androgen receptor (AR), Estrogen receptors (ER α and ER β), StAR, Aromatase and INSL-3 were upregulated at all doses indicating estrogenic/antiandrogenic activity of ATR. Fertility assessment revealed subfertility in F1 males with high pre- and post-implantation losses at 10, 70 and 100 mg/kg b. wt/day dose as compared to control. Further, F2 fetuses exhibited congenital disabilities viz. decreased weight, crown-rump length and anogenital distance with several other morphological deformities. To conclude, ATR exerted estrogenic and/or anti-androgenic activity with fetotoxic effects through the male germline.

Deciphering the Molecular Mechanism of Triclosan on Hypothalamus Pituitary Gonadal Axis

The present study was undertaken to decipher the molecular mechanism of Triclosan (TCS), an antimicrobial agent, on hypothalamus-pituitary-gonadal axis and to investigate the effect of TCS exposure on male reproductive system through epigenetic mechanism. During the reporting year, studies were undertaken to observe the transgenerational effect upon perinatal exposure to TCS at different doses (0.1, 4, 40 and 150 mg/kg b. wt. /day). The F1 male and females from respective groups were mated with naïve female and males respectively. F2 animals were sacrificed at different time intervals. At day 75, the F2 male showed decrease in % motile and % progressive sperm in the treated groups as compared to control groups. There was a significant decrease in daily sperm production as well as organ weight in the treatment group as compared to control group. There was an increase in serum levels of estradiol and a decrease in testosterone in the treatment group as compared to control group.

Identification and Characterization of Sertoli and Leydig Cell Homing Peptides

Sertoli Cell Homing Peptides (SCHP) and Leydig Cell Homing Peptides (LCHP) were previously identified using phage display peptide library. The molecular target of SCHP2 was initially identified using affinity purification mass spectrometry (APMS). During the reporting period, the target of SCHP1 was identified using the same approach. The

results show that the target of SCHP1 is HSPA2, HSPA8 or HSPA9 proteins. Cellular uptake study of the SCHP1 and SCHP2 was performed using TM4 cells and HEK293 cells using confocal microscopy. The results show the uptake of the SCHP1 and SCHP2 by TM4 cells but not by HEK293 cells, which confirms specific homing potential of the SCHP1 and SCHP2 peptides to Sertoli cells.

Exploring the Therapeutic Potential of Peptides Targeting Lysophosphatidic Acid Receptors in Ovarian Cancer

In ovarian cancer, elevated levels of Lysophosphatidic acid (LPA) and aberrant expressions of LPAR 2 and 3 activate the downstream signaling cascades resulting in cell proliferation, invasion and migration causing metastasis. There are no potential drugs available that can target the LPARs in ovarian cancer. Targeting LPAR with LPAR binding peptide may disturb LPA-LPAR interaction and delay ovarian cancer metastasis. The present study aims to identify the peptides targeting LPAR using phage display library approach. In the preliminary study, differential expression of LPARs (1-6) proteins was evaluated in human ovarian cancer cell line (OVCAR3). LPAR3 was found to be overexpressed followed by LPAR2. We selected LPAR3 as a target for the identification of peptide targeting LPAR3 in ovarian cancer. Three rounds of *in vitro* panning was carried out using rLPAR3 as a bait by Ph.D-12 phage display library. Future plan is to deduce the 12 mer peptide sequences displayed by the M13 bacteriophages by Sanger sequencing/NGS. The most frequently occurred peptide sequence will then be commercially synthesized and validated *in vitro* and *in vivo*.

Evaluation of Drugs-Cytochrome P450 Enzyme Interaction through Fluorometric High Throughput Screening Assays

Cytochrome P450 superfamily has been implicated as one of the most important drug-metabolizing enzymes because it metabolizes a wide range of pharmaceuticals. In the proposed study, ayurvedic formations were studied for their herb drug interaction (HDI) against the key marker, human CYP isoforms CYP1A2, CYP2C9, CYP2D6, CYP2E1 and CYP3A4. During the drug development process, it is vital to include preclinical (in vitro) and clinical (in vivo) interaction studies. So, these hundred formulations are validated by in-vivo and in-vitro studies for their HDI. The structure for 45 active principles of 30 traditional medicinal formulations was downloaded from the PubChem database. The molecular docking of 45 active principles with Cyp450 was performed using the CDOCKER docking optimization tool. A total of 10 conformations were generated for each active principle. Best conformation was selected based on their interaction with key residues (hydrogen bonding and pi-stacking), similar to their respective inhibitors and CDOCKER INTERACTION scores. Ricinoleic acid and Chlorogenic acid are the two main active principles that showed higher interaction scores and interactions with key residues similar to respective inhibitors in all four crystal structures of human cytochrome P50 isozymes.

REPRODUCTIVE CANCERS

PSP94 as an Adjunct Marker for Serum PSA for Differentiating between Benign Prostatic Hyperplasia (BPH) and Prostate Cancer (PCa)

Serum prostate specific antigen (PSA) test is used globally for prostate cancer screening, however, its low specificity causes diagnostic dilemma and a number of patients have to undergo unnecessary biopsies. The objective of this study was to assess the utility of PSP94/PSA ratio (PP Index) in minimizing referrals for prostate biopsies in patients having lower urinary tract symptoms and with PSA levels between 4-20 ng/ml. Based on PSA alone, 100% of the participants in the PSA range of 4-20 ng/ml were recommended for biopsy whereas if PP Index with a cut off value of ≤5.26 had been used, ~50% of prostate biopsies could have been avoided. At a cut off of ≤5.26, the PP Index had a sensitivity of 100% and specificity of 53.49%. PSP94 test when done in addition to PSA

(PP Index) in patients having PSA levels between 4-20 ng/ml, it can better discriminate between prostate cancer and BPH.

Investigating the Key Elements in Estrogen Signaling and their Contribution to Prostate Cancer

Estrogens elicit a myriad of cellular functions through estrogen receptors (ERs) i.e., ERα/β mediated genomic and non-genomic signaling. Unlike genomic signaling, wherein ERs on binding to estrogen translocate to the nucleus to regulate transcription of genes, non-genomic signaling is initiated at the plasma membrane or extranuclear sites. In addition to ERα/β, GPR30, a non-conventional ER, is also reported to be present on the plasma membrane. We previously demonstrated the presence of ERs on the plasma membranes of androgen-dependent and independent prostate cancer cell lines. Activation of these receptors using cell-impermeable estradiol led to increased invasion and migration *in vitro*. However, it is not clear whether estradiol induced effects are mediated through the conventional ERs present in plasma membrane or through GPR30. During the reporting year, studies were conducted to identify the role of GPR30 in prostate cancer. The expression of GPR30 was assessed at the transcript level in different prostate epithelial cell lines. GPR30 was found to be high in LNCaP (androgen-dependent cell line) followed by PC3 (androgen-independent cell line), RWPE (normal) and least was expressed in DU145 (androgen-independent cell line). GPR30 knockdown stable PC3 clones demonstrated increased migration and invasion in comparison to empty vector transfected stable clones. Further, *in vivo* tumorigenic ability of GPR30 knockdown clones is being assessed using NODSCID mice.

Deciphering the Mechanisms of Innate Immune Surveillance in Prostate Cancer for Immunotherapy Salient Achievement -*Ex vivo* Anti-Prostate Tumor Activity of a Recombinant Fragment of Human Surfactant Protein D (rfhSP-D): Induction of Immunogenic Cell Death and Immunomodulation

Surfactant protein D (SP-D) is emerging as a potent anti-tumoral innate immune defense molecule. Both early and late stages of prostate cancer in the transgenic mouse model (TRAMP) showed significantly decreased SP-D transcript and increased proteolytic degradation of SP-D protein suggesting impaired SP-D levels may contribute to PCa progression. Further, these studies provided a rationale to use an elastase inhibitor (Sivelestat) along with the exogenous supplementation with a recombinant fragment of human surfactant protein D (rfhSP-D) to sustain the functional efficacy in the protease enriched tumor micro-environment of murine tumor explants. The *ex vivo* study revealed that the combined therapy has a significant immunomodulatory potential and induced tumor macrophage polarization towards M1 and immunogenic cell death (ICD). The findings highlight that rfhSP-D plays an anti-tumorigenic role in PCa by transforming an immunologically unresponsive "cold tumor" into a responsive "hot" tumor.

Trop2 in Ovarian Cancer: Evaluating its Potential as Immunotherapeutic Target

Trop2 is an important therapeutic target for multiple solid cancers including ovarian cancer. Monoclonal anti-Trop2 antibody drug conjugate has got FDA approval. In an attempt to identify immunodominant epitopes of Trop2 for active immunization, the team purified truncated Trop2ECD protein (Trop2-172) and used for immunization of rats. The anti-Trop2-172 sera could detect native Trop2 protein expressed by ovarian cancer cells by immunoblotting as well as flow cytometry. The immune sera when tested in ADCC (antibody directed cytotoxicity assay) exhibited cytotoxic effect against Trop2 positive cancer cells indicting their capability to identify and target Trop2 positive cancer cells.

Assessing Trop2 Expression and Anti-Trop2 Immune Status in Ovarian Cancer Patients

Ascitic fluid and sera from 35 ovarian cancer patients were subjected to exosome isolation and detection of Trop2 protein as well as its interaction partner claudin-7. Trop2 as well as claudin-7 were found to be present in the ascitic fluid derived exosomes, however, their levels varied. The levels of these proteins are being correlated with the Trop2 and claudin7 transcripts present in the cells present in the ascitic fluid. This data may help in utilizing these molecules as prognostic markers for ovarian cancer.

Expression of Natural Killer and Natural Killer T Cell Receptors and their Association with Ovarian Cancer

The study aimed to characterize the immune profile of chemo naïve primary debulking surgery (PDS) group, chemo treated interval debulking (IDS) group and during follow up of different cycles of chemotherapy of high grade serous epithelial (HGSOC) patients. One hundred and twenty serous epithelial ovarian cancer cases and fifty healthy individuals were enrolled as control (HC) to achieve these objectives. The study highlighted a reduction in the frequency of circulatory $CD56^{B}$ NK, $CD56^{D}$ NK, NKT-like and T cells with activating receptors and alteration in immune subsets with inhibitory receptors, indicating the differential immune profile of primary and recurrent ovarian cancer patients. Increased soluble MICA in the serum of cancer cases might act as "decoy" molecule and could be a probable mechanism of decrease in NKG2D positive subsets. An elevated level of serum cytokines IL-2, IL-5, IL-6, IL-10 and TNF-α observed in ovarian cancer patients may help to identify the cytokines associated with ovarian cancer progression and their possible use as biomarker. Clinical and immunological parameters were found to be associated with progression free survival of the disease.

A Study on Expression of miRNAs in Tissue, Tumor Derived Exosomes and Body Fluids in Ovarian Cancer

The study highlighted a differential expression of specific miRNAs such as miR-182; miR-433 and miR-145 in the serum of ovarian cancer patients in comparison with healthy controls, suggesting their possible use as prognostic marker in ovarian cancer.

Primary Screening of High Risk HPV DNA by a Low Cost Molecular HPV Test for Early Detection of Cervical Precancers and Cancers among Women in Urban and Rural Community of Maharashtra

Out of 1038 women recruited in the project, 680 women were from an urban site (Abhyudaya Nagar) and 353 women were from a rural site (Dahanu). HPV DNA positivity by HC2 test was seen in 5.45% women,while the HPV positivity by care HPV test was 4.08%. Most common genotype by gene Xpert was HPV16 followed by 18 and other HR HPV Acetowhite lesion after application of 5% acetic acid (VIA test) was seen in 5.63% women. PAP results revealed ASCUS in 10 women, HSIL in 4 women and LSIL in 4 women. All the screen positives are being followed up in preventive oncology department, Tata Memorial hospital, Mumbai.

Identification of Circulating MicroRNA Signatures as Diagnostic Markers for Early Stage and Metastatic Breast Cancer

The study is being carried out to identify subtype-specific molecular profiles of differentially expressed miRNAs associated with early stage and metastatic breast cancer and to evaluate circulating microRNA signatures as biomarkers for determining the response to drug therapy and treatment outcome. The approvals of ICMR-NIRRCH Ethics Committee, Saifee Hospital and Mumbai Oncocare Hospital ethical committees were obtained. So far, breast tissues and blood samples of 30 breast cancer patients and blood samples of 10 healthy controls have been collected. The expression of miR-20b, miR-141, miR-205, miR-143, miR-26a and miR-374 was evaluated in blood samples of

patients by real time PCR. The expression of miR-141 and miR-205 which have been associated with breast cancer in earlier studies was found to be significantly higher in blood samples of breast cancer patients compared to healthy controls. For identification of novel miRNAs and cancer-related miRNAs specific to the Indian population, samples have been sent for Next Generation Sequencing and the data is awaited.

Role of Toll-like Receptors and Toll-like Receptor Agonists in Modulating Response to Chemotherapy in Triple Negative Breast Cancer Patients

The objective of the study is to analyse the Toll like receptor (TLR) expression in triple negative and identify the therapeutic efficacy of relevant TLRs associated with progression and prognosis of TNBC. The study indicates that targeting TLR4/TL8 genes along with IFNG could be a potential therapeutic strategy for treating triple-negative breast cancer patients.

Deciphering the Placental-Breast Epithelial Cell Cross Talk in Pregnancy associated Breast Cancer

The study aims to understand the effect of placental-breast epithelial cell cross talk and its relevance in pathogenesis of pregnancy associated breast cancer. Preliminary studies indicate that placental cell secretions regulate the cell proliferation/migration/clonogenic abilities of breast cancer cells.

Improving Access for Screening of Common Cancers and Non-Communicable Diseases (NCDs)Among Women in Tribal Block of Maharashtra: Challenges in Implementation

The study is a joint collaboration between ICMR-NIRRCH and District health system. In the first phase, training of master trainers, formative research using qualitative research tools like FGDs of eligible women and ASHAs, key informant's interview of CHOs and ANMs, facility survey was done to assess readiness of health system. Cervical (VIA and HPV testing), breast and oral cancer screenings were done. Also testing for common NCDs by doing blood pressure, RBS and Hb were done. Endocervical samples were tested for common RTIs. Barriers were transportation, time spent at the public health care facility and behaviour of the staff. ASHAs were found as the key connecting link between women and health system. ASHAs needed incentives for transport and some financial remuneration. Hence, ASHAs need to be incentivized to improve awareness and health seeking behaviour. There was lot of hesitancy among women to come for screening due to the fear of COVID. Health care facilities need to be upgraded in terms of infrastructure, equipment and trained manpower to implement screening services.

HEALTH TECHNOLOGY ASSESSMENT

HTA on Use of Tranexemic Acid in Management of PPH

The existing Indian guidelines on PPH management framed in 2015 recommends using tranexamic acid if oxytocin and other uterotonics fail to stop bleeding or if bleeding is partly due to trauma. The updated WHO recommendation has not yet reflected in Indian guidelines or the DAKSHATA checklist. For lack of guidance, Department of Health Research, Ministry of Health and Family Welfare, Government of India from Government of Maharashtra received a policy question regarding cost effectiveness of Tranexamic acid use in PPH management. A decision analytic model was built using a decision tree to determine cost-effectiveness of administering IV TXA within 3 hours of birth to existing management with uterotonics and supportive care to women with PPH. Results reveal that with an estimated annual cohort of 5,10,915 PPH cases in India, addition of IV TXA would result in a per-patient disaggregated societal cost of INR 6607 (USD 95) with discounted gain of 20.25 QALYs as compared to INR 6486 (USD 93) with discounted gain of 20.17 QALYs with existing standard care for PPH management. At an ICUR value of INR 1470 per QALY gained (USD

21), addition of IV TXA is cost-effective in Indian public health settings. The intervention is likely to prevent 389 maternal deaths, 177 surgeries and 128 ICU admissions per 100,000 PPH cases. Policy guidelines, training manuals and facility checklists should be updated to reflect this recommendation.

COVID-19 RESEARCH

Opposing Roles for sMAdCAM and IL-15 in COVID-19 Associated Cellular Immune Pathology

Using an integrated approach of monitoring inflammatory and mucosal migratory markers together with a key homeostatic cytokine and the gut microbiome in a cohort (n=130) of SARS-CoV-2 infected individuals we were able to show distinct depletion profiles, with relative sparing of CD8 effector memory and CD4+ regulatory T cells in hypoxemic disease within the lymphocyte compartment. An apparent increase in the frequency of intermediate monocytes characterized both mild as well as hypoxemic disease. IL-6 levels inversely correlated with those of sMAdCAM and both markers showed converse associations with observed lympho-depletion suggesting opposing roles in pathogenesis. Interestingly, IL-15, a key cytokine involved in lymphocyte activation and homeostasis, was detected in symptomatic individuals but not in healthy controls or asymptomatic cases. Further, plasma IL-15 levels negatively correlated with T, B and NK counts suggesting a compensatory production of this cytokine in response to the profound lymphopenia. Finally, higher levels of plasma IL-15 and IL-6, but not sMAdCAM, were associated with longer duration of hospitalization. Our results highlight key systemic and gut-associated parameters that need to be monitored and investigated further to optimally guide therapeutic and prophylactic interventions for COVID-19.Gut microbiome dysbiosis was observed in COVID-19 patients with symptomatic infection along with a putative protective microbiome signature in individuals with asymptomatic infection. These were further found to be associated with systemic immune responses as well as clinical features of infection.

National Registry of Pregnant Women with COVID-19 in India

More than 8000 pregnant and postpartum women with COVID-19 are registered in the Preg Covid registry. Data of 4203 pregnant women collected during the first wave of the COVID-19 pandemic (March 2020-January 2021) reported 6% pregnancy/foetal loss including stillbirths in Maharashtra. The most common complication was preterm delivery (16.3%) and hypertensive disorders in pregnancy (10.1%). The overall case fatality rate (CFR) in pregnant and post-partum women with COVID-19 was 0.8 %. During the second wave of the COVID-19 pandemic, five times higher severe COVID-19 cases, 8 times higher maternal deaths, 2 times higher stillbirth rate per 1000 births, 3 times higher spontaneous abortion rate per 1000 births, 3 times higher very spontaneous preterm births (28 to 32 weeks of gestation) were observed in pregnant and postpartum women admitted at BYL Nair Hospital, Mumbai. The evidence generated from PregCovid registry was useful for policy decision on COVID-19 vaccination in pregnant women in India.

Understanding Mother to Child Transmission of SARS-CoV-2

The study is aimed at identifying the determinants of congenital transmission of maternally acquired SARS-CoV-2. Maternal swabs, blood plasma, placental tissue and fetal cord blood plasma were collected from pregnant women infected with SARS-CoV-2. We identified a proportion of women who have a systemic infection with and without placental infection. A subset of these women mounted an immune response of antibodies against SARS-CoV-2 and transmitted it to the baby. Studies are ongoing to profile the placenta for the transcriptome changes to identify gene networks altered in response to SARS-CoV-2 infection.

Occurrence and Dynamics of SARS-CoV-2 Infection in Unvaccinated and Vaccinated Population of Mumbai, India

A retrospective analysis of the occurrence and dynamics of SARS-CoV-2 infections and their correlation with vaccination status was carried out. The RT-PCR cycle threshold (Ct) data of confirmatory genes of SARS-CoV-2 was retrieved from the in-house database for samples collected between December 28, 2020 and August 30, 2021. A total of 42,415 samples suspected of SARS-CoV-2 infection, received from unvaccinated cases (96.88%) and vaccinated cases (3.12%) were analyzed. A lower incidence of SARS-CoV-2 infection in fully vaccinated cases (5.07%) compared to partially vaccinated cases (6.5%) and unvaccinated cases (13.453%) was recorded. The vaccine efficacy (VE) in clearing the SARS-CoV-2 infection was highly significant after the first dose of vaccination. Similarly, the SARS-CoV-2 infection was significantly controlled within 30 days after first dose of vaccination through 60 days after second dose of vaccination. While Covaxin and Covishield vaccination offered protection against SARS-CoV-2 infection, the emergence of new infections persisted despite vaccination. A high viral load was observed in women and senior citizens in comparison to men and individuals with age <60 respectively. In addition, the viral loads in partially vaccinated individuals were observed to be high as compared to individuals who had taken the second dose and those who were unvaccinated.

MISCELLANEOUS

ICMR National Snakebite Project on Capacity Building of Health Systems on Prevention and Management of Snakebite Envenomation including its Complications

India is the snakebite capital of the world with about 60000 annual deaths occur due to snakebite envenomation (SBE). Poor farmers, shepherds, tribal and migrant population are largely affected by SBE. Based on the model of prevention and management of snakebites developed by NIRRCH, Indian Council of Medical Research (ICMR)-National Task Force Expert Group for 'Research on Snakebite in India' recommended upscale of the Dahanu model to a Health System Research project using a similar multi-sectoral approach for attaining the 2030 WHO goal of reducing snakebite deaths by 50%. The national snakebite project is an interventional study being conducted in Shahapur and Aheri blocks of Maharashtra and Khordha and Kasipur blocks of Odisha. As of 31 March 2022, retrospective data of about 504 snakebite cases has been collected and 28 community FGDs have been conducted in the study blocks.

PUBLIC HEALTH

Infertility and Associated Disorders

- The centre demonstrated that women with superficial peritoneal endometriosis (SUP) and only one type of endometriotic lesion were more likely to conceive post-surgery. This evidence is useful for counselling women with endometriosis, younger than 35 years of age with SUP or with only one lesion type for natural conception or ART within 6 months after endometriosis surgery.
- N-Formyl L-Aspartate was identified as a novel sperm chemoattractant using a microfluidic chip developed in house.

RTI / STI / HIV / MICROBICIDES

- Studies carried out on selected Lactobacilli suggest that they could be explored as biotherapeutics against cervical cancer.
- Identification of important pathways and novel genes of Candida spp. through in silico methods that can serve as potential drug targets.

Maternal and Child Health

- The CHARM2 intervention involved five sessions of family planning and gender equity counseling, two gender-synchronized sessions delivered separately to husbands and wives

by sex-matched health providers and a final session for the couple provided by either male or female. It was effective in increasing contraceptive use, marital communication and women's contraceptive agency among young married couples in rural India.

- An online database for precocious puberty (Precocity DB) was developed.

Disease Informatics

- Multimorbidity Risk Prediction for Schizophrenia (MRPS) is an open access comorbidity analysis tool developed for predicting the risk of morbidities in schizophrenia, based on shared gene-disease associations. It can be freely accessed by clinicians and researchers for assessing risk of comorbidity in individuals with schizophrenia at http://www.mrps.bicnirrh.res.in

Reproductive Cancers

- PSP94 as an adjunct marker along with PSA has the ability to differentiate between prostate cancer and BPH at PSA levels between 4-20 ng/ml and thus can help clinicians in better decision making for reducing prostate biopsies.
- Significantly elevated level of soluble MICA, a ligand of NKG2D, serum cytokines IL-2, IL-5, IL-6, IL-10 and TNF-α observed in ovarian cancer patients, may be used as a prognostic marker of ovarian cancer and can predict the treatment outcomes.
- Levels of specific miRNAs such as miR-182(low); miR-433 (high) and miR-145(low) in the serum of ovarian cancer patients in comparison with healthy controls, suggest their potential as a prognostic marker in ovarian cancer.
- Anticancer potential of TLR4/8 genes as candidates for improving chemotherapy response in triple negative breast cancer patients was identified that would be beneficial for treating triple negative breast cancer patients.

Health Technology Assessment

- HTA study shows that adding Tranexemic Acid to the management of PPH saves more lives, prevents surgical interventions or ICU admissions and is cost effective. The results were communicated to the Maternal Health division for incorporating the same into the guideline and Dakshata program.

COVID-19 Research

- The findings and research publications of PregCovid registry were communicated to Director General, ICMR to facilitate the policy decision for vaccination of pregnant women in India.
- It was observed that COVID-19 positive cases with Ct values ≥31 requires reduced duration to remove SARS-CoV-2 and thus, shorter isolation period for this group might be considered in order to facilitate adequate space in the Covid Care Centres
- Highlighted the importance of preparing appropriate guidelines for early diagnosis and treatment of mucormycosis in COVID-19 infected pregnant women
- Documentation of clinical characteristics, outcomes and mortality in pregnant women in the first and second wave of COVID-19 in Maharashtra, India

PATENT

- PCT application number PCT/IN2022/050237 for our Indian patent application no. 202111030956 titled "A pharmaceutical composition with a recombinant fragment of human surfactant protein-D for pulmonary infection including SARS-COV-2" was filed on March 15, 2022.
- Patent Application Number: 202211019761 titled "Vaginal Lactobacilli for urogenital health" was filed on March 31, 2022

ICMR- NATIONAL INSTITUTE OF NUTRITION (ICMR-NIN), HYDERABAD

Assessment of nutritional status of below 12 years children of Muzaffarpur District, Bihar - A rapid nutritional assessment

A rapid study was carried out to assess the nutritional status of the children in litchi growing areas of Muzaffarpur district of Bihar, where an outbreak of Acute Encephalitis Syndrome (AES) was reported. It was found that the children were subsisting on inadequate diets, both quantitatively and qualitatively. The same reflected in their nutritional status - the prevalence of underweight (AES: 31.6% & non-AES: 25.1%) and stunting (AES: 47.7% & non-AES: 38.7%) among children under 5 was high. Anaemia was high among 3-5 years children (47.7%) and children below 3 years (76.4%). The prevalence of B12 deficiency was 45.4% in children 3-5 years and 58.6% in children below 3 years. All the deceased children were from underprivileged or marginalized communities. Most children reportedly consumed Litchi fruits and were exposed to hot sun during summer. Litchi fruits contain hypoglycin A or Methylene cyclopropylglycine (MCPG) known to cause hypoglycemia and metabolic derangement. Therefore, parents were sensitized not to allow their children to skip the night meal and play outdoors in hot sun.

Efficacy of screen and treat approach for anaemia reduction among women of reproductive age

The efficacy of screening followed by treatment with iron-folic acid tablets as per the Anaemia MuktBharath (AMB) guidelines was studied among women of reproductive age (WRA), along with changes in iron status biomarkers. Young WRA (n=470), aged 17-21 y, were screened for their venous blood hemoglobin (Hb) and treated with IFA for 90 days according to their grade of anaemia, or if non-anaemic, administered prophylactic IFA, and then followed-up additionally for 9 months. At baseline, anaemia, iron deficiency (< 15 mg/L plasma ferritin) and iron deficiency anaemia (< 12.0 g/dLHb and < 15 mg/L Plasma ferritin) prevalence were 69.6%, 68.7% and 62.4% respectively. At the end of 90 days of IFA treatment, anaemia, ID and IDA prevalence reduced by 40%, 47.3%, and 4%, respectively. Moreover, significant treatment effects persisted at 365 days of follow-up with 0.5g/dL decline in mean Hb compared to 90 days. These observations suggest that screening and administering tailored doses of IFA treatment in addition to the regular IFA prophylaxis in non-anaemic WRA is efficacious in reducing the prevalence of anaemia and improving their iron status, and that the combined effects largely persist for 9 months after cessation of treatment.

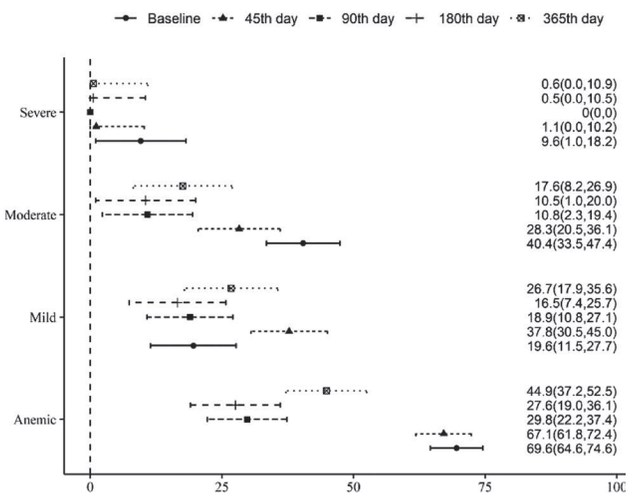


Fig. 1: Prevalence of Anemia(%).

Development of prebiotic noodles containing galactooligosaccharides

The study aimed to develop prebiotic (such as galactooligosaccharides) formulated noodles. Twelve different formulations of noodles were prepared and subjected to nutrient and sensory evaluation. The nutritional analysis showed increase in the protein content in the formulation containing Maida (74%) +Defatted Bengal Gram (DFBG) (20%) + galactooligosaccharides (5%) +1g Micronutrients (MN). The percent of carbohydrates were high in the formulation [Maida (95g) + galactooligosaccharides (5g)].

The results showed 75% acceptability for Maida noodles compared to 22% for Maida (74%) +DFBG (20%) + galactooligosaccharides (5%) +1g Micronutrients (MN)], 26% for wheat (95%) galactooligosaccharides (5%), 52% for Maida (95%) galactooligosaccharides (5%).

Consumption pattern of artificial sweeteners used in food products and as table top sweeteners among normal, overweight, obese and type II diabetes individuals located in major metropolitan cities of India

This study examined the consumers' knowledge of artificial sweeteners and quantifying levels of high intensive sugars present in various food products available. The survey on the consumption pattern of artificial sweeteners among type II diabetic subjects indicated that 86% of individuals consumed table top sweeteners. The preference for these artificial sweeteners were 27% saccharine, 25% sucralose, 23% aspartame, 10% stevia, and 4% acesulfame K. About 74% of dieticians did not recommend using artificial sweeteners, while 26% recommended AS for weight management and glycemic control. Among the Artificial sweeteners, stevia (28%) and sucralose (15%) were most recommended by the dieticians. The content of sweeteners in various food products quantified using HPLC and TLC indicated that they were in accordance with Acceptable daily intake (ADI).

Resistant starch of plant foods and its hypoglycemic effect in human

This study aimed to determine the resistant starch (RS) content in commonly consumed foods and to develop certain low GI/GL food products which may be useful for people with Diabetes. Twenty one different samples were analysed including, cereals, pulses, roots and tubers and vegetables. In cereals, high resistant starch content was present in jowar (5.717 g/100g), in pulses - red gram dal (29.4 g/100g), in roots and tubers -Colocasia (45.7 g/100g) and in vegetables - plantain (39.88 g/100g).Effect of different processing methods increased the resistant starch in cereals due to retro gradation and reduced RS content in pulses as well as in roots and tubers due to starch gelatinisation and solubilisation and starch lipid complexes respectively. Dry heat- reduced RS content due to dextrinization. Moist heat increased RS content due to gelatinisation. The food product developed using different ratios of wheat and plantain had different levels of sensory acceptability scores. These low glycemic index food products can be considered as a potential food alternative for control of Type 2 diabetes.

Effect of maternal protein restriction on body composition and protein quality control processes in the skeletal muscle of the offspring

Several studies suggest that maternal protein content and source can affect offspring health. However, chronic impact of maternal quality and quantity protein restriction, and reversible changes upon rehabilitation on body composition, and protein quality control (PQC) processes in skeletal muscle in offspring is not known. This study examined the effects of maternal low-quality protein (LQP) and low-protein (LP) intake from preconception to post-weaning, followed by rehabilitation from weaning on body composition, glucose-homeostasis, metabolic factors, skeletal muscle (SM) proteolysis, ER stress, autophagy and ubiquitin -proteasome system (UPS) in rat offspring. Wistar rats were exposed to LQP or LP isocaloric diets for 7 weeks before pregnancy to lactation. After weaning, offspring were either continued on these diets or rehabilitated with normal protein (NP) for 16 weeks. LQP and LP offspring had lower body weight, fat and lean mass, insulin and HOMA-IR than NP. LQP-offspring had higher cholesterol, T3, T4, lower triglycerides, glucose, while the same were unaltered in LP than NP. Interestingly, LP-offspring showed augmented PQC processes and increased SM protein degradation than NP-offspring. Majority of above outcomes were reversed upon rehabilitation. These results suggest that chronic exposure of rats to a maternal LQP and LP diets induced differential

adverse effects by lowering body weight, fat, lean mass and skeletal muscle proteolysis which were reversed upon rehabilitation.

Development of α-crystallin mini chaperone peptides as therapeutic molecules for diabetic ocular diseases

The protective and therapeutic effects of individual α-crystallin peptides and their combination in a 3:1 ratio in diabetic cataract and retinopathy were investigated in a rat model and cell lines. Even though systemically administered, α-crystallin peptides did not prevent hyperglycemia, however, they delayed cataract progression and preserved retinal function in the diabetic rats. Furthermore, α-crystallin peptide administration reduced the aggregation and insolubilization of protein. Additionally, hyperglycemia-induced oxidative and ER stress were also attenuated upon α-crystallin peptides administration. α-Crystallin peptides alleviated the hyperglycemia-induced apoptosis by reducing the caspase-3 activity and Bax levels. Additionally, α-crystallin peptides attenuated ER stress and oxidative stress in HeLa cells. α-Crystallin peptides preserved the retinal function, delayed the progression of diabetic cataract by attenuating the protein aggregation, oxidative stress, ER stress, and apoptosis. These studies will likely help in developing the α-crystallin peptides as therapeutic agents to delay cataract progression.

Effect of dietary zinc deficiency on skeletal muscle proteostasis and mitochondrial biology in growing rats

Zinc deficiency leads to reduced growth, mass, and work capacity of skeletal muscle. However, the underlying mechanisms in connection with skeletal muscle proteostasis and mitochondrial biology are not clear, and hence, these aspects were investigated using a rat model. Results indicate a decreased mean muscle fiber cross-sectional area and increased apoptosis in the muscle of zinc-deficient rats. Activation of the ubiquitin-proteasome system as indicated by increased levels of the E1 enzyme, MuRF1 (muscle-specific E3 ligase; muscle atrophy marker), and proteasomal activity was observed in the zinc-deficient rats. Declined autophagy (Beclin1, ATG5, and LC3), and increased ER stress markers were observed. Zinc deficiency also affected mitochondrial biology. Thus, zinc deficiency appears to affect skeletal muscle proteostasis, and mitochondrial biology, causing muscle atrophy.

Anticancer effect of cinnamon extract and its active component procyanidin B2 in a rat model of prostate cancer

This project studied the chemopreventive efficacy of cinnamon and its bioactive compounds in a rat model of prostate cancer. Histopathological changes such as hyperplasia and Prostate Intraepithelial Neoplasia [PIN] induced by the combination of chemical carcinogen and testosterone in the prostate were reversed by cinnamon and its bioactive compounds. Similar to chemo-preventive drugs, cinnamon (concentration) and its bioactive compounds led to inhibition of cell proliferation, induction of apoptosis, inhibition of oxidative stress and angiogenesis, proteasome inhibition and inhibition of metastasis in prostate tissue. The data demonstrates that cinnamon and its bioactive compounds have a beneficial effect against carcinogen-induced prostate carcinogenesis.

Effect of traditional cooking on phytonutrient content and radical scavenging activity in cereals and millets

Traditionally processed sorghum, pearl millet and finger millet (viz. cooking, fermentation with curd, fermentation without curd, addition of curd to fermented millets) were analysed for their nutritional and anti-nutritional properties. Protein content was significantly higher in the cooked and fermented with curd sorghum (20.57±0.37 g/100g) and pearl millet (20.27±0.27 g/100g). Phytic acid content in millet flours ranged from 4.77±0.07 (pearl millet) to 8.6±0.15 mg/g (sorghum) and a sharp reduction (3.28±0.09 mg/g) was observed

in sorghum after it was cooked and fermented overnight and mixed with curd. Nutrient retention of water soluble vitamins increased in all the traditionally processed millets. The millets when traditionally cooked, overnight fermented and then added with had decreased phytic acid (62.9%) and increased Fe and Zn content which may enhance the bioavailability of both the micronutrients.

Exploring the protective effect of gamma oryzanol on diet-induced model of non-alcoholic steatohepatitis

The present study investigated the protective effect of gamma oryzanol in western diet-induced animal model with Non-alcoholic fatty liver disease (NAFLD). The results demonstrated that gamma oryzanol at a dose of 300mg/kg body weight could ameliorate western diet-induced NAFLD. In addition, gamma oryzanol supplementation also reduced visceral adiposity. Given the high prevalence of NAFLD and non-availability of pharmacological interventions for their management, gamma oryzanol appears as a promising dietary intervention with potential benefits in managing NAFLD.

Association between pesticide residue concentration in tissues and with the lymphoma, leukaemia and breast cancers

It is a cross-sectional study conducted among farmers and non-farmers visiting a tertiary cancer care hospital in Hyderabad, Telangana, diagnosed with leukaemia, lymphoma and breast cancers. In addition to these groups, family members of the farmers who were not engaged in farming and not diagnosed with any type of cancer were also included as study participants under the healthy control group. Face-to-face interview conducted among them revealed that farmers when engaged actively in farming activities did not adopt any GAPs. The results of the study revealed 17 and 14 pesticide residues in their blood and tissue samples respectively while there were no residues in the non-farmers. Further, higher frequency of polymorphisms in GSTT1, GSTM1 and CYP2E1 genes and elevated levels of 8-OHdG were found among farmers as compared to the non-farmers and healthy controls.

Understanding the possible dysregulation of molecular events associated with the exposure of Lead (Pb) and Aβ peptides on Neuronal/ Glial cells

Brain cells were exposed to 80µM of Lead(Pb) and the possible dysregulation of molecular events associated with neurodegeneration were investigated. Alterations in expression levels of various proteins like CDK5, p35, Calpain, Munc18, Neuregulin, E2F1and H2AX were evaluated. Human microglial cells on exposure to lead had alterations in the phagocytosis and antioxidant markers indicating the fact that they have crucial role on progression of neurodegeneration.

Evaluation of maternal micronutrient status, inflammation and effect of COVID -19 on placentas of anaemic pregnant mothers, including fetal outcome

212 term pregnant mothers were recruited, 58% of whom were positive for COVID-19 IgG antibodies and 42% were negative, although all were asymptomatic during their entire course of pregnancy and also were RT-PCR negative for SARS-CoV-2 antigen at the time of their admission for delivery, placental histology showed that irrespective of hemoglobin status of the mothers, placental hypoxia was evident.

Oral toxicity study of a new *Salmonella* killing bio-control agent NINMB 13076 bacteriophage

Sub-chronic oral toxicity study of *Salmonella* phage conducted on mice revealed no side effects. The study revealed no difference in the probiotic microbiota population of BALB/c mice. *Salmonella* phage NINP13076 did not affect the growth of probiotic microbiota. Phages are proven to be safe, and they can be used for bio food preservation.

Microbiological safety and quality of commonly consumed herbal drugs

Ashwagandha, Shatavari, aloe vera, and amlaare the commonly consumed herbal drugs. Over 112 herbal drugs were collected. These included solid, semisolid, and liquid samples for microbiological analysis. Microbiological contamination in solid herbal drug samples was found to be more compared to semisolid and liquid herbal drug samples.

Studies on the efficacy of P995 technology to control microbiological contamination in foods

Samples collected from the top layer after processing in the Ozonator showed a good reduction in microorganisms which could be due to better exposure to UV light. The Ozonator is not significantly effective in foods having a high microbial load. The findings of the study suggest that the treatment of different food samples with ozone and UV reduces the microbiological load, but the extent of reduction appears varied depending on the food sample.

Dermal penetration of pesticide residues in farmwomen workers: Assessment of cost-effective protective gears a preventive measure

Analysis of pesticide residues/residual metabolites/ haematological parameters was carried out in dermal washings (hand/wipe/patch), blood and urine samples among 360 farm-workers (men and women) who were not using PPE (n=180); using commercially available PPE (n=60) and PPE prepared using available resources (n=120) and provided free-of-cost. The mean concentration of ten pesticide residues detected ranged from 0.002 - 246 µg/mL in hand washings, 0.002 - 198.3 ng/cm2 in patch and 0.0001 - 1740 ng/cm2 in wipe samples among the subjects not using PPE. The same were lower in hand washings (0.01 - 16 and 0.0001 - 11.44 µg/mL); patch (0.001 - 6.57 and 0.0001 - 1.82 ng/cm2); and wipe samples (0.003 - 72.9 and 0.0008 - 39.7 ng/cm2) after using commercially available and PPE prepared and provided to them respectively. Further, Dimethyl phosphate, Diethyl thio-phosphate and Diethyl dithio-phosphate were detected in plasma (1.9 – 936.1 ng/mL) and urine (0.45 – 535.03 ng/mL) samples among the subjects not using PPE; while their reduction in plasma (0.25 – 15.7) and urine (0–68.99) was observed after using commercially available/PPE prepared and provided to them. Further, increased inflammation (CRP, IL-6, IL-1β, Cortisol, TNF-α) was observed when compared to their respective normal ranges among those not using PPE.

Impact of long-term use of double fortified salt when used prenatally, on maternal iron and iodine status and cognitive development of infants in rural Meghalaya - A Pilot study

The study was conducted in two blocks of the East Garo district of Meghalaya. A qualitative research study was conducted to understand the food habits and health-seeking behaviours of Garo women during pregnancy. It was found that no special care or diet was taken during pregnancy, as it was considered a natural phase not requiring special attention. However, antenatal check-ups were considered important. Pregnant women were unaware of the need for iron-folic acid tablets during pregnancy. Consumption was not regular either due to non-compliance or non-availability. For the pilot study, a total of n=151 pregnant women (in the second or third trimester) were enrolled in the Double Fortified Salt group (n=57) or Iodised salt group (n=68). Supplementation was carried out for 8±1 months. There were no differences between the groups at baseline. At endlineHaemoglobin, C-reactive protein, Ferritin, and vitamin B12 were similar in both groups. Serum Transferrin (43.33±27.47 (DFS) 44.29±33.16 (Iodised) (nmol/ mL)) was higher (p=0.045) in the iodized salt group.

Infodemic in Pandemic - An online survey on food and nutrition related web search behaviour, food scares and changes in Knowledge, Attitudes and Practices (KAP) among Indians

This study evaluated the trend of COVID-19 associated food and nutrition news search behaviours of Indian internet users between January 2020 and

June 2021 and its impact on their perceptions and practices. The Relative Search Volume (RSV) on Google Trends (GT) of 34 popularly searched keywords showed a steep rise in search for immunity boosters, vitamin supplement brands and "ayushkadha" during the first wave (April- August 2020). With a brief period of decline, the search trend again hiked correspondingly with increase in number of COVID-19positive cases during the second wave. The online survey conducted on adult Indian internet users (n = 572) reported high (71.9%) consumption of Vitamin C rich fruits as well as Vitamin C (68.2%) and Zinc (61.4%) supplements 'to boost immunity'. Traditional Indian spices like ginger and garlic were used by 62.9% and 50.9% respondents respectively. Most respondents reported to rely on social media for COVID-19 associated health tips, however those with history of infection relied more on doctors and health professionals. This study highlighted the need of media and health literacy to advocate for the use of health information cautiously.

Impact of integrated cognitive behaviour therapy (CBT) and pranayama on sleep quality of women living in welfare hostels

The study was conducted among women living in welfare hostels. More than 50% reported sleep disturbances. The intervention with CBT was for three months. Significant mean differences between pre-and post-intervention were found. Statistically significant differences indicated that the intervention resulted in improved sleep quality. Although psychological well-being improved in all three groups, the mean difference was significantly higher for the integrated intervention group. The same trend was seen for psychological distress as well but not for perceived stress which showed all the groups benefitted similarly from the intervention.

Adaptation of the Food and Agricultural Organization's, Education for Effective Nutrition in Action (ENACT) and Food Systems' Courses for Nutrition Education in India

The ENACT (developed by the FAO for Africa) is a comprehensive hands-on Nutrition Education course that has immense applicability in community nutrition. This project aimed to adopt the ENACT course material to the Indian context. The 11 units of the resource book and student's book were adapted

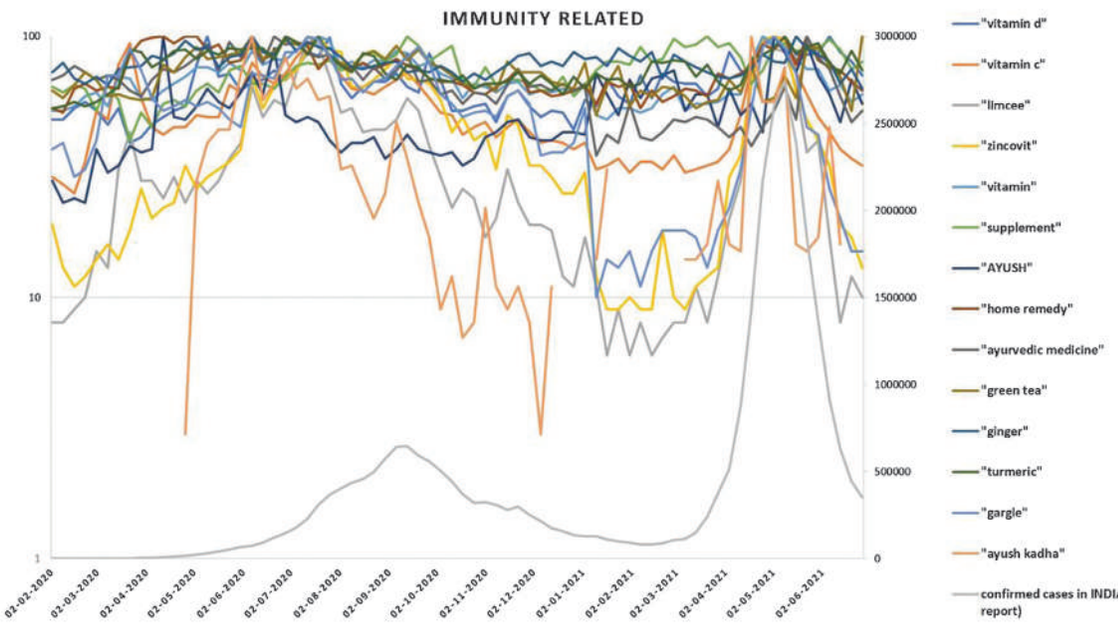


Fig. 2: positive correlation was observed between the number of COVID cases and search terms like "vitamin D", "Limcee", "grocery delivery", "vegetable sanitizers", "alcohol" etc. whereas, search terms like "street food", "junk food", "food delivery" etc. were negatively correlated to the number of cases.

to the Indian scenario by contextualizing the case studies and also the pictures and graphics. Under output-2, six e-learning modules on "Nutrition and Food Systems" on the following topics were developed. Six universities have agreed to adopt the study material and e-learning modules as add-on courses in their PG curriculum of nutrition & dietetics.

PUBLIC HEALTH

- Nutritional status of under five year children of Muzaffarpur district, Bihar has been carried out as part of comprehensive investigations of Acute Encephalitis Syndrome (AES). AES was observed in the children who had the history of litchi fruit consumption and fasting status of children. And all the children who succumbed to AES were from under privileged and marginal communities.
- Developed a training module on Nutrition and climate change and action plan for health and nutrition for State Nodal Officer, District Nodal Officer.
- Demonstrated that screening followed by treatment with iron-folic acid for a period of 3 months reduces the prevalence of anaemia and improves the iron stores. Further, significant treatment effects persisted after 9 months of treatment.
- The lower 2.5th centiles serum zinc thresholds to define low serum zinc concentrations in 1-19 year old healthy children and adolescents were derived.
- Coupled in vitro digestion/Caco-2 cell based studies showed that bioavailability of zinc from biofortified rice (developed at ICAR-IRRI, Hyderabad) is twice that of control variety
- The 'Education for Effective Nutrition in Action (ENACT) and Food Systems' modules developed by the FAO for Africa was adapted to the Indian context, by contextualizing the case studies and also the pictures and graphics to Indian settings. Six e-learning modules on "Nutrition and Food Systems" were developed and six universities were contacted to include these modules in the undergraduate curriculum.
- The intervention study using less familiar foods (mahua recipe) on primitive tribal groups (PVT) women results showed improvement of Hb, and essential nutrients. Indigenous food with high nutritional value should be mainstreamed.
- Twenty percent prevalence of frailty was observed among urban older adults and provided evidence that inadequate intake of nutrients is independently associated with frailty.
- Developed a functional food formulation for diabetic complications and partnered with an industry for developing the products for diabetic complications and age-related degenerative conditions.
- Indian regulations currently do not have microbiological criteria for herbal drugs. The data obtained on microbiological analysis of herbal drugs can be utilized to develop regulations on herbal drugs.
- The study on trend of COVID-19 associated food and nutrition news search behaviours of Indian internet users and its impact on their perceptions and practices highlighted the need of media and health literacy to advocate for the use of health information cautiously.
- As part of the committee on "Revision of Nutritional Norms under the National Food Security Act, 2013" NIN contributed significantly in revising, formulating and proposing food baskets for the beneficiaries of the food safety net programs under NFSA on principles of food diversity, balance and moderation. The technical report has been submitted to Department of the Food and Public Distribution, Ministry of Consumer Affairs, Food and Public Distribution.

EXTRAMURAL RESEARCH

FERTILITY REGULATION

Phase-III Clinical Trial with an Intravasal Injectable Male Contraceptive –RISUG®

RISUG (Reversible Inhibition of Sperm Guidance), developed at IIT Kharagpur, completed Phase I and Phase II clinical trials, and Phase III was Supervised by ICMR and supported by the Ministry of Health and Family Welfare (MoHFW). The four Participating centers in this study are LNJP New Delhi, Dist. Hospital, Udhampur, SMS Medical College, Jaipur and Dayanand Medical College, Ludhiana, Punjab. IIT Kharagpur has been mandated to manufacture a pre-filled syringe for delivery of RISUG. GMP setup of the RISUG plant to manufacture a test batch of 10000 standardized pre-filled syringes RISUG syringes is underway**.** The Central Drugs Standard Control Organization (CDSCO) directed ICMR to collect information from the RISUG (Reversible Inhibition of Sperm Under Guidance) injected subjects regarding their psychosocial and sexual behavior after the injection. This study is now ongoing at LNJP Hospital. The project will start the next Phase after approval from the Drug Controller General of India (DCGI).

Phase-I-II Clinical Trials on the Revived Recombinant Vaccine against Human Chorionic Gonadotropin (hCG)

The Phase-I and II clinical trial with recombinant beta hCG vaccine is going on at AIIMS, New Delhi, and SGRH, New Delhi, to determine the safety and immunogenicity of the recombinant hCG-LTB vaccine in women who are healthy and sexually active. The study tests vaccine efficacy in preventing pregnancy in sexually active women without inducing any impairment of ovulation, derangement of menstrual regularity, and bleeding profiles. The safety data of enrolled subjects, a detailed causality assessment report for adverse events, and a summary of animal studies were submitted to DCGI. The study is awaiting approval from DCGI to reinitiate the clinical trial.

National Centre for Technology in Family Welfare (NCTFW), IIT, Kharagpur

The "National Centre for Technology in Family Welfare," funded by the Indian Council of Medical Research (ICMR) has been established with the mandate of "Innovation and Product Development" as well as to carry out applied research to translate them into products for family welfare is established at IIT Kharagpur. The ongoing project aims to (i) manufacture a pre-filled syringe for delivery of RISUG. (ii) Synthesis and characterization of PCL-DA: PEG-DA-based polymeric blends grafted with SMA hydrogel as a bio-degradable intrauterine contraceptive implant, with an objective of fabrication of a novel flexible copolymeric scaffold grafted with RISUG® for establishing a bio-degradable form of IUCD. The findings suggest that SMA hydrogel grafted PCL-DA: PEG- DA scaffold can be developed as an intra-uterine biodegradable non-hormonal female contraceptive implant due to its excellent bio-compatibility and spermicidal activity (iii). Studies to understand the mechanism of a recurrent spontaneous miscarriage of unknown etiology is ongoing. Metabolomics has been used to understand the etiology of various complex diseases and aberrantly expressed metabolites in IRSM, which could be mainly linked to perturbations in glucose metabolism and amino acid biosynthesis. The results have revealed that glucose metabolism was significantly dysregulated in women with IRSM. PI3K (p85), PI3K (p110), p-Akt (Thr308), p-Akt (Ser473), and glucose transporters GLUT3 and GLUT4 were found to be significantly downregulated.

REPRODUCTIVE CANCERS

Development of dendritic cell vaccine for the treatment of recurrent/metastatic reproductive cancers

This ongoing study aims to (i) evaluate the utility of the identified biomarkers (SPAG9, AKAP4, HSP70-2) for early detection and diagnosis in cervical and ovarian cancer patients in southern and northern regions of India and (ii) follow up

the treated cervical and ovarian cancer patients for persistence/ progression and recurrence, (iii) employ identified biomarkers (iv) carry out the preclinical evaluation of therapeutic and prophylactic SPAG9 cancer vaccine in the animal model system; (v) evaluate cell-based vaccine therapy for epithelial ovarian cancer patients who have failed two systemic therapies(vi) carry out in-depth research on immune responses in ovarian cancer patients immunized with dendritic cell-based immunotherapy from southern and northern regions of India. Blood samples of 455 cervical cancer cases, 135 Ovarian Cancer patients, and 204 healthy controls have been collected (before or after neoadjuvant chemotherapy) for early detection and diagnosis of biomarker study. Follow-up of these patients is ongoing.

Early detection and diagnosis in cervical and ovarian cancer patients

SPAG9 gene and protein expression was carried out in 41 cervical and 46 ovarian and cervical cancers. SPAG9 gene and protein expression were detected in 90% of cervical and ovarian cancer patients. This study has immense translational value. SPAG9 has the potential to be a universal therapeutic cancer vaccine and a promising candidate for cancer immunotherapy-a true example of MAKE IN INDIA efforts.

INFERTILITY

Male infertility

Presently, three studies assess various aspects of male infertility. A study titled **"Exploring male factors in recurrent pregnancy losses: A genomics and proteomics-based approach"**- aims to understand the role of male partner's contributory molecular and genomic factors in idiopathic recurrent pregnancy losses (iRPL). The study observed higher oxidative stress levels in iRPL corresponding to increased DNA fragmentation, indicating a possible link between oxidative stress in sperm cells and iRPL. Another study on the **Genetic Intersections between Male Infertility and Cancer: Role of Yoga Intervention** is ongoing**.** This study found that the practice of Yoga improved standard sperm parameters like sperm motility and sperm telomere length increased the expression of genes that maintain DNA integrity in the DNA repair genes, reduced expression of oncogenes, and enhanced the expression of cell cycle control and tumor suppressor genes. Another study explores the **Spectrum of Sycp3 Gene Mutation in the Case of Male Infertility and their Association to MTHFR C677T Gene Polymorphism in Eastern Population of India.** The study aims to identify the frequency of SYCP3 gene mutation along with hormonal profiles to assess the endocrine gonadal axis, i.e., estrogen, testosterone, and follicle-stimulating hormone, and correlate with the genetic profile along with cytogenetic study and differential allelic frequency. The findings showed differential expression in the SYCP3 gene.

Female Infertility

Two studies are assessing the various factors associated with female infertility**.** A study titled **Immuno-modulatory effect of Intralipid in women with recurrent implantation failure with elevated uterine Natural Killer cells (RCT)** ongoing at AIIMS, New Delhi found no correlation between pNK and uNK cell levels in controls and subjects**.** A study titled **Molecular Analysis of a promising immune-regulatory pathway involved in Recurrent Pregnancy Loss (RPL)** aims to investigate the role of HLA-G and FOXP3 polymorphisms in the regulatory sequence in women with RPL. Fieldwork has been completed, and samples of 262 women are being analyzed.

WOMEN HEALTH

Evaluation of Prevalence, Regional Phenotypic Variation, Comorbidities, Risk Factors and the Variations in Response to Different Therapeutic Modalities among Indian Women with Polycystic Ovary Syndrome (PCOS)

This study was initiated in 2018. This study aims to estimate the national prevalence of PCOS. The subject enrolment is complete at all the centers. Preliminary findings show that of the 13194 women screened across rural and urban India from six different regions for PCOS, 2768 had features suggestive of PCOS. Phase II of this study will commence soon.

ICMR Centre for Advanced Research in Mechanisms leading to preeclampsia

The centre is undertaking studies to examine the possible factors involved in the pathology of preeclampsia at early and later stages of gestation and establish the role of long-chain polyunsaturated fatty acids (LCPUFA) and micronutrients in mechanisms associated with preeclampsia (PE). Women with PE were older, had a higher SLI score, were professionals and more educated, had higher BMI and systolic and diastolic blood pressure at all the time points, had a higher percentage of nulliparous women, and a higher percentage of the assisted mode of conception and cesarean sections as compared to non-PE women. Gestational age at birth was lower in the PE group than in the non-PE group. Babies born to mothers with PE had a lower birth weight and head circumference than the non-PE group. The percentage of preterm birth and SGA babies in the PE group was higher than in the non-PE group. TSH levels were higher in women with PE than non-PE women at V1.Fetal growth measures such as BPD, HC, AC, and EFW were lower at 18-22 weeks of gestation and FL at 32-35 weeks in the PE group compared to the non-PE group. Mean uterine artery PI was higher at 11-14 weeks and 18-22 weeks of gestation in the PE group compared to the non-PE group. Umbilical artery PI and fetal MCA PI at 32-35 weeks were lower in the PE group than in the non-PE group. Fetal growth measures such as AC, FL, and EFW at 32-35 weeks were negatively associated, while mean uterine artery PI at 11-14 weeks and 18-22 weeks was positively associated with preeclampsia after adjusting for confounders. The biochemical and molecular analysis for various parameters is ongoing.

HEALTH SYSTEM STRENGTHENING

Systems Approach for assessment of maternal deaths in Rajasthan, A feasibility study

This project assessed the magnitude of maternal deaths and underlying factors contributing to maternal deaths in Rajasthan. The barriers and challenges in reporting maternal deaths in Rajasthan were analysed. The total number of cases reported from Jodhpur andUdaipurare265 and 192 respectively as per CMHO list. The new cases found through the project surveillance were five and two in Jodhpur and Udaipur respectively. Maternal Death Surveillance and Response (MDSR) training was conducted for ASHA, ANMs and Medical Officers was conducted by virtual mode in Jodhpur and Udaipur districts in Two Phases for capacity building, and health system strengthening. Severe bleeding was the main cause of complications during delivery in both the districts.

RARE AND INHERITED DISEASES

National Registry for Rare Diseases and other Inherited Disorders

ICMR National Registry for Rare and other Inherited disorders (NRROID) was initiated in November 2019 in collaboration with AIIMS, New Delhi, to collect valuable data on demography, phenotype, natural history, evolution, and outcomes of specific diseases with/ without treatment. The disorders on which data is being collected have been broadly classified under six categories: Lysosomal storage disease, Inborn errors of metabolism, skeletal dysplasias, hematological disorders, primary immune deficiency, and neuromuscular disorders. Nineteen centers from all over the country are currently contributing to the registry. Data on over 7000 cases of rare diseases has been collected till date under the registry.

Study of Hemoglobinopathies and G6PD deficiency among tribal's of Tamil Nadu

The study aims to evaluate Hemoglobinopathies and G6PD deficiency among tribals of Tamil Nadu. A total of 5107 individuals belonging to three different tribal groups (Irulas, Kurumbas, and Malayalis) from three districts of TamilNadu were screened for Hemoglobinopathies and G6PD deficiency. The presence of the sickle cell gene was observed among the Irulas and Malayalis from Dharampuri and Nilgiri districts, and the carrier frequency varied from 0.7% to 20.9%, with an overall frequency of 3.8%. A high prevalence of b-thalassemia trait was observed among all the tribes ranging from 5-9%

CHILD HEALTH

To evaluate the feasibility of a multigene panel for diagnosing and managing autism spectrum Disorder in the early neonatal period

Using Chromosomal Microarray and Next Generation Sequencing Technology, this study aims to analyze DNA samples from Autistic and controls using a multigene panel and identify gene-disease relationships and variants specific to the Indian population. The centre is evaluating the predictive value of the screening tool using the latest data analysis tools and statistics to identify genes and variants specific to Indian people. Till now,90 samples and ten controls from various centers have been collected and analyzed. Chromosomal microarray and whole exome sequencing will be done for these samples, and evaluation will be done. All samples were tested using both techniques. Identification of candidate genes will be made once all samples have been processed. This will be matched to autism-specific databases and available global literature. One paper on Autism literature review has been submitted for publication.

Seven Days Versus a fourteen -days Course of Intravenous Antibiotics in the Treatment of Uncomplicated Neonatal Bacterial Sepsis

The primary objective of the study was to evaluate whether a 7-day course of intravenous antibiotics has a relapse rate that is not inferior to a standard 14-day course of antibiotics, among newborn infants (aged 0-28 days, weighing more than or equal to 1000 gm at birth) who have uncomplicated blood culture-proven septicemia and who are in clinical remission by the end of the fifth day of intravenous antibiotics. From April 2021 to March 2022 total of 1764 subjects have been screened. 1209 have been enrolled in the observational part of the study. Eighty-seven have been enrolled in the RCT part of the study carried out in CNBC, New Delhi, PGIMER, LHMC, New Delhi, IOG Chennai, IGICH Bangalore and KGMU Lucknow.

To study the bacterial etiology, antimicrobial sensitivity pattern resistance determinants, and associated risk factors of neonatal sepsis in 4 different districts of Assam

The study aims to investigate the bacterial pathogens and their sensitivity pattern, evaluate the presenting signs and symptoms of culture-positive cases, determine the associated risk factors, and prepare guidelines for empirical antibiotic therapy. Till now, 1711 neonatal blood samples have been collected. *Klebsiella pneumonia*was found at a higher rate of 63.2% (146/231) amongst gram-negative organisms, and *staphylococcus aureus* at a higher rate of 37.4% (77/206) amongst gram-positive organisms. Amongst 231 gram-negative isolates, PCR molecular confirmation has been done for 64 lactose fermenting isolates (*Klebsiella pneumoniae*= 39; *E.coli*= 25) and non-lactose fermenting isolates (*Pseudomonas aeroginosa*= 21).Rest 139 lactose fermenting and seven non-lactose fermenting isolates are yet to confirm. The molecular characterization for 26 *klebsiella pneumonia* isolates has been done, and the rest are under process. This study will provide antibiotic treatment guidelines for the clinical management of neonatal septicemia.

National Registry for COVID 19 infections among pregnant women and their neonates

The “National Registry for COVID-19 infections among pregnant women and their neonates” was initiated under the Division of RBMCH in

January 2021. The registry is collecting data on COVID-19 infections from 21 centers across India. Information on suspected cases that tested positive (RT-PCR, TrueNat, CBNAAT, Molecular Test, Serological Antibody Test, Rapid Antigen Test) is obtained from hospital records. Anonymized data is being collected from the time of the first case reported at the respective sites and will be collected until December 2023. Currently, 6222 pregnant/ postpartum women and 3229 neonates have been enrolled in the registry. The data is being analyzed, the results will be published soon.

Effect of daily supplementation with multiple micronutrients and iron folic acid compared to iron folic acid alone in children aged 6 to 59 months on anaemia prevalence and hemoglobin concentration: A randomized controlled trial in urban Delhi

A total of 15338 households were surveyed in which 4320 children aged 6-59 months were present. In 3123 children, blood was collected for baseline hemoglobin screening. Out of the 3123 children in whom screening was done, 1055 (33.8%) were non-anaemic, 139 (4.5%) had severe anaemia, and 1929 (61.8%) had mild to moderate anaemia. Out of 1929 mild to moderately anaemic children, 1573 were assessed for eligibility for enrollment in the study. In 475 children (required sample size), baseline samples at the enrolment were collected to assess micronutrient levels (vitamin B12, folate, and zinc), hs-CRP and hepcidin. End study sub-samples for assessment of iron parameters (serum ferritin, serum transferrin receptor, percent transferrin saturation and total iron binding capacity), micronutrient levels (vitamin B12, folate and zinc) and hs-CRP have been collected in 600 children (required sample size). All follow-ups and outcome sample collections have been completed. The baseline and end-line sub-samples have been sent to CMC Vellore for analysis and the process of analyzing the samples is ongoing. The data collection on cost-effectiveness is ongoing. Data on the cost incurred regarding out-of-pocket expenditure by the families has been collected in a sub-sample of 325 children (25% of the overall sample). Data on costs involved in the implementation of the study is being collected. The outcome data will be unmasked; data cleaning will be done, followed by analysis once the reports of sub-sample analysis are received from CMC.

Phase III, Multicentre, Randomized, Double-blind, Placebo-controlled Study to Evaluate Efficacy of Probiotic Supplementation for Prevention of Neonatal Sepsis in 0-2 Months old Low Birth Weight Infants in India- The ProSPoNS trial

Neonatal infections (pneumonia, septicaemia, meningitis) are responsible for more than a quarter of India's one million neonatal deaths yearly. Low Birth Weight (LBW) is an important indirect cause of death in neonates, accounting for 40% to 80% of neonatal deaths. These neonates have poor cognitive function and compromised immune functions. In LBW infants infections are known to spread rapidly leading to severe disease and death. Infection prevention in low birth weight babies would directly decrease the neonatal morbidity and mortality. Currently there are no preventive interventions available for neonatal sepsis other than general measures of hand-washing, exclusive breastfeeding etc. Management of neonatal sepsis with antibiotics faces the problem of drug resistance, attributed to availability over the counter, indiscriminate use and incomplete courses in India. Immune-modulation/immune-potentiation with the use of probiotics may prove to be an option. The proposal for this study has been awarded funding under MRC/NIHR/DFID/Wellcome Trust, Joint Global Health Trials. Preparatory phase activities included completing a tripartite agreement between the sponsor and the pharmaceutical companies for supplies of investigational products (IPs), a clinical trial agreement between the sponsor and the participating sites, staff recruitment at Collaborating sites, etc. The study protocol has been reviewed by the Research Ethics Committee of the LSTM, UK, as suggested by MRC. The trial has been registered at CTRI. The CT-NOC from

CDSCO has been obtained. During the reporting period, activities of the implementation phase of the trial have been initiated. An investigator's meeting, site feasibility, and site initiation visits were completed at the six subject recruitment sites. A Hands-on workshop for the lab technicians was conducted centrally at AIIMS, New Delhi. First Trial Steering Committee and the Data Monitoring Committee meetings were held. ICMR received a CT NOC extension letter dated 08 June 2021 for the extension of trial initiation for one year with effect from 01 March 2021. The implementation phase of the trial started in June 2021, with the first enrolment on 26 July 2021 at the Mahatma Gandhi Institute of Medical Science (MGIMS), Sevagram, followed by all five sites, including Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Pondicherry on 31 July 2021, King Edward's Memorial Hospital (KEM), Pune, Maharashtra on 13 August 2021, Subharti Medical College (SMC), Meerut, Uttar Pradesh on 19 August 2021, Asian Institute of Public Health (AIPH), Bhubaneswar, Odisha on 03 November 2021, Lady Hardinge Medical College (LHMC), Delhi on 21 December 2021. By the end of March 2022, a total of 1573 subjects had been enrolled, and 1009 completed the two months of follow-up.

THE ICMR - COCHRANE AFFILIATE CENTRE

ICMR-Cochrane Affiliate Centre has been established as part of a Cochrane India Network set up by Cochrane in India in 2021 with nine Affiliate Centers across India. The focus is on increasing the use of Cochrane's evidence in knowledge translation and policy-making activities. The Affiliate centers would promote and represent Cochrane in particular regions/areas of the country. The Cochrane India network would attract and support larger numbers of India-based authors, methodologists, and editors with requisite knowledge and expertise. A Technical Advisory Committee approved by DG ICMR has been established to support and guide the activities of the ICMR-Cochrane Affiliate centre and the meeting was convened on 23 June 2021. The Network scheduled inauguration of the Cochrane India Network on 26 October 2021. Cochrane India network also collaborated with NITI-Aayog and held a meeting on 25 January 2022 to emphasize the need for a systematic review of the effectiveness of home-based care and e-health services with policy perspective. Further, ICMR-Cochrane Affiliate centre has planned to collaborate with Campbell South Asia and recruit scientists to work at the centre for conducting Cochrane systematic reviews, organizing workshops and to perform other activities by the centre.

ICMR ADVANCED CENTRE FOR EVIDENCE BASED CHILD HEALTH, PGIMER, CHANDIGARH

During the reported period, the ICMR Advanced Centre for Evidence based child health, PGIMER, Chandigarh, has organized six workshops as part of capacity building. Based on the topics discussed in the 4 prioritization workshops, the CAR has completed five systematic reviews and meta-analysis. Of them, 3 have been published in peer reviewed journals and two have been communicated. One Health Technology Assessment (HTA) on N-95 masks and COVID-19 infection has been completed and sent for publication, another HTA on otoscope is ongoing. Three policy briefs were generated from the systematic reviews and sent to ICMR. The CAR has established networking with HITAP, Cochrane and other institutes from different countries.

NUTRITION

Effectiveness of Point of Care Anemia Testing by front line workers (ANM, AWW, and ASHA) in anemia control

The study aims to assess the validity, feasibility, and effectiveness of POCT in the anaemia control strategy. If proven successful, the study's results can facilitate the scaling up of POCT for anaemia and significantly strengthen the anaemia control measures in the country.

Biopolymer based nano-layer fortification of self-assembled micronutrients over preconditioned rice: Retention of fortified nutrients and scale-up studies

The PI and his team have successfully developed a lab-scale technology for whole grain micronutrient fortification of rice ensuring nominal processing, washing, and cooking loss of micronutrients. Two patents are also in the process of being filed based on the findings of the project.

Impact evaluation of "screen and treat" approach for anaemia reduction: a cluster randomized trial in rural Telangana"

This study aims to assess the effectiveness of population level screening followed by targeted IFA supplementation according to the grade of anaemia for increasing the mean population level haemoglobin and reducing the prevalence of anaemia as compared to the existing anaemia control program. In the seven intervention clusters, 6630 participants belonging 2179 households have been enrolled and collected demographic data. 6132(92.5%) participants provided pooled capillary blood samples. Of these, 4489 participants were eligible for intervention (prophylactic or therapeutic IFA supplementation based on the baseline Hb values as per the AMB guidelines). In control clusters, 5253 participants were recruited at baseline from 1823 households and about 569 participants provided blood samples (≈10%) at baseline to estimate the balance between the two arms. The anaemia prevalence was observed to be high among 6-59 month old children (47%), women of reproductive age (49%) and adolescent girls (41%). Anaemia prevalence was low in men (≈6%) and moderate in adolescent boys (≈17%) and 5-9 year old children (≈ 23%). These estimates are broadly comparable to the anaemia prevalence estimates from the CNNS(2016-18). The intervention delivery and data collection in the study is ongoing.

CENTRE FOR NUTRITION RESEARCH AND TRAINING (CNRT)

The Centre for Nutrition Research and Training under the Division of RBMCH & Nutrition was initiated in November 2021 with the primary objective to carry out and promote nutrition research, especially in under-represented regions of the country. The centre also aims to develop young researchers' capacity for conducting nutrition research. Besides the above, the NABL accredited Clinical Biochemistry laboratory under the centre aims to develop and standardize newer cost effective methodologies for estimating micronutrients and other nutrition biomarkers.

NORTH EAST CAPACITY BUILDING

Establishment of Health and Demographic Surveillance System in Dibrugarh District, Assam

Under the HDSS, studies are ongoing to assess risk factors and clinical outcomes of lifestyle diseases. A two years prospective study to document the progression of blood pressure in native rural Assamese and tea garden communities has analyzed 53,763 subjects out of 1,06,769, who are under HDSS surveillance. Of these, 46,762 are rural Assamese, and 60,007 are tea garden inhabitants. Of these subjects, 16,887 (31.41%) were normotensive, 22,283 (41.44%) were prehypertensive and 14,593 (27.14%) were hypertensive subjects. Another study to assess hematological and biochemical parameters of the same population is ongoing in which 2293 participants were surveyed with socio-demographic and clinical information collection.

Task Force Study on the development of indigenous reagent red cell panels for identification and characterization of blood group alloantibodies in North East India

The objectives of this task force study is to find the frequency of clinically important blood group antigens of Rh, Duffy, Kell, Kidd, MNS, P1, Lewis, Lutheran, Colton, Dombork, Indian, Diego, Cartwright, Miltenberger in population of Assam, Nagaland, Sikkim and Arunachal and to prepare indigenous panel red cells for screening and

identification of alloantibodies against the antigens prevalent in these populations and also to determine the frequency of these blood group antibodies in the patients/antenatal women from NE by using the above prepared reagent red cell panel. Currently NIIH has completed workshops for training of all staff engaged in this study and further laboratory work is ongoing.

Multicentric Task Force Study on Systemic Lupus Erythematosus (SLE) from the North Eastern Region of India: Early diagnosis to research potential for understanding disease pathogenesis

The objectives of this task force study are (i) to transfer cost effective technologies for the diagnosis and management of various autoimmune diseases in the north east region (ii) to document demographic, clinical and serological details of patients diagnosed with autoimmune diseases from North East India. Additional studies on the etiology of SLE is ongoing under this Task force study. Preliminary data collection has started for all the studies.

ENVIRONMENTAL & OCCUPATIONAL HEALTH

Research in priority areas of occupational and environmental health relevant to national needs for various working groups is actively undertaken by the ICMR-National Institute of Occupational Health, Ahmedabad, the ICMR-National Institute for Research in Environmental Health, Bhopal and ICMR-Bhopal Memorial Hospital & Research Center, Bhopal. Major highlights of various programmes undertaken by the ICMR in the areas of occupational and environmental health during the year 2021- 2022 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH (ICMR-NIOH), AHEMDABAD

EPIDEMIOLOGICAL STUDIES

Assessment of respiratory health in children residing in critically polluted areas(CPA) using Urinary Club Cell protein 16 (CC16)as a biomarker- A feasibility study

While children residing in CPA are at risk of respiratory diseases, assessing the problem by pulmonary function tests (PFT) is difficult to execute in children, since it is effort-dependent. A biomarker for non-invasive screening may be helpful to identify early respiratory diseases among children. Across-sectional study carried out with 203 children (10-13 years)showed higher urinary CC16 excretion among CPA area children in comparison to non-CPA children (2.14 ± 2.9 vs. 0.49 ± 0.72 ng/mg of urine creatinine). In addition, significant differences also existed for spirometry parameters between the two groups of children (FEV1: 1.86 ± 0.45 vs. 1.71 ± 0.39 Ltr/Sec; FVC: 2.02 ± 0.47 vs. 1.86 ± 0.42 Ltr).

Exploration of Renin-Angiotensin system in Lead-induced hypertension among occupationally exposed individuals

Blood-Pb levels (BLLs) in the occupationally exposed individuals (n=250) ranged between 6.34 - 87.80 µg/dL, with a mean BLL value of 36.79 ± 14.79 µg/dL. Mean (±SD) systolic and diastolic blood pressure (SP and DP) were recorded as 130.91 ± 15.59 and of 84.28 ± 13.50, respectively. Study subjects with BLL>40 µg/dL (upper acceptable limit recommended by OSHA) had significantly higher SP ($p = 0.029$) and DP ($p = 0.040$) than the individuals having BLL<40 µg/dL. The results for RAS parameters are currently under evaluation.

DNA methylation and its association with Pb-exposure, B vitamin deficiencies and lifestyle factors among Pb-exposed workers

Epigenetic changes like DNA methylation have been associated with many disease conditions, but very few have studied theirrole in occupational health hazards. A study was carried out among164 male workers to determine the impact of Pb-exposure, B vitamin deficiencies, and lifestyle factors on

DNA methylation (% of 5-methylcytosine). Blood Lead levels (BLLs) were measured by Inductively Coupled Plasma Optical Emission Spectrometer (ICP-OES). B vitamin status and % 5-mC in the samples were quantified by ELISA methods. Univariate analysis showed significantly reduced DNA methylation in the BLLs categories of 30-50 µg/dLand > 50 µg/dL and in the presence of vitamin B9 (Folate) deficiency. In stepwise multiple linear regression analysis, the variables such as experience (β= -0.242; P = 0.002), BLLs (β= -0.197; P = 0.011), tobacco chewing (β = -0.176; P = 0.021), and vitamin B9 (β = -0.158; P = 0.037) were all found to be negatively and significantly associated with DNA methylation.

Assessment of work-related exposures and its impact on respiratory health due to systemic inflammatory responses and immunological markers among loading and unloading workers at the vegetable market

Dust exposure among the loading and unloading workers of the vegetable market was associated with systemic inflammatory responses (SIR), abnormal blood parameters and pulmonary function tests. Workers of the high exposure group (median duration of exposure =years of exposure xthe working hours per day) displayedSIR, as measured by increased serum albumin and C-reactive protein, increased immunological markers(IgE and IgA) and abnormal PFTcompared with the low-exposure group.

Assessment of health status of vendors exposed to bioaerosols in vegetable market

Environmental bioaerosols and organic dust exposures in the vegetable markets were evaluated for their harmful effects on the respiratory health of workers. Andersan 6 stage viable cascade sampler and personal air samplers were used to collect samples from different sites of the wholesale vegetable markets of Ahmedabad and residential outdoor environment for the analysis of the microbial load by bacteria, fungi, organic dust, endotoxin and (1→3)-β-D Glucan. The highest bacterial and fungal load were observed during monsoon season followed by the winter season. The collected organic dust concentrations ranged from 1.18 to 5.21 mg/m^3. Respiratory symptoms viz., cough, phlegm, dyspnea occurred significantly more frequent in the workers compared with the residential control subjects (P<0.05).

Assessment of workplace fine particle exposure and pulmonary function parameters among ceramic tile industry workers: a cross-sectional study

Personal respirable dust (PM4) exposure was found to be highest in ball milling and spray drying sections of the ceramic tile industry with 8 hours TWA PM4 6.44 mg/m^{3}and 29.36 mg/m^3, respectively (8-hour TWA PM4permissible exposure limit (PEL) for OSHA (USA) ≤5.0 mg/m3). Thus, in the spray drying section, personal exposure to respirable dust was 6 times higher than the PEL recommended by OSHA.

Significantly deteriorated lung functions were found in the workers and supervisors as compared with the administrative staff with the mean values of FVC%, FEV1/FVC%, FEF25–75% being 3.6 ± 0.8, 81.2 ± 7.7 and 3.4 ± 1.18, respectively among the workers, 3.3 ± 0.6, 78.1 ± 8.6 and 3.2 ± 0.8, respectively among the supervisors and 4.3 ± 0.8, 90.3 ± 6.6 and 4.4 ± 1.4, respectively among administrative staff (Fig. 1&2). However, post-hoc analysisshowed no significant difference between the supervisors and the workers groups.

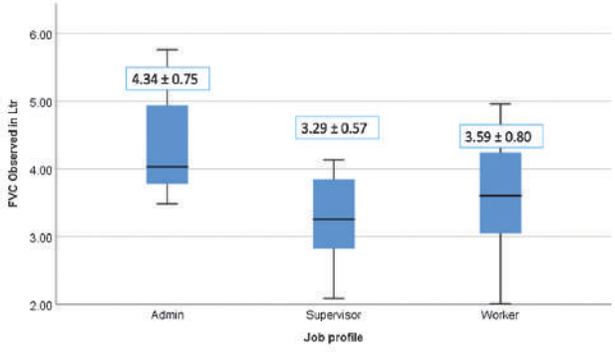


Fig. 1: Association between FVC (L) and job profile of study participants.

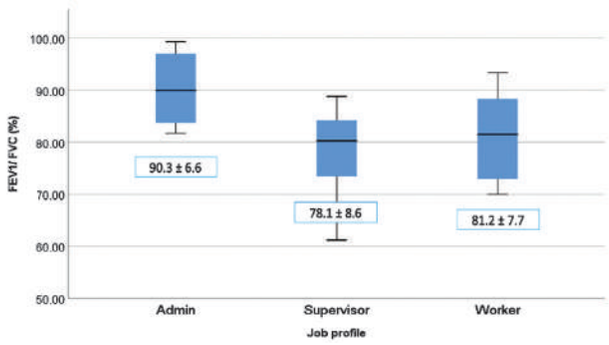


Fig. 2: Association between FEV1/FVC (%)and job profile of study participants.

Develop and validate tools for the Indian workforce to screen occupational mental health and workplace factors influencing it

An imbalance in the key organizational psychology constructs viz. "Workload", "Reward", "Community", "Control", "Values" and "Fairness" are potential factors leading to negative occupational mental health, i.e. burnout. Burnout, a psychological syndrome is the combination of emotional exhaustion, sense of reduced compassion and accomplishment. To note, the concept of occupational mental health in a nation with second largest workforce is nascent. Further, the utility of existing western tools in Indian subcontinent is limited by culturally inappropriateness, patented, less comprehensible and other factors. The study developed tools to screen occupational mental health and workplace areas. Conventional steps involved in psychological tool development, viz. construct identification, drafting of pertinent questions, content validation and field testing of questions were adopted. After series of steps, tools for screening occupational mental health and key constructs influencing mental health at workplace (workplace assessment) were developed. The screening tools exhibited adequate test - retest reliability, internal consistency / reliability (cronbach's α>0.73) and correlation (correlation coefficient > 0.6) with the general mental health in larger sample. The proposed simple and easy-to-administer tool requires development of normative scores, thereby aiding early diagnosis and management of those requiring intervention.

Table 1. Psychometric properties & reliability statistics of the scales

Tool	Cronbach's Alpha	Inter - item correlations (range)	Corrected Item-scale correlations (range)	Squared multiple correlations (range)	Pearson's correlation coefficient with GHQ - 5
Burnout screening tool	0.82	0.18 - 0.5	0.2 - 0.57	0.17 – 0.64	0.694
Workplace screening tool	0.73	0.16 - 0.45	0.21 - 0.7	0.19 – 0.6	0.586
GHQ -5	0.716	0.22 - 0.56	0.37 - 0.58	0.15 – 0.39	-

Risks and burden of musculoskeletal health problems among "work from home" and "work from office" employees of the Information Technology (IT) industry

A cross-sectional analytical pilot study Given that "work from home" became a norm for many jobs during the COVID-19 pandemic, which still continuesin many sectors, a study compared the prevalence of work-related musculoskeletal discomfort (WMSDs) and performed objective ergonomic assessment of the working postures, using the Rapid Upper Limb Assessment (RULA) tool in the "work from home" (WFH) and "work from office" (WFO) employees of the IT sector. The preliminary results showed that the overall prevalence of MSDs (in any the body regions) among IT professionals was 70%. Lower back pain was the most common (48.9%), followed by neck pain (17.8%) and upper back pain (12.2%). However, no statistically significant difference was found between the two groups (WFH/WFO) of employees. Overall RULA scores (p=0.025), the neck RULA scores (p=0.025) and the wrist RULA scores (p=0.038) were higher in the WFH group when compared to the WFO group. The poor ergonomic scores suggest a greater risk of developing musculoskeletal disorders in the longer

run. The study findings give a thrust to the idea of provision of furniture/ monetary support by the IT companies to the employees "Working from home" for the development of ergonomic home workstation.

Fig. 3: Assessments done for calculating postural angles using Imagej Software.

Evaluation of impact of pesticide usage through environmental and biomonitoring of farm workers with special reference to urinary metabolites

Occupational pesticide exposure and pesticide poisoning are unappreciated threats to the farm workers. The impact of pesticide usage and exposure through the biomonitoring of farm workers with special reference to urinary metabolites and cholinesterase activity was studied. The mean ages of exposed and unexposed subjects in our study were 45 and 50 years, respectively andthe mean exposure period of farmers was 20.21±15.27 years in the farming activity. Urine samples were processed for DAP metabolites and analysis is in progress. Mean erythrocytes acetylcholinesterase (AChE) activities were found as 4.25±1.27 U/ml and 4.60±2.65 U/ml in the exposed and unexposed groups, respectively. Plasma butyrylcholinesterase (BChE) activities weremeasured as 3.95±2.66 U/ml and 4.45±1.84 U/ml, respectively for the same groups. Thus, a significant reduction in cholinesterase activity was observed among exposed groups compared to the unexposed group. Although, there were no statistically significant differences in haematological and biochemical tests performed, higher prevalence of anaemia was observed in the exposed subjects (19% vs 5%).

Fig. 4: Pesticide Mixing by farm workers.

Fig. 5: Biological monitoring of farm workers.

Evaluation of health indices among e-Waste handling workers

Potential health hazards due to accumulating e-wastes is a major occupational as well as public health concern. A cross-sectional study carried out among 200 workers involved in e-waste recycling and related activities in Bangalore city, Karnataka showed that PPEs usage at the workplace was high. Around95.5% and 52.5% e-waste workers regularly washed hands and took bath,respectively

after work. General health complaints of the workers included backache (23.5%), neck pain (14%), muscle pain (9.0%), muscle rigidity (10.0%) and headache (13%). Blood concentrations of chromium, nickel and lead in the dismantling, segregation & processing and combined workers were significantly ($p<0.05$) higher than the supporting staff. Logistic regression analysis showed that the above workers also had higher chance for having high blood levels of arsenic and manganese compared to supporting staff. Further analysis showed no significant association between high metal levels and age and smoking habitsof e-waste workers.

Importantly, about 30% of subjects had systolic blood pressure ≥140 mm of Hg and diastolic blood pressure ≥90 mm of Hg. Hematological parameters were found to be normal, except for microcytic hypochromic and microcytic normochromic anaemia in nearly 8% and 11.5% of the workers, respectively. Comet assay showed a high frequency of DNA damage index among study participants. Significant increases in the levels of 8-hydroxy-2′-deoxyguanosine (8-OHdG) and abnormal levels of liver enzymes (SGOT and SGPT) were observed among study participants. Multinucleated and binucleated cells were also significantly higher among workers engaged in combined work ($p<0.05$).

TRANSLATIONAL RESEARCH

A carbon nanotube based miniaturized sensor for differential diagnosis of ACO from asthma and COPD

In a collaborative study with IIT Kharagpur, a Carbon Nanotube (CNT) based nanosensor to differentiate between asthma and COPD is being designed. We identified new markers that are presently being translated on the CNT based nanosensor for robust detection of the above diseases. Expression levels of 8 immunological mediators (NGAL, IL-5, MCP-1, IFN-γ, IL-6, TGF-β, IL-4 and IL-13) were estimated in the serum of COPD and controls. Since IL-13 showed significantly different expression in COPD patients as compared to healthy controls ($p>0.0001$) and its levels in serum being the highest, it was used for the development of the sensing platform.

To validate homogenous self-assembled monolayer (SAM) formation,atomic force microscopy (AFM) was performed at different regions of the SAM-modified electrode andvalidation of antibody binding with SAM was confirmed with ATR FTIR spectra.

Validation of each fabrication step was carried out using AC electrochemical impedance spectroscopy (EIS, (Fig. 6a). The obtained Nyquist plot shows significant changes in charge transfer resistance in each fabrication stage. The developed sensor was tested with varying concentrations of I-13 antigen, and the sensor output (Fig. 6b) showed distinguishable charge transfer resistance values, which will be used for the calibration curve.

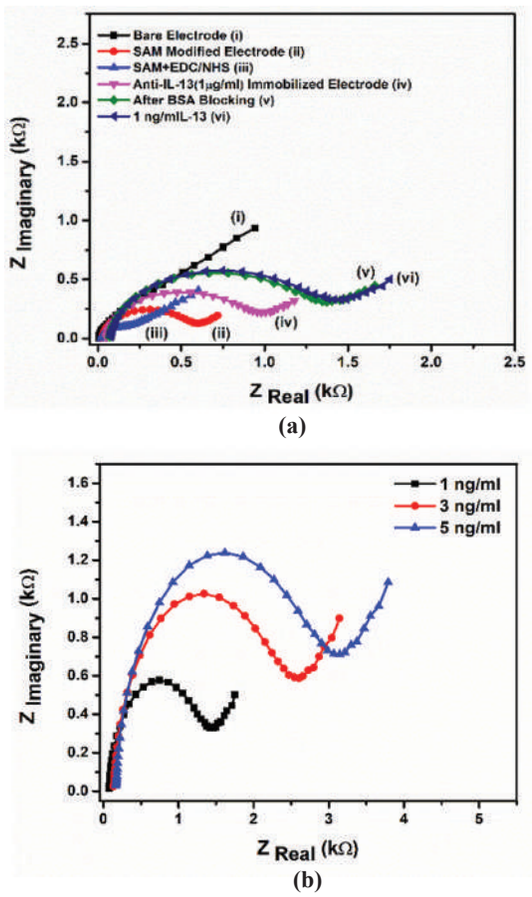


Fig. 6: Nyquist plot for (a) different fabrication stages and (b) varying concentration of IL-13 antigen.

NATIONAL TASK FORCE STUDIES

National Survey For The State-Wise Prevalence of Microbiologically Confirmed Pulmonary Tuberculosis In India

The study estimated the prevalence of microbiologically confirmed pulmonary tuberculosis for Gujarat state as 1.5 case per 1000 population. The overall notification for the state was 1,36,645 cases, with the absolute state TB burden being 95,511 (95 % CI of 53019 – 1,38,004). The state TB overall contributed to 2.2% (95% CI of 1.4 – 3 %) of national TB cases. Gujarat state was recorded as better functioning state among all states in the country with prevalence: notification ratio being 0.91 as compared to the national figures of 2.84

Population based serosurvey to estimate of SARS-CoV2 antibodies in India: Fourth phase (July 2021)

Prevalence of SARS-CoV2 antibodies for Gujarat state was estimated and > 60 % were seropositive to SARS-CoV 2, while 99 % health care workers were sero-positive.

Assessment of comparative performance (efficacy and safety) of C-TB with QuantiFERON-TB Gold Plus and 2 T.U. Tuberculin PPD RT23 SSI in Tube for detection of TB infection in general and key population

A study compared the efficacy (sensitivity and specificity) of C-TB with QuantiFERON®-TB Gold Plus and 2 T.U. Tuberculin PPD RT23 SSI in tube for the detection of TB infection in the target population with high, medium and low prevalence of infection. In addition, safety of the tests done individually or simultaneously was also evaluated. ELISA was done for 600 Participants (2400 tests) from Gujarat.

Study to Assess the Exposure and Health Effect of Pesticides

A national study on the potential toxicity and health hazards associated with endosulfan exposure was carried out to generate data which initiated scientific database at national level. Analysis of the samples from Maharashtra showed that, pesticide residues were present in 16.87 % of blood samples (106 of 628 samples)and 20.03 % of serum samples (126 out of 629 samples). 17 out of was 280 urine samples (6.07 %) showed the presence of pesticide residues.

Monitoring of Pesticide Residues at National Level

A total of 1915 samples were analysed successfully which included vegetables from farmgate and market, fruits from market, milk and surface water samples from different parts of Gujarat. Out of these only 175 samples (<10%) were detected with pesticide residues. Overall, monitoring programme showed that Acephate, Methamidophos, imidacloprid, Difenconazole. Chlorpyriphos, Malaoxon, Dimethoate, Tebuconazole, Propergite, Profenophos, Chlorantraniliprole, Ethion, Monocrotophos, Thiamethoxam were commonly present in the fruit and vegetable samples. The maximum residues were found in Bitter gourd, Brinjal, cabbage, capsicum, cauliflower, cucumber, green chili, tomato, okra, bottle gourd, cluster beans, apple, banana and mango, pomegranate and orange. This data can be used to understand the quality of food and to evaluate the possible health risk associated with their consumption.

National Environmental Health Profile (NEHP) – A multicity study

Now-a-days, deterioration in ambient air quality is a prime concern for the nations globally, as air quality closely relates to cardio-respiratory and other health parameters of the population. The present multicity study aimed to compare air quality and related health outcomes of different cities and to determine the influence of air pollution on health outcomes. The study involves the collection of three types of data: (1) air quality data from

the state pollution control board (2) meteorology data from the Indian meteorological department (3) morbidity and mortality data from selected hospitals. Also, it involves a cross-sectional community-based survey of selected urban clusters through questionnaires and point-of-care screening devices (Such as PFT). Ahmedabad study site has completed all 20 clusters, which covered 1415 households and 4021 family members. The study observed that 81.8% were residing in Pacca houses, 94% family used LPG as cooking fuel and 62% of households had isolated kitchens.Common, self-reported respiratory symptoms included sneezing and rhinorrhoea (21%), breathlessness (19.8%), cough (18.3%). Prevalence of prehypertension and hypertension among study subjects were 43% and 12%, respectively. The prevalence of obesity and pre-obesity were 5% and 40%, respectively.

RECENTLY INITIATED STUDIES

Isolation and characterization of Himalayan berries polyphenols extracts and their pharmacological evaluation in the treatment of inorganic arsenic-induced cognitive impairment in mice: DST Woman Scientists Project

Under this project, hydro/ hydroalcoholic extraction and phenolic characterization of selected Himalayan berries will be done and the berries extracts will be evaluated for therapeutic role in arsenic-induced cognitive impairment of mice.

Airborne and serum Aflatoxin B1 levels will be comparedbetween the occupationally exposed and non-exposed workers in different food industries from India. Also, Aflatoxin B1 levels will be correlated with genotoxicity and hepatic and renal function parameters among workers. No Indian study has so far compared airborne and serum aflatoxin levels and their correlations with adverse health effects among workers.

A proteomic approach to investigate lead toxicity in industrial workers

Limited human studies have been done on serum proteomic markers with reference to lead toxicity. The study will assess the proteomic profile, oxidative stress markers, and DNA methylation among Pb-exposed workers.

This study focusses on *Lagerstroemia speciosa*leaves(LSL) lectin as a preventive cancer marker, because of its relatively different agglutination patterns with normal erythrocytes as compared to the erythrocytes from the different types of cancers like Bladder (BL), Rectal (RC) and Oral (OR) and Leukaemia (LK).

Cataloguing metamobilome based environmental antimicrobial resistance patterns in pharmaceutical industries clusters of Gujarat

This newly initiated project envisioned the importance of horizontal gene based antimicrobial resistance emergences and cataloging of this information using the culture-independent methods. The study is in initial stages where the analytical methods for antimicrobial residues and whole genome sequencing based antimicrobial resistance genes (ARGs) patterns cataloging is being done. Some initial results from Operational Taxonomic Units (OTUs) based on relative abundance suggest that Firmicutes, Actinobacteria, Proteobacteria, Bacteroidetes, Chloroflexi, Verrucomicrobiota, Acidobacteria, Spirocetes, Nitrospirae and planctomycetes are some of the dominant phylum in the analyzed samples. At the family levels,Bacillaceae, clostridiaceae, Plancto-mycetaceae, Planococcaceae, Nocardioidaceae, Verrucomicrobiacea, Lactobacillaceae etc. are some of the major bacterial communities. Further, at genus levels, majorly the unclassified bacteria contributing towards the total metagenomics pool, this is also supportive to our hypothesis and selection of metagenomics approach as a method of choice for identification of microbial diversity.

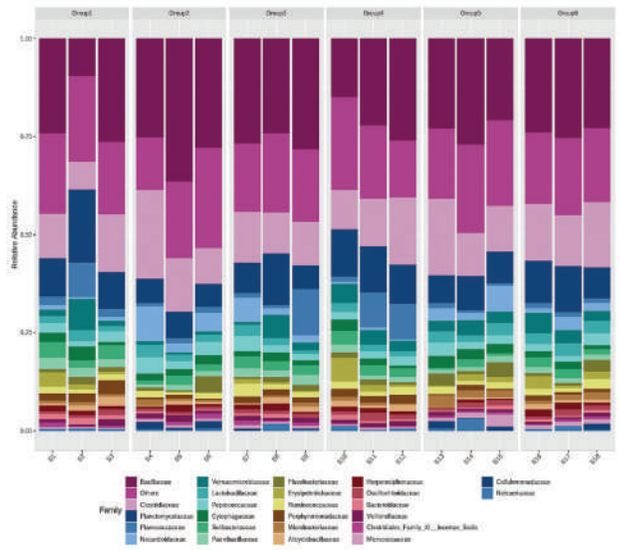


Fig. 7: OTU based relative microbial abundances at family levels in analyzed soil and waste water samples.

PRE-CLINICAL RESEARCH

Comparative evaluation of sex-dependent neurobehavioral outcomes upon various bisphenolanalouges exposure in adult mice

Present research work is an attempt to answer the research questions mentioned above where, the impact of oral chronic BPS and BPF exposure on anxiety and depression-like behaviour will be assessed in experimental rodent model (adult male and female mice). The study will provide critical information on the sex-dependent neurobehavioral outcomes upon such bisphenols exposure. Also, the effects on monoamine neurotransmitter levels (serotonine, dopamine, adrenaline and noradrenaline) will be assessed upon these exposures. Considering the structural similarity with BPA and due to the xenoestrogenic nature of these bisphenols, their effects on estrogen receptors and gluco-/ mineralo-corticoid receptors expression for neuroendocrine functions will be evaluated. Till the 8th week the anxiety related behavioral assessment using elevated plus maze suggest that males are showing more anxious behavior than females and also the effects are more pronounced with BPS and BPF than the BPA itself.

Protective effects of biochanin A and coenzyme Q10 combination against chromium induced toxicity in experimental model

Heavy metals like chromium toxicity are an important occupational health problem. Selected natural compounds like biochanin A and coenzyme Q10were evaluated for the prevention of chromium toxicity and the molecular mechanisms involved in the actions of these natural compounds at the gene levels were deciphered.

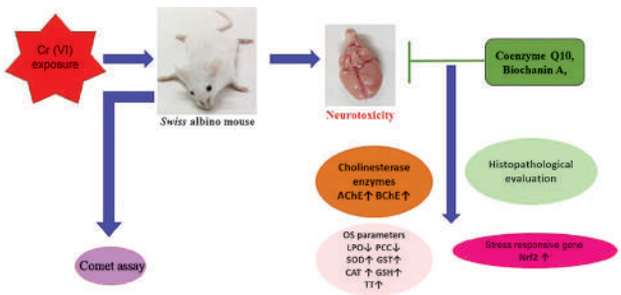


Fig. 8: Protective effects of biochanin A and coenzyme Q10 combination.

DATABASE AND REGISTRY DEVELOPMENT

Hospital Based Surveillance Using Worker's Registry for Occupational Diseases and Injury

The study involves hospital-based surveillance for disease and injuries pattern among admitted workers at ESIC hospital. The information of 600 under-treatment workers were collected from the ESIC Model Hospital, a multispecialty center. Maximum hospitalizations of workers were related to respiratory (34.83%) and cardiovascular (12.33%) illnesses. Further, nearly 10% workers reported with problems related to musculoskeletal disorders(MSD), with lower back pain being the most prevalent problem. Injury(non-fatal) at the workplace was recorded in 6.6% of the hospitalized workers. Most of the injuries were in the form of bone fractures (42.50%) and burn (22.50%). Data revealed that compliance and knowledge of the safety measureswere poor among the workers with nearly half of the injured workers not using safety gears and not having knowledge of preventive measures. These workers were engaged in work continuously for more than 8 hours before the injury. A large number of hospitalized workers reported a noisy environment (60.16%) at workplace, and nearly 65.50% workers reported the presence of dust /odour /smoke, and excessive heat at work environment.

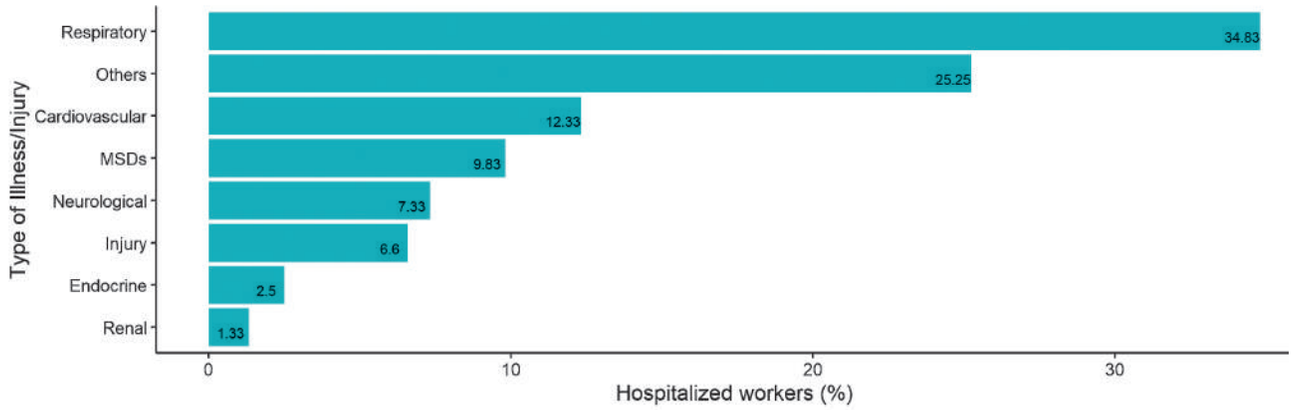


Fig. 9: Reported Illness and Injuries among hospitalized workers.

Fig.10: Chemical Burn of a worker.

PUBLIC HEALTH

1. Blood Lead levels (BLLs) were found to be significantly associated with systolic and diastolic hypertension. Individuals with the BLL>40µg/dL (upper acceptable limit recommended by OSHA) had higher systolic blood pressure (BP) (p = 0.029) and diastolic BP (p = 0.040) as comparedwith the BP of individuals having BLL <40µg/dL. Interestingly, diastolic BP significantly correlated (p = 0.025) with the quartile range of BLLs in a dose-dependent manner.
2. Epigenetic dysregulation in the form reduced DNA methylation was found to be correlated with Pb-exposure (BLLs and duration of exposure), vitamin B9 (Folate) deficiency and chewing tobacco products.
3. Extended duration of Pb exposure (product of the years of exposure and working hours per day >228) contributes to systemic inflammatory response (SIR), altered immunological markers (serum IgE and IgA), and reduced pulmonary function test (PFT) among loading and unloading workers at vegetable markets.
4. Workers (n = 132; 100 vendors, 32 loader-unloader) of the vegetable markets suffered from significantly higher prevalence of respiratory symptoms viz., cough, phlegm and dyspnea compared with the residential control subjects (n = 60) (P<0.05). The vegetable market area showed greater concentrations of endotoxin and (1→3)-β-D-Glucan in the dust samples compared with the residential areas.
5. A studyforenvironmental plastic-degrading microorganisms identified *Aspergillus* spp. as the major isolates capable of degradinglow-density polyethylene films. *Aspergillus ustus, Aspergillus fumigates, Aspergillus flavus, Aspergillus terreus*and *Aspergillus versicolor* were the main species identified. Among the bacterial isolates, *Bacillus* spp. and *Rhodococcus* spp. were found to be associated with maximum degradation of plastic films. These organisms degraded plastics at the rate of 1-2.5% per month and may be used to developlow-cost, low-technology, eco-friendly treatment modalitiesto reduce plastic wastes.
6. The prevalence of microbiologically confirmed pulmonary tuberculosis for Gujarat state was estimated to be 1.5 case per 1000 population.

7. Prevalence study of SARS-CoV-2 antibodies for Gujarat state showed> 60 % seropositivity in the general population with 99 % health care workers being seropositive.
8. Tools were developed and validated to screen occupational mental health and workplace factors influencing itfor the Indian workforce.
9. Reported registry findings are valuable source of data for OSH incidents in an occupational setting in India, the timely data in this area is not available otherwise in public domain. The findings are forming a basis for online registry in for occupational diseases and injuries.
10. Monitoring of pesticide residues in food products helps to assess the potential health risk and regulate MRLs for safe human consumption.

PATENT

Patent # PCT/IN2021/050793: A diagnostic device and method for differentiating Asthma-COPD Overlap Syndrome (ACO) from Asthma andCOPD. Filing date: Aug 17, 2021) – (Overseas Patent): The present invention relates to an interleukin-based, self-assembled monolayer (SAM)-modified impedimetric analytical device. The present invention provides a rapid diagnostic device with 98% average accuracy and 1 ng/ml limit of detection and can be a good alternative to other conventional sensors because of its cost-effectiveness, reliability and the requirement of low sample volume.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH, BHOPAL (ICMR-NIREH)

Inauguration of new green campus of ICMR-NIREH Bhopal

The permanent campus of the institute built with a budget of 1240 million Indian rupees was inaugurated on 13 March 2021 by the Union Minister of Health and Family Welfare Dr Harsh Vardhan. As a role model to the nation in the adoption of sustainable development practices, the permanent campus of the institute was constructed following the tenets of the Indian Green Building Council to maximize energy and water conservation, while safeguarding the health of the workforce as well as the surrounding environment.The campus minimizes its negative effects on the environment and ecosystem with efficient water and waste management strategies (e.g. rainwater harvesting, single-use plastic ban), energy efficiency (e.g. motion-sensitive lighting, maximum use of natural light, minimum outdoor light pollution) and green landscaping.

Fig. 11: Inauguration of new green campus of ICMR-NIREH Bhopal.

A cross-sectional study on current Health status of gas affected individuals of Bhopal: Phase II-Clinical examination of gas exposed survivors

In this study, clinical evaluation of randomly selected gas exposed survivors belonging to the exposed cohort of the ongoing Long-term Population Based Epidemiological Study was aimed with a focus on disease identification and determination of disability levels. A total 1657 gas exposed survivors (581 from severely exposed cohort + 523 from moderately exposed cohort + 553 from mildly exposed cohort) were clinically evaluated and about 76 types of morbidities recorded. The level of disability, as measured through *BarthelIndex*, was “mildly ill/near healthy

leading near normal life" (*Barthel Index*: 17-20) in over 86.4%, 91.3% and 93.7% of the examined subjects respectively in severely, moderately and mildly exposed cohorts.Hypertension (41.3% subjects), osteoarthritis (34.7%) and refractive errors (29.7%) were top 3 morbidities among 76 types of morbidities recorded. Morbidities clubbed system-wise revealed that musculoskeletal system related morbidities topped the list (67%), followed by cardiovascular system related morbidities (48%). Majority of the subjects (86.3%) clinically examined were categorized as mildly ill/near healthy leading normal life (Barthel index 17-20).

Aberrant circulating epigenomic signatures: development and validation of minimal invasive biomarkers for transgenerational monitoring of air pollution associated cancers

In this IMPRINT-India collaborative project between ICMR-NIREH, Bhopal and IIT-Kharagpur, a multi-city pan-India approach to compare the cell-free circulating epigenomic signatures of individuals living in two tiers of Indian cities categorized as low-risk and high-risk air pollution zones. The high-risk group reported marked changes in the expression levels of epigenetic modifiers (DNMT1, DNMT3a, EZH2, EHMT2 and HAT), that maintains the levels of specific epigenetic marks essential for appropriate gene functioning. These results also coincided with the observed alterations in the levels of DNA methylation (LINE-1 and % 5mC), and histone modifications (H3 and H4), among the high-risk group. In addition, higher degree of changes reported in the expression profile of a selected miRNA panel in the high-risk group indicated the probability of deregulated transcriptional machinery. This was further confirmed by the analysis of a target gene panel involved in various signalling pathways, which revealed differential expression of the gene transcripts regulating cell cycle, inflammation, cell survival, apoptosis, cell adhesion and mitochondrial integrated stress response. Together, our results provided first insights of epigenetic modifications among individuals living in different high and low levels of air pollution zones of India.

ONGOING PROJECTS

Population based long term epidemiological study on health effects of Bhopal toxic gas exposure

Due to COVID-19, the Long-term Survey 57th and 58th rounds were conducted through only telephonic communication. A total of 10,540 individuals belonging to 4,360 families of the original cohort were followed up. Overall, diseases of respiratory system (15.2%), diseases related to eye (7.9%), gastrointestinal tract diseases (2.9%) and skin problems (0.6%) were reported. The prevalence of any morbidity was 12.3% in severely exposed, 12.7% in moderately exposed and 18.4% in mildly exposed areas.

Assessment of micro-climatic variation on the population dynamics of dengue vector using a landscape genetics approach in an urban landscape

This study aims to assess the role of micro-climatic variables and landscape features on population dynamics of dengue vectors, to identify dengue hot-spots in an urban setting using landscape genetics approach and to assess the role of air quality index ($PM_{2.5}$ and PM_{10}) on dengue vector and disease dynamics. A total of 710 adult female *Aedes* mosquitoes were collected of which 47% (N=334) were *Ae. aegypti* and 53% (N=376) were *Ae. albopictus*. A higher density was observed in post monsoon period (from June to October). Highest mosquito density was observed in the month of August (per man hour density of 6.6 and 7.6 for *Ae. aegypti* and *Ae. albopictus* respectively). Both *Ae. aegypti* and *Ae. albopictus* mosquitoes were found to be prevalent in almost all the sampling sites across the Bhopal city except for sites S01, S07, S12, S16 and S27 where *Ae. aegypti* was found exclusively throughout the reporting period. Similarly, *Ae. albopictus* was found exclusively in the sites S08 and S17. Site-wise outdoor density of *Ae. aegypti* varies from 1.5 per man-hour to 15 per man-hour while that of *Ae.* albopictus varies from 1 per man-hour to 24 per man-hour.

All collected *Aedes* mosquitoes were identified at molecular level. A total of 337 *Ae. aegypti* and 276 *Ae. albopictus* mosquitoes were assessed for blood meal identification by using PCR based method. Human blood was detected in 6.5% of *Ae. aegypti* and 9.4% of *Ae. albopictus* mosquitoes collected from Bhopal city. RNA extracted from individual head-thorax of 725 female *Aedes* mosquitoes were pooled into 145 pools (5 *Aedes* mosquitoes per pool) and processed for RT-PCR based detection of dengue virus (DENV) and chikungunya virus (CHKV) infection. 4 pools were found to be positive for DENV infection (pool positivity 2.75%) and 3 pools were found to be positive for CHKV infection (pool positivity 2.07%). Serotyping of dengue positive pools revealed presence of both serotype 2 and 4 in Bhopal city.

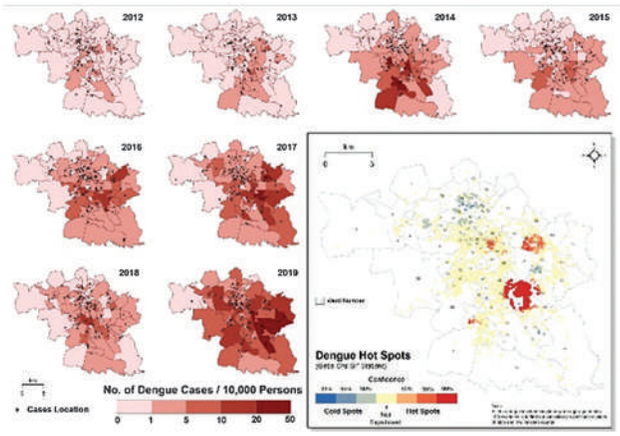


Fig. 12: Dengue hotspots in Bhopal city.

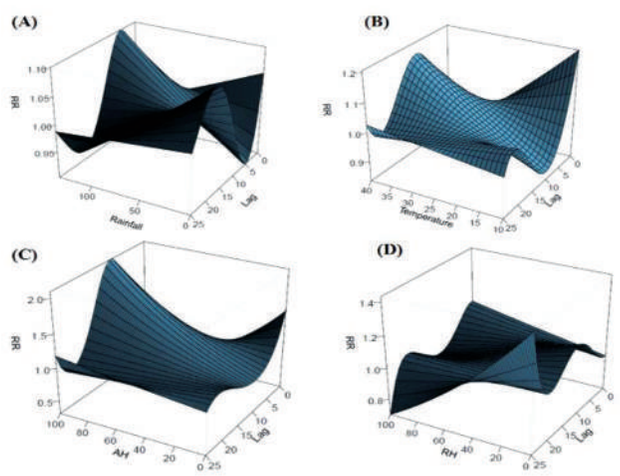


Fig. 13: Association between weekly (A) rainfall (mm), (B) Mean temperature (°C), (C) absolute humidity (g/m^3), (D) relative humidity (%) and relative risk (RR) of dengue at different lag periods.

Investigation on drinking water as a potential source of Endocrine disrupting chemicals (EDCs) to humans: An exploratory study in Jabalpur MP

In this study, the seasonal disparity and occurrence of six phthalates and bisphenol A (BPA) in the drinking water supply system and associated health risk were examined. DEHP was the most prevalent phthalate esters (PAEs) congener ranging from 1.14 - 8351.85 µg/L(winter) and 0.552 - 410.29 µg/L (summer) surpassing the permissible limit. However, BPA concentrations were found under the permissible limit. The results suggested that PAEs concentration displayed significant seasonal variations with the highest in winter and the lowest in the summer. The exposure to PAEs and BPA from drinking water was assessed, and the results indicated a possible health risk to humans with a Hazard Quotient (HQ) for DEHP. The findings necessitate an immediate scrutiny of these EDCs in drinking water supply system and are critical for implementing effective technologies at the WTP scale to ensure the quality and safety of drinking water in order to ascertain human and environmental health.

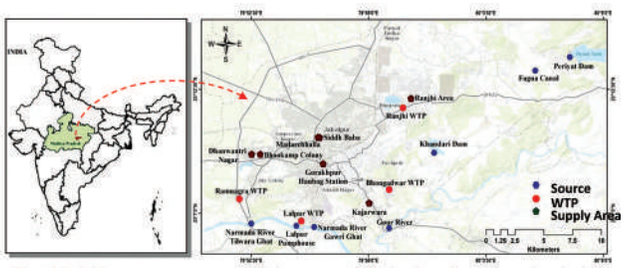


Fig.14: Drinking water as a potential source of Endocrine disrupting chemicals (EDCs) to humans.

Effects of improved information and volunteer support on segregation of solid waste at the household level in urban settings in Madhya Pradesh, India (I-MISS)

This study funded by Swedish Research Council for Environment, Agricultural Sciences and Spatial Planning (FORMAS) through Karolinska Institute, Sweden aims to develop a better understanding of household waste management for improved well-

being and ultimately societal and environment sustainability. A qualitative study was performed in Ujjain city, India. Ten focus groups discussions and eight in-depth interviews were conducted with household members in residential and slum areas. All interviews were digitally recorded, transcribed, and translated. The thematic framework technique using the Motivation-Opportunity-Ability-Behaviour theory for analysis was used. Three themes were constructed: Motivation – household members are motivated to sort waste yet fear the consequences of improper sorting; Ability – household waste segregation is rapidly gaining acceptance as a social norm; and Opportunities – convenient facilities and social support system for household members towards waste segregation.

Online Slogan Contest was conducted as the first step of crowdsourcing activity. A total of 969 entries (484 English and 485 Hindi) representing almost all part of India such as Madhya Pradesh, Rajasthan, Chhattisgarh, Uttar Pradesh, Uttarakhand, Karnataka, Delhi, Gujarat, Maharashtra, Bihar, Odisha, Haryana, Jharkhand, West Bengal, Telangana, Assam, Himachal Pradesh, Kerala, Andhra Pradesh, Chandigarh, Dadra & Nagar Haveli and Daman & Diu, Puducherry, Punjab, Sikkim, Tamil Nadu and Meghalaya were received.

PATENT

a. Patent Application titled "Fluorescent polystyrene based nanohybrid array for estimation of circulating cell-free miRs"

b. Patent Application titled "Nano-dendritic cell construct for selective targeting of tumour cells"

ICMR-BHOPAL MEMORIAL HOSPITAL & RESEARCH CENTRE, BHOPAL (ICMR-BMHRC)

The Bhopal Memorial Hospital and Research Centre (BMHRC) with and its eight Outreach Health Centres were started with a mission to provide free health care to those affected by the Bhopal Gas tragedy (1984), and to provide affordable healthcare to the public at large. The hospital was started in the year 2000, while services at the outreach centres were initiated in 1998. Healthcare services have been continuously provided since then to the victims of the gas disaster, their dependents, and to the public at large.

CLINICAL WORK

Clinical work at BMHRC involves treatment of patients in the out-patient department (OPD), investigations (Pathology, Radiology and Microbiology), procedures and surgeries, in-patient department (IPD) care and rehabilitation. 17 specialties are present at the main hospital. OPDs are run at the eight Health Centres 6 days a week, Radiological and Pathological investigation are done here too. The clinical work at BMHRC and its 8 Health Centres continued during the whole year (2021-2022) in spite of the ongoing COVID19 pandemic. COVID19 patients were also admitted in the 100-bedded isolation ward and provided all treatment facilities and services were provided round the clock.

Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB PM-JAY) started in BMHRC in January 2019 and is empanelled with the National Health Authority, New Delhi. BMHRC, Bhopal is the only Super Speciality hospital in Central India which has been empanelled for ABPM-JAY. The departments which are covered running under this scheme are Cardiology, Cardio Thoracic Vascular Surgery, Neurosurgery, Urology, Surgical Gastroenterology, Ophthalmology, Psychiatry and Pulmonary Medicine. Since the start of this scheme in BMHRC, Bhopal 1256 beneficiaries have benefited till date. During this period, despite the COVID19 pandemic BMHRC, Bhopal admitted and successfully treated 202 patients through ABPM-JAY. Approximate 31,810 samples for COVID19 testing were collected during this period at BMHRC and its eight outreach health centres. Additional sample collection was done in the

periphery (sub urban and villages near Bhopal) and Raja Bhoj Airport, Bhopal in association with district administration.

PATIENT DATA

- The OPD footfall in the hospital and its outreach health centres in the year 2021-2022was approximately 16,000 per month.
- Inpatients in the year 2021-2022 were approximately 600 per month.
- Nearly 4.5 lakh patients and their children are registered at BMHRC and its 8 health centres for health care. Free health care services are provided to all registered gas victims and their children/dependents. The doctors, nurses, paramedical staff and all employees of BMHRC (hospital and health centres) have worked continuously during this period in spite of the pandemic to provide timely and excellent health services to the patients.
- Total number of patient visits in BMHRC in the period April, 2021 to March, 2022 was2,00,301.
- Total number of diagnostic investigations done in this period are 9,98,581 (Radiology 32,934, Microbiology 4,94,439, Pathology 4,71,208 and Biochemistry). There were 4,03,257 COVID19 tests (RT-PCR, Rapid Antigen tests and Cartridge-based Nucleic Acid Amplification Tests) carried out during this period at BMHRC, Bhopal.
- 796 COVID19 suspects /cases were admitted and provided treatment in the COVID19 isolation facility.
- 22,207 doses of COVID19 vaccine were administered during this period.

Fig. 15: Ophthalmology department.

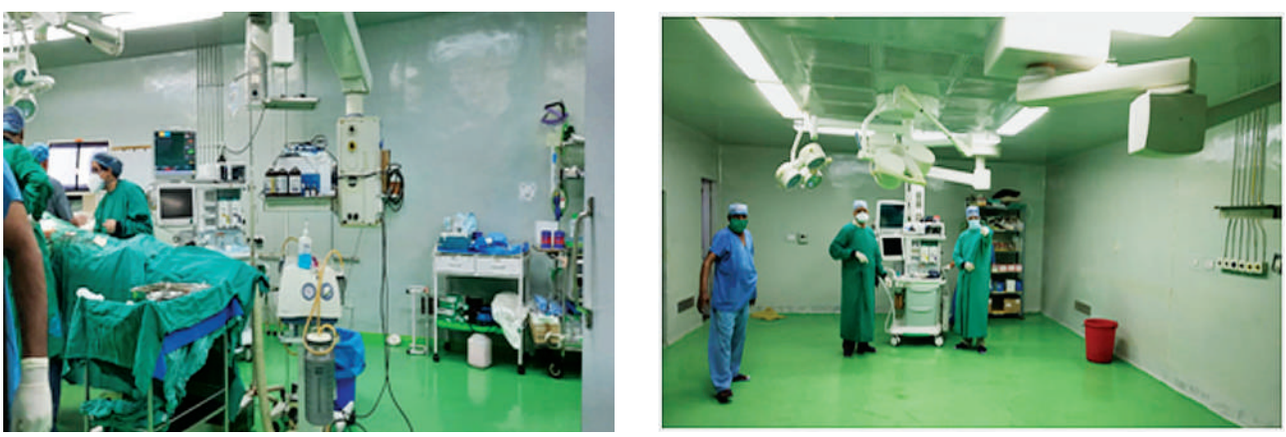


Fig. 16: Anaesthesiology and Critical Care Department.

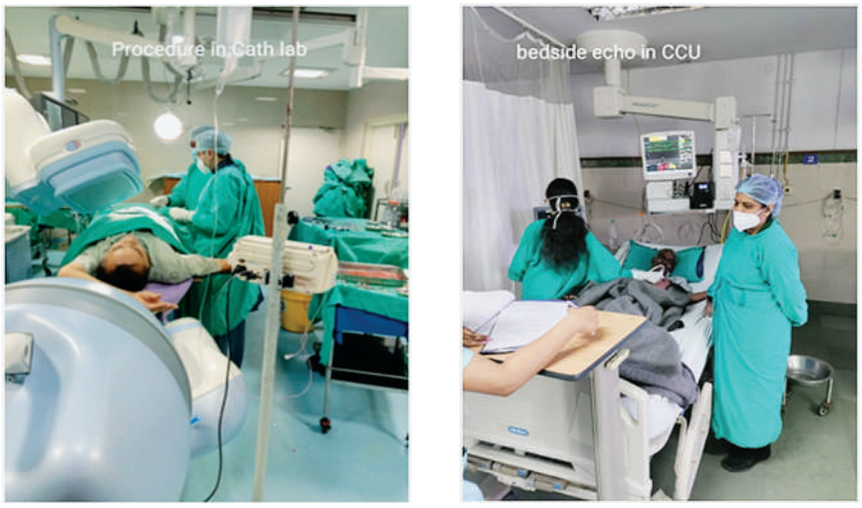


Fig. 17. Cardiology Departmen.

Fig. 18: Urology Department.

TEACHING/TRAINING ACTIVITIES

- DNB Ophthalmology course is ongoing. The second batch has been admitted.
- MD Anaesthesia course(Post Graduation) has begun in March 2022. In the 1st batch, four students have joined through NEET-PG.
- The Bhopal College of Nursing conducts the following courses: M.Sc. Nursing, B.Sc. Nursing and Post Basic BSc Nursing. These are recognized by Indian Nursing Council, MP State Nursing Council, and affiliated to MP Medical Science University, Jabalpur. Admissions were taken into Post Basic B.Sc Nursing and M.Sc. Nursing in 2021-22. Total number of admissions in the year is90. Achieved 100% results in University exam of Post Basic B.Sc Nursing and M.Sc. Nursing. Eight PG research project work were carried out.
- The Paramedical Institute at BMHRC conducts the following Diploma Courses:
  - Diploma in Anaesthesia Technician
  - Diploma in Blood Transfusion Technician
  - Diploma in Dialysis Technician
  - Diploma in Cath Lab Technician
  - Diploma in Medical Lab Technician
  - Diploma in Optometry & Refraction Technician

- PG. Diploma in Perfusion Technology
- Diploma in X-Ray & Radiographer Technician.

Total number of admissions in the academic year 2021-2022 is 58.Currently, there are 112 students pursuing their paramedical courses in the institute.

CLINICAL TRAINING / INTERNSHIP

- Twenty-eight students of Psychology underwent internship in Psychiatry during this period. Teaching program and training to students of nursing, clinical psychology, psychiatry and social work from various colleges is regularly imparted for Mental health. Internship and observer ship programs are conducted. The students of psychology are even trained to prepare for M Phil clinical/rehabilitation psychology entrance examinations.
- Mental Health Training of staff nurses of the district hospitals of Madhya Pradesh is regularly done in the department.
- 128 students underwent internship with training in Physiotherapy under the department of neurosurgery.

Trainings conducted by NRL, BMHRC, Bhopal

- Review Meeting of IRL-TB CDST laboratories linked with NRL BMHRC Bhopal for staff of IRL and C&DST Lab of MP, Chhattisgarh, Jharkhand and Goa on 25th November 2021.
- EQA refresher training for EQA Microbiologists and LTs of IRL Bhopal and Indore at NRL BMHRC, Bhopal on 27th and 28th December 2021
- Modular training for newly appointed LTs, at STDC, Bhopal from 02nd to 6th March 2022.
- LT modular training for new appointed LTs at districts from 17th to 19th February 2022.
- TrueNat training for LTs and STLS from 25th to 26th March 2022.

Trainings attended by NRL, BMHRC, Bhopal

- National Training of Trainers in Guidelines for PMDT in India-2021 from 14th to 18th June, 2021.
- National TOT in Guidelines for Programmatic Management of TB preventive Therapy from 26th to 29th July,2021.
- Training for NRL Biomedical Engineer on NTEP program, roles and responsibilities of BME, TB lab overview, TB lab equipment, Inventory management and procurement of lab equipment on 17th and18th November, 2021; 29th and 30th November, 2021.
- Assessment of LC & DST laboratories under STRIDES on 30th April, 2021.
- Meeting with STOs and the ICMR Institutes teams to discuss area of intervention for TB free districts towards End TB by 2025 on 2nd August, 2021.
- NRL Review meeting on 20th and 21st September, 2021

NACO (Integrated Counselling and Testing Centre)

- Training and support visits: 29.

Blood Safety Training for the District Blood Bank Medical Officers, Staff Nurses and Lab Technicians was conducted by the Department of Transfusion Medicine

- Medical Officers (Orientation Training Programme): 37.
- Staff Nurse: 44.
- Medical Officers (BCSU and Non-BCSU): 36.
- Lab Technicians (BCSU and Non BCSU): 96.

Voluntary Blood Donation Camps during 2021-22

During the COVID19 pandemic situation, services were provided to all needy patients. A total 40

voluntary blood donation camps as per new guidelines of NBTC were organized.

Fig. 19: Outdoor Voluntary Blood Donation Camp in Blood Collection and Transportation vehicle.

Fig. 20: National Voluntary Blood Donation Day and Felicitation Programme, 2021.

Fig. 21: National Voluntary Blood Donation Day and Felicitation Programme, 2021.

RESEARCH DEPARTMENT ACTIVITIES

- A symposium was organized on the topic 'Beat Air Pollution Reduce Carbon' during celebration of World Environment Day on 05th June 2021.
- COVID19 awareness session & management of Covid-19 pandemic was conducted by BMHRC on the 07th Jan 2022 at National Vigyan Mela, Bhopal.
- A workshop was organized on "Testing of blood biochemistry parameters for general public" on 07th Jan 2022 at National Vigyan Mela, Bhopal.
- A talk was delivered on "Radiation Response of acrocentric Chromosome Association (ACA): Biodosimetric perspectives" at a one-week online capacity building programme conducted by ICMR on 18th February, 2022 conducted at Jammu University, Jammu.

RESEARCH PROJECTS

The following are the ongoing projects at BMHRC, Bhopal

- Cytogenetic study of high-resolution CT(HRCT) scanning of chest for radiological examinations.
- Retrospective analysis of gall bladder resection specimens received in the department of Pathology, BMHRC.
- A comprehensive analysis of laboratory biochemical and hematology parameters in hospitalised COVID19 cases/suspects.
- A descriptive study to assess the knowledge regarding Management of post-partum Haemorrhage among Nursing officers of selected maternity Hospital of Bhopal.
- A study to assess the leadership style of the nurse educator perceived by nursing students.
- A study to assess the knowledge regarding partograph among nursing officers working in selected maternity hospital, Bhopal.
- Immune response to precautionary third dose of COVISHIELD / COVAXIN among healthy adult population: an ICMR Cohort study, India.
- A Demonstration Project for Reduction of Tuberculosis in India – A Multicentric Study.
- To evaluate the sensitivity and specificity of the PathoDetect™ MTB RIF & INH drug resistance kit for detection of *Mycobacterium tuberculosis* as compared to the gold standard (part A) To evaluate sensitivity and specificity

of the PathoDetect™ MTB RIF & INH drug resistance kit for detection of drug resistance in MDRTB suspects as compared to the gold standard (part B).

- To evaluate sensitivity and specificity of PathoDetect™ MTB & NTM detection kit for detection of *M. tuberculosis* (MTB) and Non-Mycobacterium Tuberculosis (NTM) in TB suspects in comparison with the gold standard.
- Study of efficacy of passive leg raising test along with tidal volume challenge in predicting fluid responsiveness in ventilated patients.
- Assessment of partakers in tumor ME for prognosis of Glioma. A DST funded project.
- Public knowledge, attitudes and practices towards COVID-19: A web-based study in India.
- COVID 19 Awareness among Health Care Professionals Associated with Hospitals of Central India.
- Multicentric prospective observational study of current analog-sedation practices and the incidence of delirium in Indian ICUs [INSTINCT study group].
- A descriptive study to assess the knowledge on breast feeding technique among prim antenatal women attending the ANC OPD in selected maternity Hospitals, Bhopal.
- Assess the knowledge, Attitude, Perception regarding myocardial infarction (MI) and associated lifestyle behaviour of the patient with MI at Bhopal Memorial Hospital and Research Centre, Bhopal.
- Assess the knowledge on objective structured clinical examination (OSCE) among graduate students.




Fig. 22, 23, 24, 25: COVID19 vaccination.

NON COMMUNICABLE DISEASES

In the area of non-communicable diseases, ICMR's National Institute of Cytology and Preventive Oncology, Noida continues to carry out research studies for prevention and early detection of cancer. The National Centre for Disease Informatics and Research, Bangalore focuses on the National Cancer Registry Programme and related activities like software module for cancer registration, patterns of cancer patient care and survival studies. National Institute for Implementation Research on Non-Communicable Diseases (NIIRNCD) has been working in the following major research areas during the reported period viz. Early detection of breast cancer, Sickle cell anemia and other studies mainly on IDD, tuberculosis, H1N1, silicosis, snake bite, etc.

Major highlights of various programmes undertaken by ICMR in the area of non-communicable diseases during the year 2021- 22 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF CANCER PREVENTION AND RESEARCH (ICMR-NICPR), NOIDA

Population Based Cancer Registry (PBCR) at ICMR-National Institute of Cancer Prevention & Research covering Gautam Budh Nagar

The PBCR has been set up to cover the rural and urban population of District Gautam Budh Nagar (G.B. Nagar), Uttar Pradesh. The total cases of cancer patients registered during the reporting period (April 2021 – March 2022) for the year 2019 and 2020 was 3115 (data collection and entry is ongoing). Total mortality in cancer cases for the year 2019 and 2020 was 269. The most frequent sites of malignancy in the region (both genders included) were found to be breast followed by digestive organs and lip, oral cavity and pharynx.

Comparative study of Genetic, Clinical and Epidemiological factors of Breast Cancer in Indian population

This study aimed to identify the mutational landscape of breast cancer in Indian population along with its putative pathway(s) through whole exome sequencing and transcriptome analysis. The transcriptomic data unraveled three differentially expressed dysregulated genes- Gene1, Gene2 and Gene3 among four different subtypes of breast cancer. Western blot analysis revealed an overexpression of these 3 genes in > 80% of the breast tumor samples as compared with their normal adjacent tissues, suggesting their important role in carcinogenesis. A significant higher expression of these 3 genes was observed with respect to different subtypes of breast cancer on validating of immunoblotting results by immunohistochemistry. Both the techniques showed good concordance. Similarly, qRT-PCRs were performed to check the mRNA level expression of these genes which also showed de-regulation among different subtypes of breast cancer. Mutational landscape of breast

cancer patients is being validated through Sanger Sequencing.

National Tobacco Testing Laboratory (NTTL) at ICMR-NICPR

The NTTL is providing analytical facilities for tobacco and tobacco products. In the year 2021-22, smokeless tobacco (SLT) samples were received from various government agencies across the country, and also from WHO reference samples for tobacco product analysis.

The lab received approximately 297 smoked& smokeless tobacco samples and performed nearly 1123 tests in the reporting period (~ 3369 test in triplicate) for the various parameters such as Nicotine, Moisture, Total sugars, Ammonia, Volatile Bases, Chloride, Humectants and pH.

Addressing Smokeless Tobacco Use & Building Research Capacity in South Asia (ASTRA)– A randomised-controlled, feasibility trial for smokeless tobacco cessation

This study is being conducted in collaboration with the University of York, United Kingdom to identify the feasibility and effectiveness of behavioural support therapy in enabling quitting smokeless tobacco (SLT) among adults. According to the preliminary findings 50% SLT users declared that they have quit tobacco after completing the 26th week follow-up. The reasons of relapse among the study participants who were unable to quit tobacco included prevailing myths such as improved concentration and ease in bowel movement, strong dependency to fulfil occupational demands i.e., to remain active in night shifts/long working hours, relapse due to advice given by the traditional healer/quacks to chew tobacco for tooth problems, and stress due to the uncertainties in employment during Covid 19 pandemic. Few participants showed disinterest in nicotine replacement therapy (NRT) use due to excessive salivation with the usage of NRT, dislike for the sweet taste of the various flavors of NRT being offered, and inability to receive NRT due to migration to their native places during lockdown leading to relapse.

Strengthening BioChemicals research policy, capacity building and cessation support to advance smokeless tobacco control in India

This study has been initiated for characterization of the common microorganisms present in processed tobacco products and to understand the molecular mechanism involved in the development of lesions of oral cavity among smokeless tobacco users. The predominant bacterial genera in SLT products (STP) were *Acinetobacter*, *Bacteroides*, *Bacillus*, *Prevotella*, *Faecalibacterium*, and *Pseudomonas*. The prevalent fungal genera in STPs were *Pichia*, *Sterigmatomyces* and *Mortierella*. Saprotrophic fungi were high in number in STPs that can ferment the constituents of STPs and convert them into carcinogens like TSNAs. Further, the oral microbiome analysis showed that the core oral bacteriome of SLT users having oral lesions were dominated by *Prevotella*, *Streptococcus*, *Veilonella, Haemophilus, Neisseria, and Fusobactrium*. SLT users having oral lesions had high bacterial and low fungal α-diversity along with distinct β-diversity compared to non-users. Aqueous extract of STPs like *Mainpuri Kapoori*and *Ghudakhu* caused serious damage to the cell lines via the production of reactive oxygen species, inducing cell death pathways, and stimulating the migratory potential of cells.

ICMR Task Force Study on Smokeless Tobacco (SLT) and Reproductive & Maternal Health (ICMR SLT-RMH Study)

This study has been designed to understand the socioeconomic and cultural norms towards SLT and areca nut use among women of the reproductive age group and to develop and test a behavioral intervention package to change the attitude and practices using Information Education Communication (IEC) strategies. In-depth interviews with pregnant and lactating women using SLT revealed that friends and relatives had major influence during premarital stage, while in-laws, especially elderly female relatives along with women in the community had more influence in

post-marriage period for initiation of use. Perceived health benefits, urge to consume mud during pregnancy, social influences turned out to be the major factors of SLT initiation. Women were found more aware of its harmful effects during pregnancy in comparison to lactation period.

WHO FCTC Knowledge Hub on Smokeless Tobacco

The Knowledge Hub carried out the following dissemination and capacity building activities

a. **National Consultation on Global Youth Tobacco Survey (GYTA)-4: Emerging Challenges and Way Forward** was organized on September 2, 2021

b. The hub team participated as a resource faculty in **"The National Conference on Tobacco or Health (NCTOH) 25th-27th September 2021"** organized by PGIMER, Chandigarh.

c. Three-day webinar on "**Role of dental health professionals in smokeless tobacco cessation**" conducted from November 30 – December 2, 2021.

d. The **KH-SLT supported the proposed amendments to the Food Safety and Standards (Labelling and Display) Amendment Regulations, 2021** regarding warning on Pan Masala packages and submitted a detailed suggestion to the proposed amendment relating to the warning on the label of Pan Masala Products.

Prevalence of concurrent cervical and anal cytologic abnormalities and High-risk HPV infections in HIV infected women: An exploratory study

In this study, 135 HIV-positive cases and 160 HIV-negative controls were recruited. Low-grade cytological abnormality was seen in five (3.7%) HIV-positive and three (1.8%) HIV-negative women. Among the cervical smears, 15 low-grade lesions and four high-grade lesions were detected in 19 of 135 (14.1%) HIV-positive women while five (3.1%) low-grade lesions were seen in HIV-negative controls.

Of the HIV-positive cases, 28 (20.7%) anal and 39 (28.8%) cervical samples tested positive for HR-HPV. Among HIV-negative controls, 14 anal samples (6.1%) and 15 cervical samples (6.9%) were positive for HR-HPV infection

Development of a Low-Cost Automated Screening System for Cervical Cancer (CerviSCAN II) – a collaborative project of CDAC (T) and RCC-T

CDAC (T) has developed an indigenous slide digitizer (DiGiSmear AS20) along with indigenous auto-stainer and cytocentrifuge for the project. Artificial intelligence-based algorithm for detection of abnormal cells using deep learning approach had been developed and tested against screening of cervical smears by cytotechnologists at RCC-T.

In the validation phase of the project, the indigenously developed system was installed at ICMR-NICPR. For this validation, 250 cervical samples were processed on this system and the interpretation of direct microscopy of the smears prepared through the mega funnel technique (MFT) was compared with that of the digitally scanned smears and the artificial intelligence-enabled selected fields.A good concordance (85%) was found between the direct microscopy of the MFT smear and scanned images for the detection of cervical lesions. The use of this low–cost automated device can augment cervical cancer screening in low resource settings fraught with paucity of trained cytotechnologists.

Scaling up of implementation of primary HPV screening by self-sampling

Women aged 30-65 years, residing in East district of Sikkim were offered HPV test on the self-collected samples. A total of 1138 samples have been collected during the reporting period. Of these, 10% were positive for HPV. All screen test positive women underwent VIA and precancerous lesions were treated as per the guidelines. The results are being analyzed in detail for further recommendations.

Genomics of Gall Bladder Carcinoma in Indian Population

This study aims to elucidate the genetic alteration in GBC etiopathogenesis using NGS platform followed by validation, in Indian population. Whole exome sequencing was performed in 57 paired samples. The data demonstrated the highest occurrence of missense mutations followed by nonsense mutations and frame shift deletions (Fig). The RNA sequencing data found a total of 29837 genes to be differentially expressed. After filtering the genes on the basis of log2 fold change and p value, a total of 238 genes were found to be upregulated and 166 genes to be downregulated in tumor samples.

Brain derived neurotrophic factor (BDNF) and its receptor, TrkB in gall bladder carcinoma: potential biomarkers and prognostic markers

Of the 40 cases recruited in the study during this period, 37 cases showed features of chronic cholecystitis with or without cholesterolosis while three cases were diagnosed as gall bladder carcinoma. RNA isolation, cDNA preparation and qRT-PCR was performed. With chronic cholecystitis as a reference control and 18S gene as an internal control, the three cases of gall bladder carcinoma showed a 19-fold, 17-fold, and 17-fold, amplification for BDNF gene.

Capacity building of healthcare providers in screening & early detection of common cancers using a hybrid model as a part of the population-based cancer screening program in India

Five courses (two each for Medical Officers and Nurses and one for healthcare providers in Africa) were conducted on ECHO platform and contact hands-on-training.

Feasibility of integrating tobacco use screening and tobacco cessation services with routine antenatal care services: a pilot study in district hospital of Gautam Budh Nagar

Focus Group Discussions were held with Community Health Workers (ASHA). Most of the ASHAs had knowledge regarding tobacco products and their harmful effects on women in general and pregnant women. But they routinely did not screen pregnant women for tobacco use and had limited knowledge regarding where to refer them for cessation counseling. In-depth Interviews with Gynecologists revealed that majority had knowledge regarding the adverse effects of tobacco on baby's and mother's health but they did not apply that knowledge in routine antenatal care.

PUBLIC HEALTH

1. A **High Throughput Viral Diagnostic Laboratory (HTVDL) for Covid-19 testing** was established at ICMR-NICPR. A total of 21,57,148 samples were tested by RT-PCR for Covid-19till March 2022. For the period under report (April 2021-March 2022), 11,78,948 samples were tested at the laboratory at NICPR. This facility catered to western Uttar Pradesh and Delhi (Fig. 1).

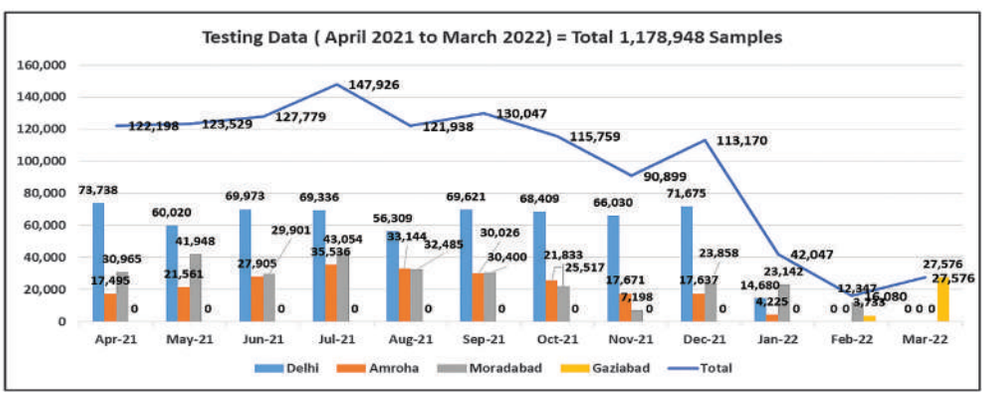


Fig. 1: Graph depicting Covid-19 testing statistics at ICMR-NICPR.

2. **National population-based sero-surveillance for SARS-CoV-2 infection transmission in India: Fourth round (June-July 2021)**. ICMR-NICPR was one of the nodal centres covering three districts (Amroha, Saharanpur and GB Nagar) and 30 clusters.In the fourth round of survey during 28th June – 4th July 2021,the Covid-19 sero-positivity ranged from 51.3% - 68.9% among general population and 86-91% among health care workers.

3. **National survey for state-wise prevalence of microbiologically confirmed pulmonary tuberculosis in India (ICMR & WHO Collaborative project):**ICMR-NICPR has carried out the survey among individuals >15 years of age in 9 clusters of Delhi, 17 of western Uttar Pradesh and two of Haryana. In Delhi, microscopically confirmed tuberculosis was detected in 25 out of 7839 eligible persons. In Uttar Pradesh, 49 of 13,600 eligible individuals were confirmed to have tuberculosis (Fig. 2).

Fig. 2: Pulmonary tuberculosis survey.

CAPACITY BUILDING PROGRAMS

a. **DHR-funded Hands-on workshop on Research Methodologies in Molecular Biology** (Nov 30 – Dec 03, 2021). Nineteen participants (19) from various disciplines (MBBS/MD/MS; MDS/BDS; AYUSH; PhD) participated in the workshop (Fig. 3).

Fig. 3: Basic Molecular Biology Techniques Relevant to Cancer Research – Hands on Training - Tissue Culture related Techniques.

b. **Capacity building of various cadres of Health Care Providers in cancer screening** through NICPR-ECHO program - Medical Officers-3 batches, Dentists-2 batches, and Nurses-2 batches.

c. **ICMR-AU-STRC Training Program on cancer screening** for health care providers in Africa through ECHO platform, Mar-Jun 2022 (12 participants).

d. **Hands-on training on Cervical cancer screening and treatment of precancer for Medical officers (in association with MCH Wing, NPCDCS, Chhattisgarh)** on December 15-17, 2021 and March 02-04, 2022 attended by 60 and 75 participants, respectively (Fig. 4).

Fig. 4: Hands-on training on Cervical cancer screening and treatment of precancer for Medical officers.

e. **1st Virtual workshop on cervical cancer screening for pathologists** (July 26-30, 2021). The workshop was attended by 50 participants from across the country. In addition, NICPR-ECHO Online Certificate Course on Cervical Cancer Screening for Pathologists was held from 23rd February till 29th April 2022 and was attended by 42 participants (Fig. 5).

Fig. 5: NICPR-ECHO Online Certificate Course on Cervical Cancer Screening for Pathologists.

f. **Oral cancer screening workshop for health care workers** on March 28-29, 2022 (18 participants).

g. **Hands-on Workshop "Molecular Docking, Pharmacaphore modeling and Machine Learning"** (March 15-16, 2022) attended by 106 participants.

PATENT

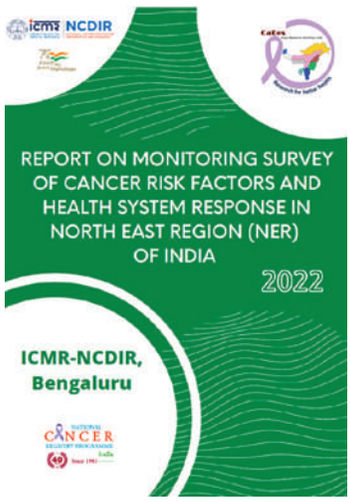
Patent filed for Diagnosis of Covid-19 using nucleic acid extraction free Real time PCR system.

ICMR-NATIONAL CENTRE FOR DISEASE INFORMATICS AND RESEARCH (ICMR-NCDIR), BENGALURU

Monitoring survey of cancer risk factors and health system response in the Northeast Region of India

The project was conducted during 1 November 2019 - 30April 2021. A total of 21321 respondents spread across a total of 480 Primary Sampling Units (PSUs) in the 12 cancer registry areas participated in the survey. The survey included household and individual level interviews. This study generated key cancer and other NCD related risk factors and health system response indicators in the 12 Population Based Cancer Registries in 8 states of North East India.

The report describing findings from pooled analysis of all state results was released on 4th February 2022 on the event of World Cancer Day.



https://ncdirindia.org/All_Reports/NE_Report_2022/Default.aspx

Fig. 6: Report on Monitoring Survey of Risk Factors and Health System Response in North East Region (NER) of India.

KEY FINDINGS

The proportion of solid fuel use was high in rural areas (79%), 51.3% of the population (rural and urban combined) used wood as cooking fuel. Nearly half of the respondents (48.6%) were current tobacco users, comprising 61.7% men and 34.8% women. Close to a quarter (22.8%) of the respondents reported to have consumed alcohol over the past 12 months. The mean number of days on which either fruits or vegetables were consumed was 0.8 days in a week. According to the WHO criteria, the proportion of those who were obese was 5.2%, while the prevalence of obesity was higher (27.6%) using Asian cut off points. The prevalence of raised blood pressure was 28.7%. The proportion of respondents whose blood glucose level was over 126 mg/dl was 5.1%.

Over a quarter (26%) of the cancer patients were self-financing their treatment; 5.8% were covered

by health insurance. Cancer screening for all three types of cancers (cervical, breast, oral) was available in 19.1% of the PHCs', 20.4 % of the CHCs' and 35.7% % of the District hospitals. A few CHCs' had a specialist in position in the following departments of surgery (17.3%), medicine (39.8%) and gynaecology (36.7%). Less than 50% of the General Duty Medical Officers at the CHCs' and District hospitals had been trained for NPCDCS/ NHM (NCD related)/State program.

Overall, addressing cancer control in the NER requires a multidisciplinary approach at all the levels of prevention, from primordial to tertiary, coupled with community participation and multisectoral coordination to ensure optimal outcomes which would be evidenced by cancer incidence and outcomes in terms of survival rates and mortality.The individual State Reports have been prepared and sent to the registries for release by the concerned State Health authorities / dignitaries for more impact.

Publication of the Volume I of the Reference Book entitled "Biomedical Ethics- Perspectives in the Indian Context"

ICMR Bioethics Unit under the aegis of ICMR had collated a reference book on biomedical ethics which was published by Jaypee Medical Publishers. This was the first-of-its-kind book in India with a comprehensive and unique compilation of topics addressing ethical aspects in various kinds of research in Indian context. The contributors to the book were national-level experts in their respective domains who have shared their expertise and knowledge on specialised topics that have been articulated in a manner to understand the intrinsic ethical challenges faced by researchers, clinicians, students and ethics committee members involved in biomedical and health research in India. The book is comprehensively curated to serve as a tool for teaching and training purposes. It is intended to provide guidance to students, researchers and ethics committee members. The book was released on World Health Day 7th of April 2022 by DG, ICMR and being disseminated to various medical institutions and research organisations across the country.

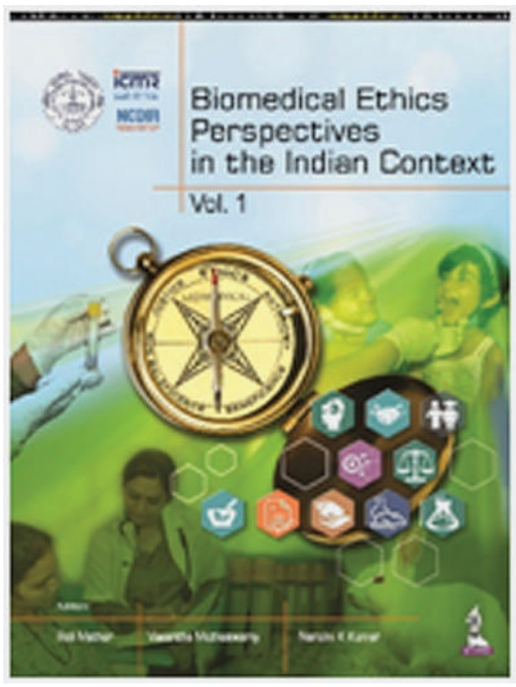


Fig. 7: Reference Book on Biomedical Ethics - Perspectives in the Indian Context Vol 1.

Release of "Clinicopathological Profile of Cancers in India: A Report of Hospital Based Cancer Registries, 2021" on 24 September 2021, on World Cancer Research Day

https://ncdirindia.org/All_Reports/HBCR_2021/

Fig. 8: Report on Clinicopathological Profile of Cancers in India: A Report of Hospital Based Cancer Registries, 2021.

The Report consolidated the data collected during the years 2012-19 from 96 Hospital Based Cancer Registries (705,395 cases) under NCRP. 52.9% cases were males and 47.1% were females.

Key findings

33.3% of total cancers were in sites associated with tobacco use (48.7% males and 16.5%% females). Among women, gynaecologic cancers (including breast cancer) accounted for over half (51%) of all cancers. Cancers of the head and neck region accounted for nearly one-third (31.2%) of the cancers. Cancers in sites associated with tobacco use comprised 48.7% of cancers whilst Childhood cancers (0-14 years) comprised 4.0% of all cancers. The age group of 45 to 64 years reported the highest proportion of cancer from all sites except for prostate cancer (over 65 years) among males. Cancers of lung were diagnosed at a stage of spread to distant sites followed by gall bladder cancer and prostate cancer. Over one-third of patients with cancers of the tongue, larynx, thyroid, corpus uteri, kidney (including children), bladder and retinoblastoma had localized disease at the time of presentation.

Chemotherapy was the most typical treatment modality for many cancers regardless of the clinical extent of disease at presentation. Most cancer patients were initiated on cancer-directed treatment within 8 to 30 days of diagnosis, regardless of the organ site and clinical extent.

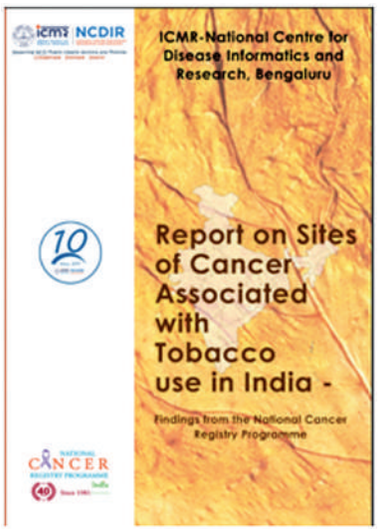
Profile of Cancer and Related Factors for Ten States – Factsheet

The Cancer Fact Sheets were released 24 September 2021. They had the information on the epidemiological profile and pattern of cancer from 10 states (Delhi, Gujarat, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Punjab, Tamil Nadu, Telangana and West Bengal), based on the findings from the 'Report of National Cancer Registry Programme 2020'. In addition, related information on the socio-demographic profile, health status indicators and health infrastructure were also presented. These have a significant bearing on the occurrence and outcome of cancer.

https://ncdirindia.org/All_Reports/State_Factsheet_21/default.aspx

Fig. 9: Profile of Cancer and Related Factors for Ten States – Factsheet.

Release of Report "Sites of cancer associated with tobacco use in India-Findings from the National Cancer Registry Programme" on World No Tobacco Day, 31 May 2021



https://ncdirindia.org/All_Reports/TRC_Report/Default.aspx

Fig. 10: Report on Sites of cancer associated with tobacco use in India-Findings from the National Cancer Registry Programme.

The report focusses explicitly on tobacco related cancers (TRCs') that constitute about 40-50% of all cancers and widespread tobacco use poses a huge avoidable burden on health. The report is based on data generated from 28 Population and 58 Hospital based cancer registries.

Key Findings

The highest Age Adjusted Incidence Rate (AAR) of cancer in sites associated with tobacco use is 161.3 per 100,000- males and 58.1 per 100,000-females are reported in the East Khasi Hills district of Meghalaya. The probability of developing any cancer type (cumulative risk) in the age group 0 – 74 years is highest in the East Khasi Hills district (1 in 5 for males and 1 in 14 for females). In all the regions, the relative proportion of sites of cancer associated with tobacco use to all cancer caner sites was higher in males than that of females.

Lung cancer is the most frequently observed site of cancer associated with tobacco use among males, followed by mouth, tongue and oesophagus in both genders. The majority of the cancers in sites associated with tobacco use are reported to have presented in the locoregional stage in both genders. Trend analysis of AAR over time indicates a significant increase in Aurangabad, Mizoramstate, Kamrup urban, Delhi, Kollam district and Chennai among males and in Bhopalamong females. On the other hand, AAR has declined significantly over time in Sikkimstate, Dibrugarh district, Mumbai and Barshi rural among males and in Sikkim state, Dibrugarh district, Mumbai, Bangalore and Chennai among females. The projected number of incidence cases for cancer in all sites associated with tobacco use by the year 2025 is 427273, of which the number of lung cancer cases would be the highest (111328) and constitute 27.2% of all cancers.

Cancer Epidemiology Surveillance Training (CanEST) Programme

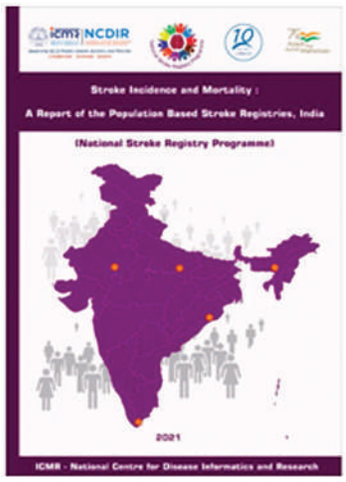
Cancer Epidemiology and Surveillance training programme (CanEST) was developed by in-house specialists experienced in handling Registry data, in consultation with National subject experts. The specific objectives of this training were to (a) Develop skills to analyze, interpret data and infer current registry data more efficiently and initiate and develop a strengthened surveillance system for Cancer in a defined geographical area. (b) Develop Research protocol for undertaking epidemiological research, both hospital-based and population-based; initiate, and oversee all phases of research activity. (c) Comprehend current Policies, Programmes, and Practices and help strengthen Cancer Prevention and Control. (d) Network with the Government Health system, the Private sector, and NGOs in Cancer Prevention and Control. The training was inaugurated on 22 October 2021.

Two batches of Research Scientists (19) from the registries have undergone the training till March 2022.The training was well received by the participants.

Fig. 11: Launch of Cancer Epidemiology Surveillance Training (CanEST) Programme.

Online Release of the Report 'Stroke Incidence and Mortality: A Report of the Population Based Stroke Registries (PBSR), India'

The first comprehensive PBSR report was released online on 10th November 2021. The report described the incidence and mortality patterns of stroke in five populations in the north, northeast, west, south, and east regions in India. The report has been disseminated among the stakeholders.



https://ncdirindia.org/All_Reports/pbsrbook/default.aspx

Fig 12: Report on "Stroke Incidence and Mortality: A Report of the Population Based Stroke Registries (PBSR), India".

Key Findings

There was regional variation in stroke incidence. Highest Crude Incidence rate(CR) (Males - 217.4 and Females - 156.6) was observed in Cuttack PBSR and the lowest CR (Males-123.4 and Females - 69.4) was observed in Cachar PBSR. Incidence of stroke was higher in rural areas than urban areas as observed in Cachar, Cuttack and Tirunelveli. Ischemic stroke was the most common type. The proportion of hemorrhagic stroke was high in Varanasi (35.1%) &Cachar (26.8%). Hypertension, diabetes &tobacco use was the prominent risk factors. Case fatality rate (deaths due to stroke within 28 days of onset of stroke) was high in all registries.

Access to Health Care among Individuals with Diabetes during COVID Pandemic in a Rural Setting in Karnataka

ICMR-NCDIR had conducted a community-based study to understand access to care for diabetes mellitus among 69 diabetes individuals in three villages in Devanahalli taluk. These patients were interviewed over phone following oral consent during the lockdown period using questionnaire on physician consultation, medicines, laboratory investigations & life style NCD risk factors.

Key Findings

Majority (95.7%) had reported that they monitored the blood glucose levels in the baseline. During the pandemic period the proportion who continued to do blood glucose monitoring reduced to 75.4% due to closure of laboratories, clinics and hospitals, non-availability of transport and glucometer strips, crowded hospitals and lockdown restrictions. 85.5% had reported blood glucose levels under control in the baseline, as compared to 70.5% who reported blood levels under control during the COVID-19 pandemic. Nearly three fourth (72.5%) had reported regular medication intake in baseline which reduced to two-third (65.6%) in the follow-up because of non-availability of pharmacy and transport, change of medicine brands and change of health facility of consultation due to the pandemic. More than two third (67%) preferred to use teleconsultation during the COVID-19 pandemic.

Strengthening Medical Certification of Cause of Death (MCCD) by development of mortality audit systems framework, online MCCD modules and standardize e-Mor application-Technical collaboration with WHO

Phase I of this project has been completed. The various deliverables completed under this project include:

- Content of training module on Medical Certification of Cause of Death (MCCD) has been developed.
- IRIS software training was conducted by experts of IRIS Institute. The purpose was to understand use of IRIS software for standardization of e-MoR software.

- Position paper on the framework of MCCD audit at hospital was developed. It has been reviewed by experts, CBHI, DGHS and the WHO. The report, 'Framework for audit of Medical certification of cause of death at health facility' has been developed for publication in collaboration with CBHI, DGHS and WHO-India.

Patterns of Stroke care in Ayushman Bharat – Pradhan Mantri Jan Arogya Yojana (AB PM-JAY) empanelled Hospitals

ICMR-NCDIR collaborated with National Health Authority (NHA) to describe the patterns of stroke, stroke care and outcomes in beneficiaries treated in empanelled hospitals of Ayushman Bharat PM-JAY scheme. The study revealed patterns of stroke care in 11 states/UTs and the need for strengthening data collection methods through the AB PM-JAY scheme to monitor stroke management in empanelled hospitals.

Integration of ICMR-NCDIR e-Mor cause of death software module with Tamil Nadu Civil Registration System (CRS) software is completed. All hospitals and local registrar offices in Tamil Nadu started using the integrated CRS software to record medical certification of cause of death (MCCD) from September 2021.

ICMR - Central Ethics Committee on Human Research

ICMR-Central Ethics Committee on Human Research (CECHR) appointed by Director General (DG), ICMR, works at the national level for the development and updating of National Ethical Guidelines, policies to address emerging ethical aspects of biomedical and health research, review research of national importance with complex issues being led by ICMR and its network of institutions or referred to it by government ministries and departments. Central Ethics Committee on Human Research (CECHR) was reconstituted by Director General(DG)with increase in membership (17 Members) as well as its scope and mandate to undertake review of high-priority COVID and non - COVID research in a relatively short period of time. The term of the committee came to an end on 6th May '22. DG, ICMR has now extended the term with existing members for 1 year (7th May 2022 - 6th May 2023). The mandate of the committee was mostly limited to COVID-19 research in the wake of pandemic during the last 2 years, however, now it is extended to all types of research being conducted by ICMR Headquarters/Institutions. Besides this the committee will be guiding the development of ethics policy and guidelines for the country. It will be able to appoint various subcommittees under its aegis as per need and requirements to undertake closer oversight of all proposed nationally important activities.

Public Webinar - Reducing Health Inequalities in NCDs - Towards a Healthier Nation on 7th April 2021

Fig. 13: Public Webinar - Reducing Health Inequalities in NCDs - Towards a Healthier Nation.

ICMR- NCDIR, Bengaluru organised a webinar 'Reducing health inequalities in NCDs - Towards a healthier nation' based on the World Health Day theme "Building a fairer, healthier world". The webinar aimed to educate the public and health professionals about the stark disparities within communities that impact health outcomes. Public Health experts Dr Rajani Ved, and Dr Yogesh Jain, explained the impact of inequities on NCDs and the framework of health system response to reduce inequities. Dr Vipul Aggarwal, Dy CEO, National Health Authority shared on the role of the Ayushman Bharat Pradhan Mantri Jana Arogya Yojana. The Question & Answer session discussed the challenges and opportunities to reduce health inequities for prevention and control of Non-communicable diseases in India.

ICMR-NATIONAL INSTITUTE FOR IMPLEMENTATION RESEARCH ON NON-COMMUNICABLE DISEASES (ICMR-NIIRNCD), JODHPUR

The study entitled "Strengthening State Non-Communicable Disease Programme for Early Detection of Breast Cancer Involving Strategic Education and Awareness Among Women" a joint program of ICMR-NIIRNCD and State Government

The National Programme for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases and Stroke (NPCDCS) in India was initiated in 100 districts in 2010, and later expanded to about 468 districts by 2012. The focus of NPCDCS is to enable screening for common non communicable diseases, at district and CHC levels, through setting up of NCD clinics. This study was initiated by the institute in March 2017. Breast Cancer Project staff has been regularly monitored, motivated and trained to do qualitative work. Information regarding knowledge, awareness and practice about signs & symptoms and risk factors of breast cancer have been collected from 47943 women (30-65 years).

A total of 58553 women have also been imparted training for breast self- examination and also to make them aware about signs and symptoms and risk factors of breast cancer. During this period, 175 suspect cases of breast cancer were identified. These cases were referred to the Government Tertiary Healthcare Centre and out of which two case has been found to be confirmedcase. One PHC of Jalore district has been covered for screening of women for cervical cancer. Phone call based follow up for BSE compliance was provided to 22901 women have been covered during 1st phone call follow up for BSE and 65164 women in round 1st and round 2nd respectively.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and The Effect of Early Intervention in Management of the Disease in Tribal Population

The study was undertaken for the newborn screening for Sickle cell anaemia (disease) in tribal populations of Rajasthan. The objectives were (a) early detection (b) to understand the magnitude of the problem and (c) to understand the barriers for undertaking such programme. To establish a cohort to study the clinical trajectories of affected individuals. To assess the benefit of early comprehensive care of affected babies. The study was carried out at Kotda, Jhadol and Gogunda blocks of Udaipur District. Since the initiation of screening at the above two blocks, 4501 new borns have been tested for various hemoglobinopathies. Among the new born screened for sickle cell disorder, 627 found sickle cell positive. Among the sickle cell positives, 600 (13.3%) were found to be Sickle Cell carriers and 27 (0.59%) Sickle Cell Disease. The mean Hb level of the SCD new borns varied between 8.1 to 9.4 g/dl (interval of 3 months). During the reporting period following incidence of clinical events in SS cases occurred including anemia. Acute febrile illness (AFI), Acute respiratory infection (ARI). The mean WBC count was recorded to be increased up to 6th Follow-up visit and found to be decreased after 7th visit. The RBC counts in follow-up visit found to be lower except in one follow-up visit. The variation of the Hb, HbS and HbF could not be correlated with the follow-up visit due to the less number of participants**.** During the reporting, one enrolled newborn died. No hospitalization required for the newborns during the reporting period. No hydroxyurea treatment required for the newborn during the reporting period. Among the 27 SD newborns, 3 SCD newborns died.

Screening of Tribal Population for Sickle Cell Anemia in selected blocks of Rajasthan

Imparted training to Medical Officers & 144 Para Medical staff for the screening of Sickle Cell Anaemia and its management. Screening of Sickle Cell Anaemia was carried out by ICMR-NIIRNCD,

Jodhpur jointly with State Medical and Health Department. A total of 43908 population screened for Sickle Cell Anaemia and prevalence of 7.49% (3,365) reported. Among them 2,223 were sickle cell trait and 96 were sickle cell disease. Sickle status card was distributed to the participants along with counselling.

Spatial Epidemiological Approach to Malaria Elimination Research (SEAMER)

Elimination of malaria demands an in-depth understanding of the dynamics between the contextual determinants and the human responses indifferent to ecological regions of the country. This study aims to discover the contextual variability of malaria transmission across eight states of India.

The 6 objectives of the project are as follows:

1. To provide the spatial distribution of parasite infection prevalence.
2. To map the behavioural risk factors and barriers.
3. To study the transmission potential of the identified hot spots using geo processing tools.
4. To understand the effect of various geographical, meteorological, socio-economic and behavioural determinants of malaria transmission.
5. Todevelopspatio-temporalmodelsoftransmissio nofmalariaanditsdeterminants.
6. To develop a dashboard for monitoring and surveillance in malaria elimination.

It is important to note that objectives 3 to 6 are dependent on the completion of data collection in the first two objectives. Data collection pertaining to the 2nd objective has been initiated, and the team will start receiving data from the sites by April 2022. The preliminary work related to the 1st objective is ongoing. Nevertheless, almost all preparatory work, including procurement, training, etc., is nearing completion.

Defining and Mapping Implementation Research on Non-Communicable Diseases (NCDs) in India

Along with rising burden on NCDs, it is important to note that the prevention and control of these diseases entail longer and larger social and economic commitments on the part of governments. In this context, it would be a logical move to understand the quantum, diversity, and quality of implementation research (IR) done in this field. Being a considerably larger domain, it seemed prudent to narrow down the focus to three specific sub-domains in NCDs, viz., cardiovascular diseases, diabetes mellitus and mental health ailments. Thus, this project was conducted as an Agreement to Perform Work (APW) with the WHO Country Office, India, aimed at conducting three systematic reviews of implementation research on Cardiovascular Diseases, Diabetes & Mental Health done in the country, with an overarching aim to examine how IR was done to advance prevention and control of NCDs in India, and how evidence from these studies could be better applied to support the large-scale impact of NCD interventions in India.

A Single-arm Feasibility Trial of Community-based Pulmonary Rehabilitation for Adults with COPD in slum areas of Jodhpur, Rajasthan

In this project, we propose to carry out feasibility study of implementing a community-based low cost rehabilitation programme for COPD patients. This will be administered at community setting with the help of trained nursing personnel. Therefore, the aim of this study is to devise an appropriate community-based PR programme and then determine the feasibility and acceptability of this programme for adults living with COPD in the slum dwellers and residents of LIG colonies in the Jodhpur and assess the potential for a future trial of its effectiveness. This study was started in March 2022. Recruitment of the staff and procurement of the instruments were completed. Till 31st March,

survey of the 240 household was completed for COPD.

Study to evaluate the effectiveness of BCG vaccine in Reducing Morbidity in Elderly individuals in COVID-19 Hotspots in India

Prospective cohort of 60-80 years old, living in hotspots for SARS-CoV2 infection in multiple cities in India were enrolled in the study between July-November 2020. Those who were negative for SARS-CoV2 infection on RTPCR and IgG antibodies were vaccinated with one dose of 0.1ml BCG. All were followed for 6-months post-vaccination with weekly telephonic calls and in-person visits at 3rd and 6th month when repeat RT-PCR and antibody testing were done. Study outcome was to determine the incidence and morbidity among the vaccinated. Incidence of COVID included positives by RT-PCR or antibody testing during follow-up. Plasma inflammatory cytokines were measured in a subset. In this study 3612 individuals screened, 1566 individuals (54% males; mean age: 67 years) met the study criteria and were vaccinated. BCG vaccinated elderly individuals showed fewer symptoms, good recovery, and less cytokine storm resulting in less inflammation after exposure to SARS CoV2 suggesting that BCG can be a potential adjuvant in the prevention of SARS CoV2 related morbidity and mortality.

Social Determinants of Low Birth Weight: A Hospital Based Study

Low birth weight continues to be a significant public health problem globally and is associated with a range of both short- and long-term consequences. LBW is a major public health problem worldwide especially in the developing countries. The maternal risk factors are biologically and socially interrelated.

The study was initiated in February, 2021 in Ahore Block of Jalore District. A total of 745 deliveries have been recorded. Out of the total, single baby born deliveries were 736 and 11 deliveries were recorded as twin babies. We have included mothers delivering live born singleton term baby with birth weight less than 2500 gm or more. Hence, 25 deliveries were found in low birth weight category. The team has enrolled 25 subjects in case group i.e. LBW delivery and 25 subjects under control group.

National Survey for the State wise Prevalence of microbiologically confirmed pulmonary tuberculosis in India

The team Rajasthan covered 19 clusters. A total 14432 participants were eligible for the surveys. Of the total chest X-rays, 92.2% were normal and 7.2% were abnormal. Prevalence of microbiologically confirmed pulmonary TB among population aged ≥ 15 years in the state (per 100 000 population) was 484.

Nationwide study to estimate incidence, mortality, morbidity and economic burden due to snake bite in India

The proposed study has sites in 13 states located in the 5 different geographical zones covering 1-4 districts in each state. Study districts in Rajasthan include Jaisalmer, Bikaner and Udaipur. The study proposes to include data from outside the hospital, directly from the community and would be first prospective study on snakebite burden in the country. This study shall also attempt to create the first computerized national registry for snakebite. Data collection is in progress.

Early diagnosis and development of referral system for sandstone miners

Silicosis is the most common and oldest occupational lung disease. But there is no uniformly available referral system for workers having occupational dust exposure. The current study involved clinical assessment of those working in mines and quarries in Jodhpur, Rajasthan, and explore the possibility of a referral system for symptomatic mine workers. Workers working in mines and quarry workers in the Jodhpur district were screened after choosing the quarries randomly. Demographic information

and detailed occupational history was recorded. Respiratory symptom score (RSS) was evaluated using a numeric score. A total of 386 mine/quarry workers (M:F=383:3) were assessed clinically. A total of 73 workers were symptomatic (19%) and salient hypoxia was present in 104(27%). Both groups of these subjects were referred to nearby community health centres for further evaluation. Awareness levels among the workers were poor as only 95/386 (25%) workers had some idea about the prevention among workers. Regular mask usage was present in 7.7% (30/386). Camp approach was used for subjects who were symptomatic and evaluation by a 3-member clinical board was done in vicinity of the community health centre, demonstrating a referral system. Those suspected of having silicosis were referred to pneumoconiosis board for further evaluation.

Assessment of Iodine status among pregnant & lactating women and 6-11 years children in selected districts of Rajasthan

This project initiated in January, 2021 with aim to carry out cross sectional study to assess the urinary iodine level among pregnant & lactating women and 6-11 years children in Rajasthan & to estimate the iodine content in edible salt samples collected from household of study along with Nutritional counseling for population for IDD program of Govt. of India. A total of 2901 households have been covered from 300 villages of Barmer & Balotra blocks of Barmer district and Gogunda Block of Udaipur district out of which 1452 were school children (6-12 years), 939 pregnant women of third trimester, 938 lactating & 941 NPNL women. Analysis of salt Iodine in 1694 sample revealed that 49.5 percent household use adequately Iodized salt i.e. 15 PPM &Analysis of urinary Iodine revealed that 49.4 percent pregnant & 46.1 percent lactating women suffered from mild to moderate iodine deficiency disorder. whereas in the NPNL women & school children, it was 26.1 & 6.3 percent respectively. In the present study, 50.8 percent pregnant women had urinary iodine below 150 µg/l which needs attention as per WHO guidelines. Project is in progress.

Assessment of Iodine adequacy in Urban Slum Population of Jodhpur city (Funded by ICMR in collaboration with CNRT)

This project is initiated with aim to assessment of urinary iodine status among 6-11 years children, pregnant and lactating women; determination of iodine level in edible salt samples collected from households and Nutritional counseling for population for IDD program of Govt. of India. The data has been collected from 30 wards covering 1140 households i.e. 900 school children (6-12 years of age), 200 pregnant women of 3rd trimester and 200 lactating women were examined for their Socio-demographic profile, Anthropometry& dietary intake along with a casual urine samples for estimation of Urinary Iodine Excretion (UIE) levels and salt Sample to estimate Iodine content of salt sample. Educational printed material, in local language/Hindi, in the form of pamphlets and pictorials were distributed. Analysis of UIE revealed that 31.4 percent lactating and 41.7 percent pregnant women suffered from mild to moderate iodine deficiency disorder whereas in the school children group it was only 21.8 percent. Severe iodine deficiency disorder was 5.8 percent in both pregnant and lactating women.20.8 percent pregnant women had UIE below 50 µg/l which needs attention as per WHO guidelines. Analysis of salt iodine revealed that only 27.7 percent HHs consume adequately iodized salt (15 ppm & above). Project is in progress.

An Intervention study for the promotion of 'COVID-19 Appropriate Behaviour' using culturally and socially appropriate methods among rural Population (Extramural Project funded by ICMR, Delhi)

This project initiated in February, 2022 with aim to assess and compare the culturally and socially appropriate methods as an intervention for improving acceptance of 'COVID-19 Appropriate Behaviour' in selected rural areas against the routine intervention & to assess the feasibility, acceptance, adoption and fidelity of the culturally

and socially appropriate methods for improving of 'COVID-19 Appropriate Behaviour' in rural areas. Interventions will help us understand the utility of socially appropriate methods in improving 'COVID-19 Appropriate Behaviour' (CAB) among rural women. Project is under progress.

Community based Nutrition Intervention models using local food preparations of Pearl Millet & food habits to address the problem of anemia & malnutrition in Rajasthan

This is an intramural project initiated in February, 2021 with aim to address the problem of anemia & malnutrition in Rajasthan *(Leads of Translation Project on Pearl Millet);* to do the improvement in the food practices of the rural population pertaining to local pearl millet preparations and to study the barriers, if any, related to it; promotion of inclusion of Pearl millet in Public Distribution System and Promotion of Inclusion of Pearl millet products in the Mid-Day Meal Program for the school children a state level program involving Ministry of Women & Child Development and Human Resource Development. Due to COVID-19, two online trainings & two Zoom Webinar Virtual training were conducted in which all the program managers i.e. AD (Nutrition), ICDS and all the Deputy Directors, CDPOs and LS of seven zones including all the 33 districts of Rajasthan had been sensitized with findings and benefits of the earlier studies on pearl millet undertaken by ICMR NIIRNCD, Jodhpur and their benefits in reduction of anaemia and management of MDDs and malnutrition. Imparted training and delivered a lecture on 'Local food preparations of Pearl Millet to address the problem of anemia and malnutrition in Rajasthan'. Number of participants were 1588. This will facilitate NACP program. This project is in progress.

ACTIVITIES

- Organized Symposium on 'Implementation Research in Health: Perspectives, Relevance and Challenges' on 27th June, 2021 in online mode (through both the Zoom and YouTube Live platforms) at ICMR NIIRNCD, Jodhpur. 579 participants across the country attended the Symposium. Dr. Abhijit Banerjee, Professor, MIT & 2019 Nobel Laureate in Economics, delivered the Chief Guest's Address on Economy & Implementation Research in NCDs'.
- Organized a workshop on 'Systematic Review and Meta-Analysis', on 20th & 21st September, 2021, at ICMR National Institute of Implementation Research on Non Communicable diseases, Jodhpur. Facilitators were Dr. Dheeraj Shah, Professor, Dept. of Pediatrics, UCMS, New Delhi, Dr. Khan Amir Maroof, Professor, Dept of Community Medicine, UCMS, New Delhi, and Dr. Shalieja Yadav, Resident, Dept of Community Medicine, UCMS, New Delhi. Total Number of participants were 13.
- Organized a Symposium on 'Implementation Research (IR)' on 5th October 2021, at ICMR National Institute of Implementation Research on Non-Communicable diseases, Jodhpur. Facilitators were Mr. Rajeev Sadanandan, Former Additional Chief Secretary, Health & Family Welfare, Govt. of Kerala and CEO, Health Systems Transformation Platform, New Delhi, Prof. (Dr.) Dorairaj Prabhakaran, Vice President (Research and Policy) and Director, Centre for Control of Chronic Conditions, Public Health Foundation of India, Dr. Abhijit Das, Clinical Associate Professor, Global Health, Department of Global, Department of Global Health, University of Washington & Director, Centre for Health and Social Justice, India, Dr. Jashodhara Dasgupta, Independent Researcher & Co-Convenor of the Feminist Policy Collective, Dr.Rakhal Gaitonde, Professor, Achutha Menon Centre for Health Science Studies, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Trivandrum.
- ICMR has designated four institutes as a central depot and 16 institutes as Regional Depots to coordinate and distribute test kits throughout the nation. Among these 16 regional depots,

this institute has been designated as a regional depot for 25 government labs spread over 19 districts of Rajasthan performing real-time RT-PCR tests to diagnose COVID-19.

- A total of around 4.7 kits distributed to government labs in Rajasthan under proper packaging and transportation conditions (maintenance of cold chain).
- The Institute has tested 45,202 Covid-19 samples.

Fig. 14: Inauguration of the GIS laboratory by Dr Samiran Panda, Addl. DG ICMR, Dr RS Dhaliwal, NCD Division Head - ICMR and Prof. (Dr.) Sanjeev Misra, Director, AIIMS Jodhpur.

Fig. 15: Official release of the report "Implementation Research on Cardiovascular Diseases, Diabetes Mellitus and Mental Illness in India - A Systematic Review".

EXTRAMURAL RESEARCH

CENTRE FOR ADVANCED RESEARCH & EXCELLENCE

This scheme encourages research in causation, progression, management, and/or prevention in identified research areas to get a better insight into the diseased condition. In 2019, 10 Centres for Advanced Research (CARE) including those in area of heart failure, young diabetes, acute myeloid leukemia, virtual autopsy, clinical pharmacology, kidney diseases-biomarkers and newer therapeutics, exhaled breath condensate, neuromodulation, pancreatic diseases and intestinal diseases were initiated. In 2021, two new CARE in neurosciences for developing early stage biomarker for Amyotrophic Lateral Sclerosis (ALS) and disability and assistive technology were initiated.

Under CARE –HF, a national heart failure database has migrated data from 25,156 patients from 4 registries in the country. Mortality rate in these patients was 18.25 in first year. Ischemic heart disease was responsible for HF in 69% of patients whereas rheumatic heart disease was present in 5% of patients. Heart Failure Biobank has been established; Detection method of NT-proBNP, a diagnostic marker for heart failure, in the lateral flow strip with colloidal gold as labels has been developed. Efforts are being made to use fluorescence based detection methods to improve the detection limits of this assay.

Under CARE-clinical pharmacology for drug development and pharmaco- economics for cancer therapeutics, formulation of powder for oral suspension (PFOS) of 6-mercaptopurine has been scaled up to industrial scale and batch stability has been tested. CARE-acute myeloid leukemia observed that the genes involved in regulation of apoptotic processes, cellular response to cytokine stimulus and negative regulation of transcription were up regulated in leukemic stem cells (LSC) as compared to the blasts. The LSC high group had significantly shorter overall survival, event free survival and relapse free survival compared to LSC low and LSC neg group. This finding has clinical implications in management of these patients.

CARE-kidney disease showed increased shedding of miR-24-3p through urinary exosomes (UE),

suggesting its biomarker potential for differential diagnosis. Under CARE-Paediatric Uropathies and CKD, NAG and TGF-beta have been found to be the best indicators of renal injury in individuals at high risk of End Stage Renal Disease (ESRD) due to congenital uropathies. CARE- intestinal diseases has developed Inflammatory Bowel disease **Nutri Care App**, a mobile app to help patients in recording their real time diet data on a regular basis, wherein 2000 individuals have been already enrolled.

CARDIOVASCULAR DISEASES

Risk Factor Control Initiative: IHCI India Hypertension Control Initiative (IHCI)

The goal of IHCI is to reduce cardiovascular diseases, particularly by improving the control of high blood pressure, a leading risk factor for heart attacks and strokes. The implementation partners include the Ministry of Health and Family Welfare, State Governments, ICMR, and WHO-India. The Resolve to Save Lives is a technical partner. The initiative uses five key strategies: state specific drug- and dose-specific protocols developed through consensus workshops, uninterrupted medication supply using forecasting tool based on morbidity, patient-centric care closest to home, task sharing to improve health care team efficiency, and a simple information system (SIMPLE App) to support and monitor the project.

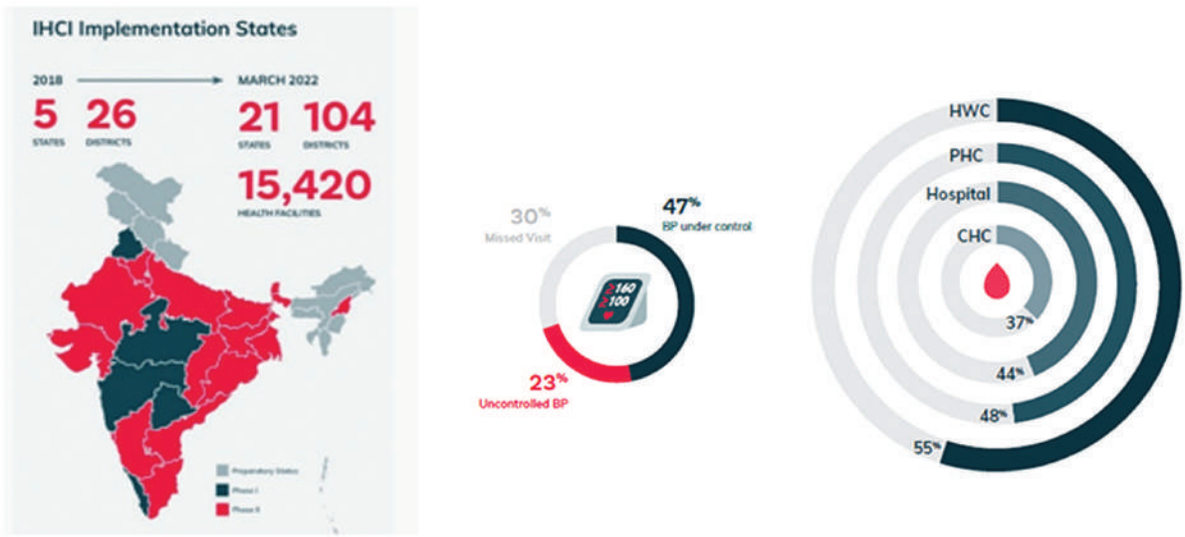


Fig. 16: High blood pressure outcomes in IHCI.

Phase -I IHCI was initiated in 2018in 26 districts across five states- Punjab, Kerala, Madhya Pradesh, Telangana, and Maharashtra. By March 2022, the IHCI phase-II has expanded to 104 districts in 21 States. Around 15,420 health facilities (66% of which are health and wellness centres [HWCs]) in these districts are implementing IHCI with 24 lakh registered hypertension patients. A unique cohort monitoring mechanism developed under IHCI revealed that the five IHCI strategies improved BP control rate to 47%. Control rates vary by the type of health care facilities (37% in community health centres [CHCs] to 55% in HWCs). Decentralized care and task sharing at the primary health centres (PHCs) have been found to be successful, wherein follow-up blood pressure monitoring and medications are provided by the ANMs/ Community Health Officers (CHOs) at the sub-centres or HWCs. The best practices from IHCI have been incorporated into NPCDCS program. Integration of features of IHCI's Simple App into CPHC NPCDCS app are on the way.

HEART ATTACK MANAGEMENT

ICMR Stemi Act

The aim is to examine whether the creation of a network of hub (medical college) and spokes

(secondary public health facilities - district hospitals and community health centres) in a district can improve thrombolytic rates in ST elevated myocardial infarction (STEMI) patients through a physician based tele-ECG-guided thrombolytic therapy model. The project has been initiated in districts of Shimla, Chandigarh, Ludhiana, Shillong, Varanasi, Tirupati, Rewaand Jodhpur.

Shimla district witnessed an increase in thrombolytic rate after capacity building of medical officers, nurses and technicians at spokes centres (66.4%) as compared to baseline (23%). The median time for symptom-to-first medical contact and symptom-to-thrombolysis (210 vs440 min) were significantly lower at spokes as compared to the hub centre which highlights the importance of providing thrombolysis in the peripheral centers. ICMR has contributed to revision in STEMI guidelines under NPCDCS based on learning from this project.

Delhi Emergency Life Heart-Attack Initiative: Mission Delhi

To avoid delays in ST elevated myocardial infarction STEMI care, this project was initiated to develop, test, and implement a 24-hour emergency response system for a pre-hospital thrombolysis service, using a bolus-dose of thrombolytic agent for the treatment of STEMI. The project uses nurses on a motorcycle as 'First Responders' for treating heart attack patients. During the feasibility phase (Phase I: May 2019- November 2021) of the study, a total of 448 calls were received on the toll-free helpline number. Among these, 290 were emergency chest pain calls, for which fully equipped motorbike ambulance for STEMI care with trained nurses were dispatched. Of the 290, 21 were STEMI patients, 11 of whom were thrombolysed at patient's doorstep. The validation study (phase II) aiming to establish the effectiveness of the use of 'First responders' on motorcycle ambulances at Ballabhgarh and RML has been initiated.

Fig. 17: Control Room.

Fig.18: Motorcycle ambulance.

HEART FAILURE

Trivandrum Heart Failure (HF) Cohort

ICMR continued its support to country's first heart failure patients' urban rural cohort at Trivandrum City and the rural Athiyannoor block Panchayat. The registry had enrolled 1205 HF patients, mean age of 61.2years. One out of every six patients reported chronic kidney disease (stage III or greater). At the end of 7 years, 1085 (90%) have been followed up and the cumulative mortality is 68.6%. This younger cohort of HF patients from India reported higher 5-year mortality rate (59%) versus Western countries (50%)

National Heart Failure Registry Program (NHFR)

This largest nationally representative heart failure registry in the country, established in 2018, had 53 centres and registered 10,700 patients. The mean

age of HF patients was 60 ±13.5, which is 10 years younger than the western population. Patients with reduced ejection fraction have higher risk of life threatening complications like cardiac arrest. Sixty three percent of patients were HF patients in this registry were with reduced ejection fraction (HFrEF). The most common cause of HF in these patients was IHD (72.3%). Rheumatic heart disease was responsible for HF in 6% of patients. The project was completed in March-2022. It is planned to follow up the patients in this registry from 9 nodal centres as a longitudinal cohort. This will first of its kind attempt in the area of HF in India.

Effectiveness of Yoga-based Cardiac Rehabilitation (Yoga-CaRe) programme in heart failure

This is a prospective, multi-centre open-label randomized controlled clinical trial (PROBE design) being undertaken with 3500 heart failure patients. Trial intervention, cardiac rehabilitation program has been developed.

CONGENITAL HEART DISEASES

Assessing the neurodevelopmental outcomes in infants undergoing surgery for congenital heart defects in five clinical centres

This multicentric study in 5 centres has enrolled 725 children with CHD undergoing corrective cardiac surgery. Neurodevelopmental assessments in 237 of these children done till date showed that 27% and 18% had delayed motor and mental development, respectively. The in-hospital mortality rate was highly varied between sites from 3 to 28%, the most common cause being septicemia. Study is being planned to understand and prevent high post-surgical mortality.

RHEUMATIC HEART DISEASE

'Effectiveness of digoxin in patients with rheumatic heart disease in the prevention of mortality and worsening of heart failure using a randomized placebo-controlled trial' of 1800 patients in nine clinical sites; and 'A study on the differential expression profile of miRNAs (total and exosomal) from rheumatic fever and rheumatic heart disease patients undergoing mitral valve replacement (MVR) or double valve replacement (DVR) surgery' are ongoing.

CHANNELOPATHIES

Contemporary Outcomes in Cardiac Channelopathies Guided by Genotype and Phenotype Based Management

A systematic investigation of 500 patients with suspected channelopathy and their available family members to understand the genetic variations landscape in cardiac channelopathies and also to study the outcomes of genotype-phenotype guided management strategy in these patients using North and South Indian patient cohorts. The North and South Indian cohorts have recruited 64 probands and 125 first-degree relatives so far. Genetic studies are being carried out.

NEUROSCIENCES

Stroke, Surveillance and Population-based Registries

Surveillance and Management System through Community involvement and Technology in rural Tirunelveli

Of the 218 stroke patients registered in the study, about 88.1% were ischemic stroke, 61% and 46.3% had hypertension and diabetes mellitus. Maximum cases (61%) were in the age group of 51-70 years. Most common mode of transportation used by the patients was hired vehicle (62%); 108 ambulance was used by only 8.7% of the patients. Only 22.3% patients reached the hospital within the golden hours (<3 hrs). The reasons for the delay were non-recognition of symptoms, non-availability of transport, delay in referral and imaging process. This project developed a mobile application named "SMART" (Stroke Mobilization and Rapid Treatment) for reducing the onset to door time to enhance the Management of Stroke patients

effectively and reduce mortality and morbidity. The App is being validated.

Establishment of Population Based Stroke Registry in Dibrugarh, Assam

The population based stroke registry in two blocks of Dibrugarh has registered 4829 cases (male: 64.4%). Ischemic stroke (62.3%) were in majority of patients, whereas haemorrhagic 31.2% and undetermined 6.5%. Majority (76.5%) of the cases reach Assam Medical College Hospital. Mortality rate within 28 days was 40.2%.

STROKE CARE PATHWAYS IN NORTHEAST

In view of the large burden of stroke and absence of care facilities in Assam, ICMR is building stroke Care Pathway models at Dibrugarh and Tezpur, Assam. The aim is to decrease response time of stroke victim through establishment of 24-hour Stroke Emergency Helpline, a 6-7 bedded stroke care unit at a Stroke Care Facility, a Mobile Stroke Unit (MSU) - 'State of Art' ambulance with mobile CT scanner, telemetry and facility to provide thrombolytic therapy in consultation with neurologist.

Establishment of Clinical Stroke Care Pathway using Mobile Stroke Unit in Tezpur

The present study was initiated in January 2019 in three blocks of Tezpur district with establishment of Baptist Christian Hospital (BCH) and Tezpur Medical College Hospital (TMCH) as stroke ready facilities. BCH & TMCH set up a 24-hour stroke emergency helpline 9126091260. Training programs and awareness activities were conducted to increase the awareness of stroke, symptoms in community and public health facilities. The stroke helpline has received total 109 calls, of which 25 calls were of suspected strokes for which MSU was dispatched. Out of these 25 stroke patients 10 were hemorrhagic, 6 were ischemic, 6 were stroke-mimic, 2 TIA, and one expired. The median distance travelled by the MSU to reach the stroke patient was 35kms and the median time to reach patient from the time of the call was 45 minutes. All the six ischemic strokes were out of window period and therefore, the thrombolysis could not be done. All stroke patients were loaded with drugs for acute care and shifted to BCH or TMCH. Recently integration between 108 ambulance and MSU has been done to reduce the time to reach the patient and provide a 'one stop' to access stroke care facility.

Pre-stroke unit set up, 214 (51.6%) hemorrhagic and 200 (48.3%) ischemic stroke patients reached BCH, a private hospital. Only 56 ischemic stroke patients reached hospital within the window period and 4/56 patients could be thrombolysed because of non-availability of neurologist. Post-stroke unit set up, so far 434 stroke patients have been admitted at the BCH- ischemic 53.2% and hemorrhagic 46.8%. Only 48 ischemic stroke patients reached hospital within the window period and 17 were thrombolysed. The median door-to-needle period improved from 1 hr 25 minutes pre -stroke unit to 52 minutes post stroke unit set up and door-to-CT time for patients reduced from 18 minutes to 13 minutes.

TMCH has only physician and no neurologist. This physician led model established a six bedded stroke unit at TMCH and implemented the Green channel pathway. Following this, a total of 555 stroke patients have been recruited of which 29.4% had ischemic stroke and 70.6% had hemorrhagic stroke. Out of the total 17 patients with ischemic stroke, 8 reported within the window period of 4.5 hours and all were thrombolysed. The median door-to-needle period was 1 hr 23 minutes and door-to-CT time for patients within the window period was 25 minutes. Differences in stroke types seen in BCH and TMCH may be accounted by differences in socioeconomic status of patients being catered by two hospitals.

Establishment of Clinical Stroke Care Pathway using Mobile Stroke Unit in Dibrugarh"

Thrombolysis was not being done at Assam Medical College Hospital (AMCH), Dibrugarhbefore this project was initiated. Stroke Unit was setup

at AMCH in March 2021. Emergency alarm system (Green Channel) and patient care pathway for patients attending casualty of AMCH was developed. A total of 1266 stroke patients have been admitted at AMCH, of which 29.4% had ischemic stroke and 70.6% had hemorrhagic stroke. Only 286 stroke patients reached hospital within window period of which 33 of had ischemic stroke and 27 were thrombolysed. The median door to CT time was 22 minute, a huge reduction from 6 hour before stroke unit was set up and door-to- needle time was 1 hr 19 minutes. The MSU ambulance is parked regularly at PHCs, CHC and sub-centres for generating awareness in community. 458 calls were received by the stroke helpline number at AMCH, of which 25 calls were related to stroke patients. MSU was dispatched in 23 cases and CT was performed in the periphery. The average door to thrombolysis time was 28 minutes. Out of 23 patients, 17 were hemorrhagic and 6 were ischemic stroke. Three patients of ischemic stroke were thrombolysed, 2 cases were out of window period and in one case attendant didn't give consent for thrombolysis.

Establishment of the Indian Stroke Clinical Trial Network (INSTRuCT)

The Indian Stroke Clinical Trial Network (INSTRuCT) was setup in 2017, with the objectives to establish a state-of-the-art stroke clinical trial network and to conduct pharmacological and non-pharmacological stroke clinical trials relevant to the nation. This network is the 4th government sponsored network of the world and only of its kind in developing world. **With the successful setup of the INSTRuCT network in Phase I in 30 centres. INSTRuCTPhase II** network has been initiated recently and extended to 50 centres. Four new clinical trials have been initiated recently under this network

1. **STENOSIS- Long-term Single versus Dual Antiplatelet Therapy In Patients With Ischemic Stroke due to Intracranial Atherosclerotic Disease: A Randomized Trial.** The trial aims to assess if long-term (12 months) DAPT with aspirin and clopidogrel is superior in preventing recurrent stroke and safe (in terms of any intracranial hemorrhage (ICH) or any bleeding or TIA) when compared to aspirin monotherapy alone.

2. **RE-OPEN- Randomized Trial of Biosimilar TNK Versus TPA during Endovascular Therapy For Acute Ischemic Stroke Due To Large Vessel Occlusion.**The aim of the trial is to assess whether the Indian biosimilar tenecteplase (TNK) during bridging therapy compared with tissue Plasminogen Activator (tPA) leads to better outcomes.

3. **INTRINSIC Trial- Indian Trial of Tranexamic acid in Spontaneous intracerebral haemorrhage :** This study proposes to assess whether tranexamic acid in addition to intensive blood pressure reduction improves outcome (7 day mortality) in adult patients with spontaneous intracerebral haemorrhage.

4. **MOBILITY- Medical Application based Post Stroke care Strategy for survivors and their caregivers: A Randomized Controlled Trial:** The aim of the study is to train the caregivers of stroke patients using a mobile application which has elaborative which would help them in caring for the patients at home.

Following trials were conducted under Phase-I INSTRuCT network

Secondary Prevention By Structured Semi-Interactive Stroke Prevention Package in INDIA (SPRINT INDIA)

This was initiated on 30.3.2017 with a total of thirty one participating centres. The recurrent rates of stroke are high in India ranging from 15 to 20%. The aim was to see whether '***Structured Semi-Interactive Stroke Prevention Package***' could prevent recurrent strokes, myocardial infarctions and deaths. The intervention package including

short messages, videos and workbook was developed in 11 languages namely, English, Hindi, Punjabi, Malayalam, Tamil, Telugu, Kannada, Bengali, Assamese, Gujarati and Marathi. A total of 4298 patients were randomized to intervention (n=2148) and control (n=2150) groups. The number of vascular events were 5.9% in intervention and 5.3% in control arms. Among the secondary outcome measures, alcohol and smoking cessation were higher in intervention as compared to control arm. Medication compliance was better in intervention arm. Trial was stopped for futility due to fewer vascular events occurring in both groups than that reported in literature. The intervention did not reduce the risk of vascular events compared to standard care.

Ayurvedic Treatment in the Rehabilitation of Ischemic Stroke patients in India: A Randomized controlled trial (RESTORE)

This study aims to assess the safety and efficacy of Ayurvedic treatment in improving the motor functions of stroke patients in a single-blinded randomized trial. This project was initiated at AIMS, Kochi; SCTIMST, Trivandrum; JIPMER, Pondicherry; and CMC, Ludhiana on 31st May 2018. So far, 138 patients from all four sites have been recruited. One month and three months follow ups are completed for 123 and 111 subjects, respectively. Serious adverse event was reported in seven subjects within the study period which were not related to the study treatment. The project is ongoing.

INDIAN STROKE RESEARCH NETWORK

Fever, hyperglycemia, swallowing and hypertension management in acute stroke: A cluster randomized controlled trial (Indian Quality Enhancement in Stroke Care study-InQuEST) Phase 1

FeSSH intervention can reduce 90 day deaths and dependency as shown in Table. The InQuEST Phase 1 was a pilot study initiated in 2018 to set stage for using FeSSH interventions to manage acute stroke in Indian settings. A total of 3012 patients were screened across 6different medical colleges and 6 district hospitals connected to these medical colleges. The study found that medical colleges treat a relatively high volume of stroke patients and have significant monitoring and management gaps that allow for quality improvement. Following training, significant knowledge improvement in temperature management, glucose monitoring, and swallowing management was observed. After the successful piloting in phase-I, a full-fledged step-wedge randomised control trial in twenty medical colleges (clusters) has been initiated.

Development and validation of a comprehensive clinical and neuropsychological test battery (NCTB) for use in the Indian context for patients with Vascular Cognitive Impairment

A multidisciplinary research group, for the first time in India, developed a comprehensive neuropsychological and behavioural test battery, the Multilingual Dementia Research and Assessment Toolbox (MUDRA) (previously called) ICMR Neuro Cognitive Tool box (ICMR-NTB), in five different Indian languages that can be used to assess cognitive impairment due to stroke and other dementias in different populations within India. The ICMR NTB meets diverse needs: a short version for the busy OPD to a comprehensive version for more in-depth testing or research purposes. The process involved adaptation of existing tests, and developed novel tests for a heterogeneous population. The tool MUDRA was launched in 2021 and made available to clinicians and researchers. In phase-II a project 'Development of a skill-based Neurocognitive testing protocol to assess cognition and diagnose dementia in a context of complex skills and low literacy has been initiated.

Indian Multiple Sclerosis and allied demyelinating disorders registry and research network (MS-Registry) (IMSRN)

ICMR's 'Indian Multiple Sclerosis and allied Demyelinating Disorders Registry and Research Network' is the country's first nationwide

database on rare diseases like multiple sclerosis (MS) and related demyelinating conditions of the Central Nervous System. This project was started in August 2021 and has 25 centres around the country. In this study, online portal for adding and accessing patient records from the site https://imsrn.icmr.org.in/ have been developed. Two portals under this site: one for the extensive clinical record forms (CRF), and the other for MRI imaging data, to track disease progression. The registry has already registered 909 cases- Multiple Sclerosis (MS)-350, Neuromyelitis Optica Spectrum Disorder (NMOSD)-83, Myelin oligodendrocyte glycoprotein (MOG) antibody disease-72, Clinically Isolated Syndrome (CIS)-15, Chronic relapsing inflammatory optic neuropathy (CRION) - 12, Acute disseminated encephalomyelitis (ADEM) -8 and Radiologically Isolated Syndrome (RIS) -5.

Brain Bank Network India Initiative: Establishment of satellite Brain banks in India for neuroscience Research

The aim of the study is to promote establishment and networking of Brain Banks to facilitate neuroscience research in the country and networking of satellite brain banks at PGIMER, Chandigarh and AIIMS, Bhubaneshwar with NIMHANS as a nodal centre. The project aims to develop, standardize and harmonize protocols for collecting, processing and storing the biological samples and conduct training in Biobanking practices. Total 26 cases brain tissue samples have been collected so far. The cases include COVID, road traffic accidents, suicides and others causes of deaths.

Establishment of a High Risk Autopsy Suite and a National Biorepository of Biospecimens for Emerging and Re-emerging Infections

ICMR has initiated the autopsy project to gather biospecimens from neuro infection related autopsies at NIMHANS, Bangalore. Well annotated samples from long COVID cases and other neuro infections requiring BSL3 facilities will also be collected.

ONCOLOGY

Cancer Management Guidelines

A total of 20 guidelines have been published in journals so far (Buccal Mucosa, Gastric, Colorectal, Gall Bladder, Tongue, Non Hodgkin's Lymphoma, Soft Tissue Sarcoma, Multiple Myeloma, Breast, Oesophagus, Paediatric and Soft Tissue Tumors and Lymphomas; Cervix, Larynx and Hypopharynx Cancers, Pancreas, Hepatocellular Carcinoma, Neuroendocrine Tumours).

Screening and Early Detection of Cervical, Breast and Oral cancer in Cachar, Assam: a pilot project

A successful model at Cachar district has been developed helping in undertaking a systematic population based cancer screening and assessing the prevalence and incidence of these 3 cancers. The model builds capacity by training of ASHAs in screening of cervical, breast and oral cancer and work up of screen positive cases for referral and treatment.

Strengthening State Non-Communicable Disease Programme for early detection of Breast Cancer involving strategic education and awareness among the women: a joint programme of State Government and ICMR-Desert Medicine Research Centre, Jodhpur

The study aimed to strengthen state breast cancer screening programme through training different cadres of health staff, developing a referral system for diagnosis and treatment at state medical colleges/ district hospitals and creating awareness amongst 30+women about the disease and practice of breast self-examination (BSE). In study districts of Jalore, Jodhpur and Pali, only 70% women in suspected case group had heard about breast cancer and 11% were aware about BSE. Overall, women had poor knowledge about signs and symptoms of breast cancer. Follow up of the subjects through phone call showed BSE practice of 69% and 66% at 1st follow up and 2nd follow up; 55 and 28 suspected

cases were identified at each follow up. The lessons from this project are being handed over to state Government for further uptake.

Concurrent evaluation of Human Papilloma Virus (HPV) vaccine program & vaccine acceptance among adolescent girls in Punjab, 2017

The study was aimed to review the implementation of the program in first phase in four program districts in Punjab and to understand its acceptance at the community level. Cross sectional survey among girls receiving 1st and 2nd dose of HPV vaccine in government/private schools in 2017 in Bhatinda and Mansa districts showed an acceptance rate of above 98% in all the group and 96% among parents of unvaccinated children. Overall, 4-8% of the girls reported minor side effects such as pain at the injection site, fever and giddiness. Awareness about HPV vaccine's role in prevention of cervical cancer ranged from 7% - 21.8% in various groups.

Comparative study of Genetic, Clinical and Epidemiological Risk Factors of Breast Cancer in Indian Population

A multi-centric study observed that median age of patients with breast cancer is 49 years. Exome sequencing data revealed highest mutations in 10 genes- TP53(54%), TTN (47%), PZP (29%), MUC4(28%), MUC16(28%), OBSCN (28%), PIK3CA (34%), DNAH11(20%), PIKD1(20%) and SSPO (20%). Preliminary analysis of data collected by Regional Cancer Centre, Thiruvananthapuram showed family history of breast cancer, other cancers and benign breast disease (BBD) was associated with 60%, 40% and 30% increased risk for the development of breast cancer respectively. Women who attained menopause after age of 50 years have a slightly higher risk for the development of breast cancer. Physical inactivity and High Waist Hip Ratio (WHR> 0.85) was associated with 2.8 and 3.4 times high risk, respectively, for the development of breast cancer.

Cancers in North East Region

As per ICMR Cancer Registry data, Mizoram has highest incidence of cancers of all sites in males and Arunachal Pradesh for all cancer sites in females. Risk factors are different in this part of country owing to different food habits. Two studies are ongoing.

Comprehensive microbiome characterization in esophageal, stomach & nasopharyngeal cancers of North Eastern India by Cachar Cancer Hospital and Research Centre, Silchar, Assam

The microbiome profiling of oesophagus, rectum, colon and cervix samples showed that 25% were positive for Prevotellaceae families of bacteria followed by 20.8% Fusobacteriaceae, 16.5% Porphyromonadaceae and 8.7% Bacteridaceae. Only cervical and rectum samples were found positive with Papillomavaridiae family of viruses and 100% of Streptococcacae positive samples were found in oesophageal tumor.

Comprehensive study on upper Gastrointestinal Cancers: Esophageal, Stomach and Nasopharyngeal cancer in Northeast India

The study has been initiated at Assam Medical College and Hospital, Dibrugarh; Naga Hospital, Kohima, Nagaland and JNIMS, Imphal, Manipur with an aim to identify risk factors, mutation profiling of major cancer pathway genes, gene expression profiling of major cancer pathway genes and to determine the association of important pathogens.

India Cancer Research Consortium (ICRC)

India Cancer Research Consortium (ICRC) was established under the aegis of the ICMR-DHR in April 2019 with seed grant of 20 crore. Six thematic areas; viz (i) Prevention and Epidemiology; (2) Diagnostics; (3) Therapeutics; (4) Palliative Care; (5) Innovation; and (6) Basic Biology were identified. In response to 1st call for proposals, 13 projects are ongoing and in response to 2nd call,

22 proposals are being processed for review and subsequent funding.

INDO-EUROPEAN UNION COLLABORATION ON CANCER

Role of HPV in Head and Neck cancer in Rural and Urban India

An epidemiological study in 1320 head and neck cancer cases and 1924 controls in Mumbai and Barshi revealed that 'Ever' smokers/alcohol had elevated risk for oropharynx cancer; bidi smoking, tobacco chewing, gutka chewing, drinking country spirit showed elevated risk for all HNC sub-sites with highest risk for causing oral cancer. The overall HPV prevalence in HNC was 39.43%; the prevalence sub-site wise was oral cancer-36.27%; oropharynx-50%; hypopharynx-50% and larynx-26.32%. The most prevalent HPV genotype was HPV16 amongst all HNC sub-sites.

WHITE PAPER

Alcohol use and abuse has increased in India in the past decade and no concrete data or policy is available on alcohol-related cancers. A white paper on 'Alcohol and Cancers' was published during the period.

DIABETES

Guidelines for Management of Type 1 Diabetes

Guidelines for management of type 1 diabetes using leads from ICMR's Young Diabetes Registry data were developed. The document addresses epidemiology and diagnosis, lifestyle, drugs, monitoring, acute, microvascular and macro vascular complications, education and special group. Document is available on ICMR website.

ICMR-INDIAN NATIONAL DIABETES STUDY (ICMR-INDIAB)

The study was aimed to estimate prevalence of pre- diabetes and diabetes among rural and urban population of the country. The study spans 28 states and 2 UTs enrolling 1,13,106 individuals.

The overall weighted prevalence of diabetes is 9.6%, varies from 4% in Uttar Pradesh to 23.6% in Kerala, 13.3% in urban and 7.8% in rural areas. Overall weighted prevalence of pre-diabetes is 14.0% and varies from 6% in Mizoram to 31.8% in Sikkim. The overall prevalence of general obesity is 27.1% and varies from 11.8% in Jharkhand to 45.9% in Puducherry with significantly higher in urban (37.0%) than rural areas (22.8%). The overall prevalence of abdominal obesity is reported to be 36.9% (urban-48.2%; rural-32.1%) and varies from 16.9% (Jharkhand) to 58.2% (Kerala).

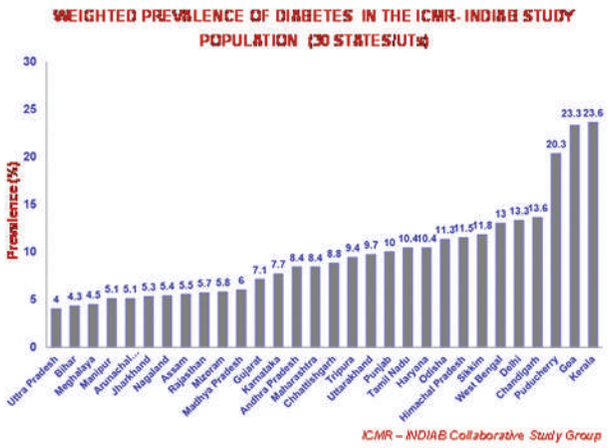


Fig. 19: Weighted Prevalance of Diabetes.

The overall prevalence of hypertension is 31.7% ranging from 22.2% in Madhya Pradesh to 44.4% in the state of Sikkim. The overall prevalence of hyper-cholesterolemia is 22% (Urban-25.7%; Rural-20.7%) and varies from 4.9% in Jharkhand to 49.9% in Kerala. The overall prevalence of hyper-triglyceridemia is 30.8% (Urban-33.9%; Rural-29.5%) varying from 20.4% in Chhattisgarh to 44.9% in Punjab. The overall prevalence of low HDL cholesterol is 67.1% and varies from 52.4% in Gujarat to 81.1% in Meghalaya. The ICMR-INDIAB study shows that burden of diabetes and pre-diabetes is high in India. From this study, fourteen publications have come out so far. In the year 2021, four states (HP, Uttarakhand, West Bengal and Odisha) completed survey.

Registry of People with Diabetes in India with Young Age at Onset

The project is aimed to understand disease pattern or types including the geographic variation and incidence and prevalence rate of complications. The phase I and phase II of study enrolled 5546 and 20351 young diabetes patients respectively and were completed in 2012 and 2021 from around 300 centres. Annual follow ups of patients were done. Phase 3 has been initiated which includes cohort creation for long term studies. Based on region wise data from this registry, three studies and a diabetes cohort for long term studies were initiated in Phase III.

Phenotyping North East Indian Young Type 2 Diabetes (PHENOEINDY-2)

Young Diabetes Registry of ICMR showed a disproportionately higher prevalence of thin type 2 diabetes patients in the NE states of India. The predominantly rural, young onset type 2 diabetic patients were short and thin (average BMI~ 23 kg/m2) but centrally obese (~90%) and adipose (~60% on DXA). Comparison between 246 diabetic patients and 252 healthy controls showed that patients had similar BMI, higher waist-hip ratio and lower mid-arm circumference, lower DXA fat (only in females), higher triglycerides and lower HDL-cholesterol. HOMA indices showed that B-cell secretion defect was the predominant abnormality. The findings demonstrate that young onset type 2 diabetic patients in NE India are thin-fat and centrally obese. Severe insulin secretory defect is the predominant abnormality but insulin resistance is also evident in metabolic abnormalities.

Fetal Growth, Neonatal Size and Its Relation to Composition and Insulin Resistance upto 8 years of Age-a Feasibility Study (PHENOEINDY-P)

The study subjects are 300 children delivered to mothers in 200 km radius area of Dibrugarh at AMCH between the years 2008 and 2011 and are 6-10 years of age at present. During 2018-2019, 71 children with BW <2.5kg were enrolled as cases and 110 children with BW >2.5kg as controls. Children with low birth weight were observed to have relatively low IQ level.

Penetrance of Susceptible and Protective Genes in Familial Clustering of Type 1 Diabetes Mellitus and its Co-association with Celiac Disease

It was aimed to study allele polymorphism of HLA class I and class II loci in families affected with T1DM and CD with a putative target to delineate susceptible and protective genotypes for familial clustering of these diseases in two geographically and ethnically different regions of India (North Indian population (Indo Eurasians) and North East (Indo Tibetans) population. 25 families were enrolled in group having multi sib affected families at PGIMER, Chandigarh and AMC Dibrugarh have been enrolled for the study. None of the patients with both T1DM and CD was recruited. Antibody profiling and NGS sequencing has been undertaken. Data is being analyzed.

DIABETES COHORT STUDY

It is a longitudinal study in urban and rural subject to be followed up for 5 years that would help understand the factors involved in the development of Type 2 Diabetes Mellitus & its complications and provides opportunities for interventions at different levels. At baseline (n=2680), high proportion of study participants showed glucose intolerance (38% prediabetes and 16% NDDM). Family history of diabetes was present in 74% of subjects in NDDM group and 50% in NGT group; approximately 2/3rd had a 1st degree relative with diabetes. Obesity/central obesity, low HDL and high TG were common. 40% had family history of obesity and hypertension. NDDM group was twice likely to have hypertension, 1.6 times likely to have micro and or macro albumin-urea and had lower physical activity as compared to NGT Group. Approximately, 60% of participants in prediabetes and NDDM groups had metabolic syndrome. Wheat was the staple cereal in 90% of study participants.

Serum insulin and c-peptide levels were found to be increased from NGT to prediabetes to NDDM. Serum adiponectin levels were highest in NGT subjects, whereas serum leptin and HsCRP levels were highest in prediabetes group. Females had three times higher levels of serum leptin levels than males. On one year and 2 year follow up, 14% and 20% of NGTs progressed to IFG and 13% progressed to IGT and or IFG respectively; among the IGT and or IFG individuals (at baseline), 15% and 16% reverted to NGT, 19% reverted to IFG and 6% and 8% progressed to NDDM. Around 6% and 8% of prediabetes individuals converted to NDDM in those who reported at 1 year and 2 year follow up respectively.

Establishing Biorepository Facility

It is aimed to procure, process and preserve biological samples related to non-communicable diseases (NCDs) in a centralized bio repository facility and to develop national and international collaborations to harmonize bio specimens to efficiently prioritize, retrieve, disburse and track specimens whenever required as driven by research protocols. Samples collected from every 5th individual and the diabetic subjects in ICMR-INDIAB study are stored at MDRF The biorepository at MDRF is planned to provide essential support for samples collected for the ICMR funded projects.

IMPACT OF YOGA ON CHRONIC CARE

A multicentre open label parallel arm RCT evaluating whether yoga can prevent worsening of glycemic control in patients with type 2 diabetes mellitus on oral anti-hyperglycemic drugs

In this two-arm parallel lifestyle intervention randomized controlled trial, T2DM subjects on oral glucose lowering agents, aged 30-70 years, with HbA1c of ≤8.5% and with no limitation to perform physical activity were included. A total of 249 participants were randomized to yoga intervention (n=129) or usual care (n=120). The participants were aged 53.7±9.2 years, has baseline BMI 27.7± 4.4 kg/m^{2}and HbA1c of 7.2±0.6 %. The rise of HbA1c by 0.5% occurred in 31.6% participants on follow up of one year, with similar event rate observed in 36.7% participants in usual care and 34.1% in yoga arm (p=0.673). There was also no significant difference in ITT analysis between 2 arms for HbA1c at 4, 8 and 12 months, nor in any of the metabolic or psychological parameter evaluated in this study except fasting plasma glucose at 4 months.

To study the effect of structured long term yoga intervention on biomarkers of stress, oxidative stress and inflammation in subjects with prediabetes

It was aimed to determine whether structured long-term yoga can improve stress (cortisol, DHEAS and prolactin), oxidative stress (malondialdehyde (MDA), inflammatory (hsCRP and IL-6) biomarkers, markers for DNA damage and others (adiponectin, leptin and 25-OH-Vit D) in non -diabetic subjects with IFG/IGT at 12 and 24 months follow up. The pre- diabetic subjects received 40 minutes of structured yoga in addition to lifestyle advice in one group and in the other group, subjects receive lifestyle advice alone for 3 years. More subjects in the placebo group (lifestyle alone) reached the endpoint of incident diabetes as compared to the yoga group (yoga + lifestyle) both at one and two years. Postprandial glucose levels significantly declined in both groups but remained significant after 2 years in the yoga group only. Fasting plasma glucose levels worsened significantly in the placebo group after 2 years. Insulin resistance as indicated by HOMA-IR and adiponectin levels improved significantly in the yoga group after one year and remained so even after 2 years; whereas rise in the lifestyle group occurred much later only after two years. Yoga when added to standard lifestyle measures appears to improve antioxidant capacity and restrict oxidative damage in pre-diabetic individuals.

Impact of yoga on stress, metabolic parameters and cognition of Indian adolescents

The project was planned to assess the effectiveness of an intensive 25 session yoga intervention (twice a week for 2 months, followed by weekly once session for next 2 months and finally a refresher session) in adolescents studying in grades VIII – X (~ aged 13-15 years) in north (Delhi) and south (Chennai) India in a school based setting on stress, metabolic parameters and cognition (attention & concentration). The study included 1807 adolescents aged 13-15 years from 12 schools (6 private and 6 government schools) from Chennai and Delhi. Intervention group students underwent 17 yoga sessions. Awareness talks on healthy lifestyle were delivered monthly once to the control group. The mean stress scores post intervention reduced from 14.2 to 12.8 in the intervention group and increased from14.3 to 16.1 in the control group. Intervention group participants as compared to control group showed minimal increase in salivary cortisol levels (0.4 vs 2.8 ng/ml), statistically significant decrease in systolic/diastolic blood pressure and pulse rate, statistically significant ($p<0.05$) increase in LCT scores (19.3% vs 9.6%), significant improvements in physical activity and less consumption of junk foods.

Investigations of Association of Mutations in MODY and NDM by Translational Genomic Research

The main aim of the project was to identify the genetic etiology of monogenic diabetes and congenital hyperinsulinism (CHI), tailor treatment on the basis of the genetic defect identified and follow up the patients systematically in order to understand the disease course and progression. In Maturity-onset diabetes of the young (MODY) and Neonatal diabetes mellitus (NDM) patients with pathogenic /likely pathogenic variants, a comparison between the base line and follow up showed a significant reduction in the HbA1c levels and blood glucose respectively between them. In Congenital hyperinsulinism (CHI) patients with pathogenic /likely pathogenic variants, a comparison between the base line and follow up showed a significant increase in the blood glucose levels. Through this project investigators were able to successfully deliver precision medicine to 75% of the genetically proven MODY patients and to 90% of genetically proven NDM patients. The results showed that the diagnosis and treatment based on genetic etiology has helped in translation of laboratory findings to the bedside during this project work.

INDO US COLLABORATION IN DIABETES RESEARCH

Harmonization of Existing Registries (Indian YDR and the SEARCH registry in U.S) of Diabetes in Youth

The study showed that it is possible to harmonize diverse registry data and also possible to analyze multiple harmonized datasets with a single query run by all sites, with summary data only sent to a central location or shared by all locations.

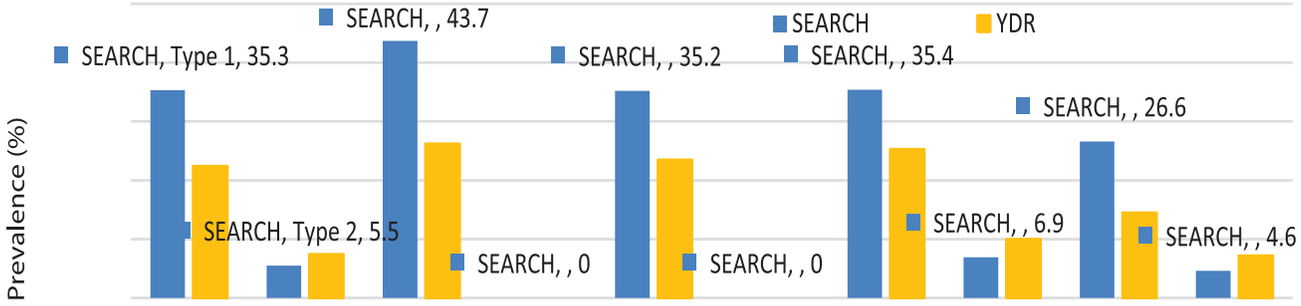


Fig. 20: Prevalence of DKA at onset, by diabetes type and age group in SEARCH and YDR.

It was observed that youth in India had elevated A1c levels compared to SEARCH for both T1D and T2D and regardless of treatment regimens, but T1D youth in India had lower DKA prevalence near onset vs SEARCH. Through collaboration with SEARCH, YDR has implemented additional procedures to collect duplicate cases across sources and use capture-recapture methods to estimate completeness of ascertainment. This may allow the YDR registry to accurately report on incidence of T1D and T2D in India in the future. 4 abstracts and 4 manuscripts were published.

Genetics of Type 2 Diabetes- a Multi-centric Population Specific Study

Genetic determinants of T2D were determined using family-based cohorts from four distinct Endogamous Ethnic Groups (EEGs) representing two Northern (Punjab [Sikhs: SI] and Rajasthan [Agarwals: AG]) and two Southern (Tamil Nadu [Chettiars: CH] and Andhra Pradesh [Reddys:RE]) states of India and to examine whether the previously established 8 South Asian T2D risk loci are relevant to the AG, CH, and RE EEGs. Data and samples were collected from three EEGs: AG (N = 530, Families = 25, mean age = 43y, mean BMI = 27, T2D = 37%); CH (N = 518, families = 21, Age = 47y, BMI = 27, T2D = 33%), and RE (N = 500, Families = 22, Age = 46y, BMI = 27, T2D = 36%). Each of the families from an EEG was ascertained by a proband with T2D. Similar characteristics for the SI EEG (N = 1260, Families = 324, Age = 51y, BMI = 27, T2D = 75%) were obtained previously. Other T2D-related traits (e.g., BMI, lipids, blood pressure, insulin, glucose) in AG, CH, and RE EEGs exhibited strong genetic influences (h2 range: 15% [triglycerides] - 90% [glucose; non-T2D]). The findings highlighted high burden of T2D in Indian EEGs with significant additive genetic influences on T2D and its related traits.

COVID AND NCDS

Comparison of Seroprevalence of SARS-CoV2 among people with and without diabetes and/or hypertension among existing cardio-vascular community cohort in National Capital Region (NCR) of Delhi

A follow up study is designed in two pre-existing community cohorts for cardio-vascular diseases established in urban and rural areas of Delhi NCR. The study intends to estimate and compare sero-prevalence of SARS-CoV2 among people with and without diabetes and/or hypertension. The study will also explore the knowledge, attitude and health seeking behavior of people and the impact on disease management and control with diabetes and/or hypertension during the pandemic.

SARS-CoV-2 infection (COVID-19) related clinical outcomes among people with and without diabetes and/or hypertension in India- A hospital based observational study

This is hospital based registry among adult COVID-19 cases (>18 years) diagnosed and admitted to dedicated COVID-19 facilities, at the All India Institute of Medical Sciences (AIIMS), New Delhi from 1st April 2020 to 31st December 2020. The data will be analyzed to study the role of two major NCDs (diabetes and hypertension) on severity and mortality of COVID complications, according the WHO criteria.

INDO GERMAN COLLABORATION

Identification of metabolic biomarkers for risk stratification in obese adolescent population in India – IMERSAI

Project IMERSAI is aimed to analyze metabolic profiles associated with obesity in adolescent population. The metabolite profiles between the two study groups were compared using partial least square discriminate analysis (PLSDA) and heat map analysis. The heat map analysis showed the changes in lipid profiles with respect to body mass index (BMI). Both saturated and unsaturated lipids were found to be significantly altered. The results indicate that specific metabolite correlation with insulin resistance and obesity among adolescent population.

CLIMATE CHANGE

Epidemological Study of Foci of Visceral Leishmaniasis in Himachal Pradesh

The aim is to understand the transmission dynamics of Visceral Leishmaniasis in Himachal Pradesh and delimit the focus and climatic and ecological determinants of Visceral Leishmaniasis. It appears that the CL in Himachal is atypical leishmaniasis (close to dermal leishmanoid) as the detected parasites from patients were *Ldonovani*, *L.tropica* as well *L. major*.

Vulnerability Assessment and Adaptation Measures Towards Potential Impacts of Climate Change on Malaria in Hot spots of India

The Himalayan region in India emerged as most vulnerable new foci for malaria due to increase in temperature. States like Orissa may witness reduction in malaria due to extreme temperatures. Malaria transmission is very low in Kangra district. In Uttarakhand, transmission windows were suitable for 10 months in study villagesof Tehri and Pauri Garhwal. Expression of HSP-70 and HSP-90 proteins was detected in *An. culicifacies* exposed to temperatures (38-40°C) indicating that mosquitoes can adapt to high temperature. Evidence of malaria parasite was detected in 18 *An. culicifacies* collected from cattle shed.

Multi centric Study of the Impact of Exposure to Ultraviolet Radiation (UVR) and aerosols exposure on Ocular Health in India

The findings of phase I showed significant association of cataract, dry eye and pterygium with sun exposure. Additional factor in Gurgaon was exposure to unsafe kitchen fuels for more than 15 years. In Guwahati, significant association between sun exposure and cataract alone was noted. Phase II is ongoing.

MUSCULOSKELETAL DISORDERS

Human Skeletal muscle disease biobank

The skeletal muscle biobank at NIMHANS is the first of its kind in the country and aims to establish a comprehensive database of neuromuscular disorders. The skeletal muscle biobank has stored 501 skeletal muscle tissue (portion remaining after diagnosis), 182 serum and 192 DNA samples from patients with neuromuscular disorders (muscular dystrophies, neurogenic atrophy, inflammatory myopathies, congenital myopathies and metabolic myopathies) in ultra-low freezers.

Pathogenesis of Osteoarthritis: Integrated approach based on transcriptome, proteome, microRNAome analysis during progression of knee osteoarthritis

This microarray analysis in synovial fluid from osteoarthritis patients has shown upregulation of type 1 collagen alpha1 (COL1A1) and amelotin (AMTN) genes in osteoarthritis patients as compared to rheumatoid arthritis (RA) patients, as well as among different grades of OA. Significant downregulation of miR-4505, miR331-3p and miR-7975 was observed in late OA synovial fluid samples as compared to early OA. A total of 28 significantly modulated proteins were identified in both different grades of OA versus RA comparison and intergrade OA comparison. From this data, key genes (COL1A1, AMTN), miRNA (miR-7975, miR-1273g-3p) and proteins (ACAN, COMP, VCAN, CA1, COL1A1, Fumarylacetoacetase and Cathepsin G) have been identified that not only differentiate between OA and RA but also late OA from early OA and hence can be further evaluated as biomarkers for severity of OA.

MENTAL HEALTH

Consortium on Vulnerability to Externalizing Disorders and Addictions [cVEDA]

Under Indo-UK collaboration, this consortium was one of the largest international neurodevelopmental cohorts, designed to study the development of mental illnesses. Five Indian population specific brain templates for children, adolescents, young adults and elderly, to serve as reference templates for Indian brains undergoing MRI scans have been developed. This template is freely available

for both clinical and research purposes. Brain developmental growth atlases to track normal and psychopathological development as well as cognitive, emotional capacities in young Indians, metric for brain age estimation from cortical features using machine learning to be used for early prediction of several mental disorders has been developed. The project has enabled 3 PhD, 2 DM, 4 MD Psychiatry dissertations and a DBT-Wellcome Training grant and numerous Training workshops and an annual lecture series.

Capacity Building under National Mental Health Programme (NMHP)

A capacity building initiative for developing clinical skills and alternative mental health workforce with reference to NMHP mandates involved 12 studies, 5 multicentric and 7 single site studies. A web-based tool i-MANN (ICMR Mental Health Assessment National Network) has been developed to manage data collected from these projects. The studies have led to 33 publications, 12 awards at scientific conferences and development of 5 manuals.

GASTROENTEROLOGY

Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) and its association with cardio- metabolic disease risk factors in North India

The prevalence of non-alcoholic fatty liver disease (NAFLD) was 66% in urban as compared to 61% in rural areas. Urban females and rural males had higher prevalence. Prevalence of NAFLD increases with increase in BMI.

Efficacy of Metformin in reduction of hepatic fat fraction and insulin resistance in overweight adolescents with NAFLD: RCT

The study aims to assess if metformin given in conjunction with diet and lifestyle is superior to diet and lifestyle alone in reduction of hepatic fat fraction, BMI, body fat percentage, and insulin resistance in Indian overweight adolescents with non-alcoholic fatty liver disease. The study has enrolled 128 subjects.

Burden and Risk factors of Acute and Chronic Pancreatitis

This study aims to estimate the disease burden and economic burden due to acute and chronic pancreatitis and other gastro-intestinal diseases in India through a combined approach of population survey and hospital based surveillance.

ORAL HEALTH

Assessment of Emotional and Behavioral Problems and Quality of Life among Children and Adolescents with Cleft and Lip Palate (CLP)

This project assesses the kind and severity of the emotional and behavioural problems experienced by children and adolescents with CLP. In the current sample of 30 participants, the results highlight that the CLP group has lower self- esteem and quality of life with more difficulties as compared to the control group.

GERIATRIC MEDICINE

A task force project study on CVD risk factors concluded that the HbA1c, Creatinine, HDL-C, ferritin and hsCRP can be reliably measured from dried blood spot (DBS) samples and are readily transferable to a liquid phase for analysis offering a convenient alternative for monitoring of CVD risk factors.

ICMR-FORTE (Sweden) collaboration

Five projects were completed on various aspects of homecare of the elderly. Second call for proposals was released in January 2022 with focus on a) public health, prevention, and health promotion b) Organisation and provision of care for older people.

DISABILITY AND ASSISTIVE TECHNOLOGIES (ATS)

National List of Essential Assistive Products (NLEAP)

ICMR initiated the steps to prepare a list of assistive products on the pattern of WHO's Priority

Assistive Products List (APL-WHO). Bureau of Indian Standards and Ministry of Health & Family Welfare (provided ISO-BIS standards) supported the development of National List of Essential Assistive Products (NLEAP). On National Expert Committee's (NEC) recommendations4 sub-groups on public health, physical medicine & rehabilitation (PMR), geriatrics and engineering were created. The list has been classified as : age-wise (different requirements in different age groups), disability-wise (21 disabilities as per RPwD Act 2016 or Visual, Hearing, locomotor, cognitive, communication, self-care), system-wise (primary, secondary or tertiary health care systems), cost-wise (low, medium or high), provision-wise (govt., private, insurance, welfare, NGO), indigenous vs. imported (available in India or to be imported), ISO-BIS Standards, and technology-wise (simple, complex, advanced including softwares). List was prepared after referring to Safdarjung list, CGHS list, Dr Shipra's list, ALIMCO list, Mobility India list, EU list, BIS–ISO list, text-books, and National Trust (with a network of more than 700 NGOs). The document was published on ICMR website for public comments. The list has been updated based on the comments received from more than 1700 experts/specialists. The Regional and National Consultation are being planned in collaboration with WHO to finalize the list.

National Centre for Assistive Health Technology (NCAHT)

Majority of the people with disabilities (PwDs), which are either a manifestation of NCDs, injuries, mental health disorders etc. are not able to afford suitable ATs to live an independent life. There is an urgent need to address the various challenges for assistive technology and devices such as innovation, design, redesigning existing devices, materials and technology available, accessibility, affordability for assistive in India. This calls for building an ecosystem for development, production and dissemination of affordable assistive technologies in India. It is proposed to establish a model centre for advanced research and excellence for assistive technologies in collaboration with UCL and DFID to address this area of concern. The scientific evidence obtained from this centre shall be useful for prioritising government programs related with assistive technologies /devices.

SNAKEBITE

Nationwide Study to estimate incidence, mortality, morbidity and economic burden due to snakebite in India

This study has been initiated in 13 states, 34 districts, 336 Blocks across the country with about 6.14% population as 2011 census in the Phase 1 and shall be expanded depending on the findings from Phase 1.

ICMR National Snakebite Project (INSP) on capacity building of health system on prevention and management of snakebite envenomation including its complications.

This study has been initially piloted covering 2 states (Odisha from East and Maharashtra from West) covering one district each and then gradually be expanded to national level including states of North Eastern Region.

TRAUMA, EMERGENCIES, INJURIES AND BURNS

Multi Centric community-based study of prevalence, KAP (knowledge, attitude & practice) for prevention & First Aid of Burns, Quality of Life and Out of Pocket Expenditure of Burn injury and evaluation of IEC interventions

This study has been initiated for a period of 3 years in 11 centers across India to enable us to understand the regional distribution of this endemic trauma.

Patent

1. Patent applied for: An Imaging Probe for Detection of Key Biomarkers in Alzheimer Disease. Under Adhoc project "Development of exosome-based drug delivery system for

naturally inspired novel multifunctional Neuroprotective molecules and their biological evaluation in Alzheimer's disease models" under Gyan Prakash Modi, BHU, Varanasi.

2. Patent applied for: Novel gastro-floating sustained release tablet of penicillin V potassium. Under Adhoc project "Pre-clinical Development of Penicillin Drug Delivery System for Prophylaxis of Rheumatic Heart Disease" under Dr Arvind Bansal, NIPER, Mohali.

3. Copyright applied for App stroke Mobilization Assessment & Rapid Treatment -TAEI-SMART Invention developed under task Force project "Surveillance and Management System through Community involvement and Technology in rural Tirunelveli' under Dr P Manickam, NIE, Chennai.

BASIC MEDICAL SCIENCES

The Basic Medical Science division coordinated intramural research in the field of basic medical sciences at the National Institute of Pathology (NIP), New Delhi, National Institute of Immunohaematology (NIIH), Mumbai and National Institute of Traditional Medicine (NITM) at Belagavi. The extramural research was undertaken in several areas viz. Genomics, Stem cell research, Nanomedicine, Haematology, Biochemistry, Pharmacology, Physiology, Human genetics, Allergy, Immunology, Translational Neuroscience, Drug development initiative and Toxicology. The division also coordinated NAC-SCRT secretariat and Standing committee on national list of essential medicines (NLEM). Interagency partnership programs were pursued in traditional and folklore medicine with Department of AYUSH. The Division assists Drug Controller General of India for evaluation of Investigational New Drugs (chemical, biological & Stem Cell / Cell based Therapy) dossiers for approval of clinical trials/ marketing of new drugs in the country.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY (ICMR-NIIH), MUMBAI

Assessment of Neonatal Screening Approaches for Sickle Cell Disease (SCD) and The Effect of Early Intervention in Management of the Disease in Tribal Populations

The primary objective of this study was to undertake neonatal screening for SCD in the tribal population and measure the benefits of early comprehensive care for affected individuals. It is a multicentric project undertaken in 7 centers in 6 states of India. The seven centers have screened 30,079 newborns by HPLC. Of these, 10.7% of babies were SCD carriers and 0.78% SCD. 197 (83.8%) babies were followed up and comprehensive care in the form of prophylactic antibiotics, folic acid, and vitamin B12 supplementation was initiated in 189 (78.7%) babies. Hydroxyurea is being administered to 10 babies. Death was reported for 10 (1.64%) sickle cell babies. Genetic modifiers are being studied to understand the genotype-phenotype correlation.

Training of in-service clinicians from Government Hospitals and Outreach Program for Aspirational districts

The main objective of the project was to conduct 6 monthly training programs for clinicians regarding the genetic diagnosis of inherited diseases and to establish a satellite centre in the 'aspirational district' Nandurbar for genetic diagnosis and counseling of hemoglobinopathies and metabolic disorders. This year a total of 2550 newborn babies were screened for five metabolic disorders among which three samples (3/2550, 0.1%) showed deficiency (G6PD: 2 cases; Galactosemia: 1) and 34 newborns (0.95%) with SCD. In the antenatal component, a total of 4534 ANC women were screened among which 549 (12.1%) were found to be HbS trait, 33(0.72%) were identified as sickle

cell disease and2.77% were detected as beta-thalassemia trait. 230 ANC were captured in the first trimester of which 101 spouses (43.91%) of ANC women were followed up.

Assessing the role of microRNAs in clinical severity of Thalassemia Patients and hydroxyurea-mediated HbF induction

The main aim of the study was to assess the role of microRNAs (miRNA) in the clinical severity of thalassemia patients and hydroxyurea-mediated HbF induction. A global miRNA microarray profile consisting of 754 miRNAs was studied in thalassemia intermedia patients at base/3/6 months of HU.12 highly upregulated and 6 downregulated miRNAs were selected for functional analysis. The predicted targets of miRNAs were critical HbF regulators: BCL11A, MYB, KLF1 and GATA-1. These were functionally validated by in vitro transfection of miR-mimic/antagomiRs of 18 miRNAs in K562 cell lines and demonstrated their critical role in the regulation of the γ-globin gene and HbF production through significant ($p<0.001$) inhibition of BCL11A, KLF-1, GATA-1 and MYB.

Platelet phenotyping (surface receptors, granules, secretion and signal transduction) and genotyping of unclassified heritable thrombocytopenia and platelet function disorders

The objective of this study was to establish laboratory diagnosis and to identify the underlying molecular pathologies for rare inherited platelet disorders.242 clinically suspected platelet function disorder patients were studied. 40 patients with unclassified platelet defects were identified. 10 of those patients (25%) were found to have homozygous variants of significance in the *RASGRP2* gene and 30 patients with variants in other genes predisposing to rare platelet disorders. In this study, we could not only identify the rare mutations in the *RASGRP2* gene affecting the platelet function in our group of patients, but also highlight the relatively high occurrence of defects that are otherwise considered rare in the published literature.

Comprehensive genomic and functional evaluation of factors influencing CAD and Myocardial Infarction (MI) in young patients

Molecular study using next generation sequencing (NGS) of 55 patients with MI upto the age of 40 years have been studied, 61 damaging variants have been identified in 48 genes, most of them not frequently reported. 34 novel, damaging variants identified. 17 patients with damaging heterozygous autosomal dominant variants in multiple genes. Strong family history of MI in young age in these patients. The data has yielded novel variants in infrequently reported genes in young patients with MI. Further functional studies on more samples may aid in understanding specific markers or mechanisms that may be either independently or synergistically associated to AMI/ CAD.

Centre of excellence for Research, Diagnosis and Management of Primary Immunodeficiency Disorders (PID)

This study has been undertaken with the objectives of establishing diagnostic facilities for PID and creating human resource for early diagnosis and optimum management of PIDs. Centre has strengthened and established various assays for enumeration, characterization and functional analysis of different components of immune system. To date, study has evaluated a total of 11510 cases suspected with PIDs, out of which diagnosis was achieved in 909 cases referred from >150 centres across India. The team has generated large cohorts of patients with specific IEIs over last 5 years including SCID, MHC II deficiency, DOCK8 deficiency, WAS, HIES, XLA, CVID, CGD,LAD-I HLH, MSMD, ALPS.Team established facility for prenatal diagnosis and helped 64 affected couples preventing birth of affected children. The centre has prepared SOPs for various assays useful for diagnosis of common PIDs. More than 600 participants from various institutions all over the country have been trained through CMEs and workshops.

Study of clinical and genetic predictors of prognosis in Myelodysplastic Syndromes

The objective of the study was to identify clinical and genetic predictors and understanding their role in prognosis of Myelodysplastic syndromes. The study was carried out in 152 patients with myelodysplastic syndromes. Molecular study revealed 73% of gene mutations. The splice factor gene mutation (61.2%) (SF3B1, SRSF2, and U2AF1), and epigenetic gene mutation (33.3%) (ASXL1, DNMTA3A, EZH2, IDH1, IDH2, TET2) were frequently observed in our study group. The survival analysis revealed that the mutations in TP53, JAK2/3, KRAS, NRAS and ASXL1 were significantly ($P<0.05$) associated with poor survival of the patients. The survival analysis of study also showed that the M-IPSS-R were more significant in separating the patients as per their risk than the IPSS-R alone.

Study of the molecular pathology of Idiopathic Aplastic Anemia

The aim of the study was to study genomic changes and phenotype correlation of subjects with aplastic anemia. The study was carried out in 93 aplastic anemia patients. The telomere shortening was observed in 43% of aplastic anemia patients (AA). Significantly elevated plasma Thrombopoietin (TPO) levels were observed in 23% of patients indicating dysregulation of megakaryocytes & bone marrow hematopoiesis. Therefore, study suggests that telomere length and plasma TPO levels may be considered as molecular markers for AA and should be monitored during the therapy.

Molecular analysis revealed 50% germline variants in telomere regulating genes (TERT, TINF2, NOP10, RTEL1) DNA repair genes (RAD50, ATM, NBN, ERCC6L2, DUT), proto-oncogenes (MPL) and genes involved in cell function and regulations (EPB41, KIF23, CDAN1, SPTA1, SPTB, WAS, SBDS) and 47% somatic variants as pathogenic and disease-causing.Molecular analysis is essentially important for the diagnosis and management of the disease.

Centre of Excellence for Advanced Research in Immunohematology and Transfusion Medicine and create a National Rare Donor Registry

The primary objective of this project was to establish reference laboratory for immuhaematology and to create rare donor registry for India. The study has established cost effective NGS facility for blood group genotyping for all 300 antigens for 43 blood group systems which can be utilized for diagnosis of unrsolved cases in transfusion medicine. Studt has also established genotyping facility and strategy for correct RhD, noninvasive fetal RhD and HNA typing.

By screening 3425 regular 'O' group blood donors for clinically important blood group antigens using serological methods, the team identified 446 rare donors, negative for a combination of clinically important common blood groups. The team is in the process of establishing a rare donor registry for the first time in India.

Study of genetic factors and immune parameters focusing on the transmission of HBV in household contacts of classical HBV cases

Identification of Occult HBV cases among family members of HBV positive patients was done using molecular methods. Twenty-two members (9.05%) tested positive for HBsAg whereas, 90 members (37.03%) were positive for HBcAb with/without HBsAb positivity, indicating exposure to HBV. Sangers sequencing was performed and analysis is in progress tofurther elucidate the viral mutations observed in OBI cases.

A multicentric study on Systemic Lupus Erythematosus (SLE) from the North Eastern (NE) Region of India: Early diagnosis to research potential for understanding disease pathogenesis

First hands-on training and workshop on serological techniques for diagnosis of Autoimmune diseases

at Assam Medical college, Dibrugarh,were conducted.

PUBLIC HEALTH

- Establishment of the "Centre for Research, Management and Control of Hemoglobinopathies" at Chandrapur. This centre will provide diagnostic services including genetic diagnosis and prenatal diagnosis, support state and district administrations for control and management of haemoglobinopathies, carry out basic and translational research in the area of haemoglobinopathies and strengthen the capabilities of the government medical colleges in the region through collaborative research and contribute to human resource development.
- Under the multicentric newborn screening program, 213 SCD babies have been diagnosed after screening of 30,079 newborns from 7 centres in high prevalent states. After screening, comprehensive care has been initiated.
- Under the DBT UMMID initiative, the team established facilities for antenatal screening for hemoglobinopathies and newborn screening for six inherited diseases in 'Aspirational District' Nandurbar and started a fellowship program in 'Clinical genetics' for in-service clinicians aimed at focused training in the diagnosis of various inherited haematological and immunological disorders. So far, trained 6 clinicians from different parts of the country.
- Study on platelet disorders has established cohort of these rare bleeding disoders which has helped us in understanding the spectrum of these disorders in India and their clinical manifestations.
- Under the mutlicentric study on Systemic Lupus Erythematosus (SLE) from the North-Eastern Region of India diagnostic facilities for autoimmune diseases have been established in 5 centres in the region.
- Molecular immunohaematology reference laboratory to resolve problems in blood grouping and crossmatching and identification of rare blood groups has been established by ICMR-NIIH under the centre of excellence for transfusion medicine.
- Under the centre of excellence for transfusion medicine, centre has established cost effective NGS facility for blood group genotyping for all 300 antigens for 43 blood group systems,andnoninvasive prenatal diagnosis for fetal RhD typing for management Rh-HDN for the first time in India.
- The team has identified 446 rare donors negative for a combination of clinically important common blood groups after screening of 3425 regular 'O' group blood donors using serological methods. These donors along with already known rare donors will be included in the rare donor registry for India.
- For the first time, indigenous red cell screening panel, suitable for Indian population has been prepared and distributed to 78 blood banks all over the country for detection of antibodies.
- The centre established the state of the art diagnostic facilities including panel for targeted NGS and functional validation for Primary Immunodeficiency Disorders (PID) at ICMR-NIIH under the 'Centre of Excellence for Research, Diagnosis and Management of PID' which have benefitted >11,000 patients from >110 centres across India.
- The centre established normal ranges for 34 important lymphocyte subsets in paediatric populationfor the first time in India which can be used for interpretation of the results during the diagnosis of PID and other immune disorders.
- The team prepared SOPs for various assays useful for diagnosis of common PIDs. These can be useful for centres establishing facilities for the diagnosis of PIDs.

- The technology for rapid, simple and cost-effective lateral flow immunoassay for the diagnosis of severe Haemophilia A and von Willebrand disease developed by the institute has been transferred for commercialization to Bhatt Biotech and has been approved by CDSCO for marketing.
- The lateral flow immunoassay for the point of care diagnosis of Glanzman's thrombasthenia (GT) has been developed and applied for patent by ICMR. It is in the process of external validation and will be transferred for commercialization.
- Cost effective, simple assay for G6PD deficiency has been standardized and externally validated and currently is in the process of applying for patent.
- Under the multicentric study on 'Systemic Lupus Erythematosus (SLE) from the North Eastern Region of India: Early diagnosis to research potential for understanding disease pathogenesis' facilities for diagnosis for these disorders has been established at 5 centres in NE region.
- ICMR-NIIH is contributing in the national rare disease registry of ICMR and asa nodal centre for Hemoglobinopathies, PID and Bleeding disorders, the team has designed the proforma and is involved in the quality control exercise of the registry.
- Specialised diagnostic services are provided by different departments, including transfusion medicine, hematogenesis, hemostasis and thrombosis, paediatric immunology and leukocyte biology, cytogenetics, and clinical and experimental immunology. More than 15,000 patients from India and abroad have availed these diagnostic facilities.
- The Institute offers prenatal diagnosis for various inherited disorders to couples referred from different parts of the country including thalassemia, sickle cell anemi and hemophilia and more than 300 affected families take advantage of these services every year.

PATENT

i) Indian patent granted :A kit for extended blood group determination and method thereof; patent number 389461

ii) Patent granted in Europe & U.S: "RHD gene allele associated with a weak D phenotype and its uses"

iii) A kit for extended blood group determination and method thereof – Application No.201721046817 Filed in 2017 Published in 05/07/2019

iv) "Simple, novel and cost-effective Lateral Flow Immunoassay for diagnosis of Glanzmann Thrombasthenia" the patent application has been filed on January 21, 2022 for this invention and patent application number is 202211003648.

ICMR-NATIONAL INSTITUTE OF PATHOLOGY (ICMR-NIP), NEW DELHI

Screening of Inhibitory Molecules against KIFC1, KIF4A, KIF15 and KIF20A and Evaluation of Anticancer Activity of the Identified Molecules on Breast Cancer Cells

Breast cancer is the most common cancer among women worldwide, representing nearly a quarter of all cancers. The mitotic spindle proteins are well tested targets for chemotherapy. KIFs KIFC1, KIF4A, KIF15 and KIF20A were found to be over expressed in breast tumors using microarray. In the present study we proposed to screen for inhibitory molecules against these kinesins which can effectively kill breast cancer cells. The 3D coordinates of the two kinesins KIFC1 and KIF15 were retrieved from RCSB (https://www.rcsb.org) to perform docking and simulations studies.In the present study, natural compounds library from InterBioScreen (IBScreen) database consisting of 68000 natural compounds was used to screen for

inhibitory molecules for the KIFs selected. In silico screening of KIFC1 with IBS natural compound library resulted in top hits having a Glide score equivalent to or lower than ΔG = -6 kcal/mol**,** the following are the top 5 ligands STOCK1N-XX288, STOCK1N-XX180 (-6.673), STOCK1N-XX785(-6.671), STOCK1N-XX853 (-6.564),and STOCK1N-XX135 (-6.429) ΔG was given in brackets, suggesting them to be the likely binding with the KIFC1.Similarly, the following top 5 hits having top Glide score were selected after screening against KIF15. STOCK1N-XX811(-8.768), STOCK1N-XX540 (-7.772), STOCK1N-XX945 (-7.451), STOCK1N-XX245 (-7.175), and STOCK1N-XX646 (-7.025),suggesting them to be likely having binding with KIF15 and may server as inhibitors against these kinesin, which need to be validated *in silico* and *in vitro* further establish their inhibitory role.

Deregulated Proteome Analysis of Lymph Node Metastatic Gallbladder Carcinoma to Identify Novel Therapeutic Targets

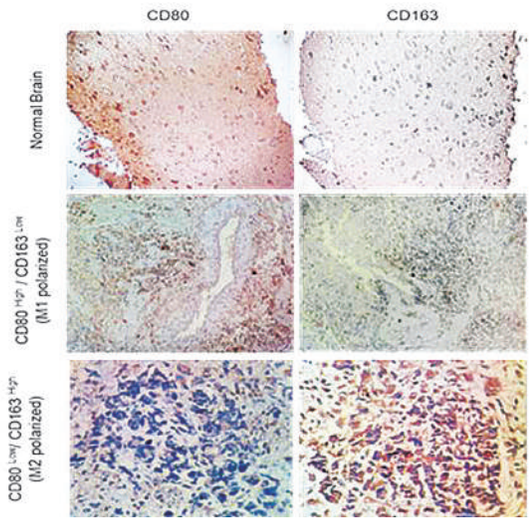
Lymph node (LN) metastasis is the earliest sign of metastatic spread and an established predictor of poor outcome in gallbladder cancer (GBC). Patients with LN positive GBC have a significantly worse survival (median survival- ~ 23 months) than patients with LN negative disease (median survival- ~ 7 months) in spite of standard treatment which includes extended surgery followed by chemotherapy, radiotherapy and targeted therapy. Therefore, effective targeted therapy for LN positive GBC is an urgent need for the improved survival of these patients. In the present study, iTRAQ-based quantitative proteomic analysis using tissue cohort comprising of primary tumor of LN negative GBC, LN positive GBC and controls was performed to identify proteins associated with lymph node metastasis. A total of 58 differentially expressed proteins (DEPs) were found to be specifically associated with LN positive GBC based on the criteria of p value ≤ 0.05, fold change ≥ 2 and unique peptides ≥ 2 .These include the cytoskeleton and associated proteins such as keratin, type II cytoskeletal 7 (KRT7), keratin type I cytoskeletal 19 (KRT19), vimentin (VIM), sorcin (SRI) and nuclear proteins such as nucleophosmin Isoform 1 (NPM1), heterogeneous nuclear ribonucleoproteins A2/B1 isoform X1 (HNRNPA2B1), which are already been reported to be involved in promoting invasion and metastasis. Bioinformatics analysis of the deregulated proteins in LN positive GBC using STRING database identified 'neutrophil degranulation' and 'HIF1 activation' to be among the top deregulated pathways. Western blot analysis further confirmed the overexpression of KRT7, KRT19, SRI and NPM1 in LN positive GBC in comparison to LN negative GBC. These proteins may be further analyzed in large cohort of samples and explored for their therapeutic applications in LN positive GBC.

Identification Of Extracellular Vesicles-based Circulatory miRNAs for Early Detection of Gallbladder Carcinoma

Early detection of GBC may significantly improve the survival of the patients, however, its detection is limited by non-specific symptoms, undetectability in radiological imaging and lack of effective screening approaches or molecular markers. There is an urgent need for a highly sensitive and specific panel of biomarkers for early detection of GBC. RNA was extracted from FFPE tissue specimens (~200 mm^2 tissue section, 9 µm thick) from Gallstone disease patients (non-tumor control) (n=6), early stage GBC (n=6), and advanced stage GBC (n=6) by using QiagenmiRNeasy FFPE kit according to the manufacturer's protocol. Total RNA including miRNA was then eluted in 16 µl of RNase-free water.RNA concentration was then quantified by spectrophotometer (Nanodrop 2000, Thermo) and RNA quality was analyzed using RNA nanokit (Agilent Technologies, US) by calculating RNA integrity number (RIN) using the Agilent 2100 Bioanalyzer. Quantitative miRNA analysis in blood plasma-derived EVs and tissue samples will be performed using 'Nanostring technology'.

Understanding the effect of crosstalk between microglia and glioblastoma cells on vasculogenic mimicry in Glioblastoma

This study aims to explore the role of microglia and tumor associated macrophages (TAM) in supporting vascular mimicry (VM) formation and maintaining and conferring resistance to anti-VM therapeutics in glioblastoma. Primary cultures of microglia/TAMs showed M2 polarization. The factors released by these cells impacted anti-VM potential of reparixin-l-lysine in U-87MG cell line. In presence of these factors anti-VM action of reparixin-l-lysine was completely stalled while M1polarized macrophages obtained from THP-1 cell line did not interfere with anti-VM effect of reparixin-l-lysine. Treatment with reparixin-l-lysine and anti-IL-8 affected VEGFR2 phosphorylation. Majority of GBM cases (approximately 65%) exhibit M2 polarized state of microglia and TAMs, while 35% of GBM cases with M1 polarized TAMs may be benefited with anti-VM drugs (Fig 1).



M1 and M2 polarization in FFPE GBM samples.

CD80 ^{High} / CD163 ^{Low} (M1 polarized)	CD80 ^{Low}/ CD163 ^{High} (M2 polarized)
7/20 (35%)	13/20 (65%)

Fig 1: Immunohistochemistry analysis with anti-CD80 and anti-CD163 antibodies on archival FFPE brain tissues. Images of adjacent normal brain and CD80 ^{High} / CD163 ^{Low} (M1 polarized) were taken at x200 resolution and images of CD80 ^{Low}/ CD163 ^{High} (M2 polarized) were taken at x400.

Since the response to drug is better in M1 polarized microenvironment, this gives direction for designing drugs for modulating M2 polarization to M1. Furthermore, IL-8/CXCR1/2 axis appears to promote VM formation via activation of VEGFR2 in GBM which appears to be the converging factor.

Identification of metabolic markers in Rheumatic Heart Disease (RHD) with Atrial Fibrillation using untargeted LC/MS based Metabolic Approach

To understand the difference in pathways leading to stroke in patients of RHD with Atrial Fibrillation (AF) and Normal Sinus Rhythm (NSR) metabolic markers in Rheumatic Heart Disease (RHD) with Atrial Fibrillation were identifiedusing untargeted LC/MS based Metabolic Approach.

Achievements: Total of 284 metabolites were identified in blood plasma through UHPLC-MS/MS analysis. PCA analysis was performed to understand the aggregation and description of the samples and cross validation analysis using 100 random permutations was performed. Those features with 1.5-fold difference and t-tests threshold of (y) 0.05 were considered. 13 metabolites were significantly upregulated and 18 metabolites were significantly down regulated among AF patients. Hierarchical Clustering analysis identified significant features in AF and NSR patients. The heatmap clearly distinguished the metabolic profiles of the AF group from the NSR group. Significantly altered metabolic pathways are illustrated in Fig 2.

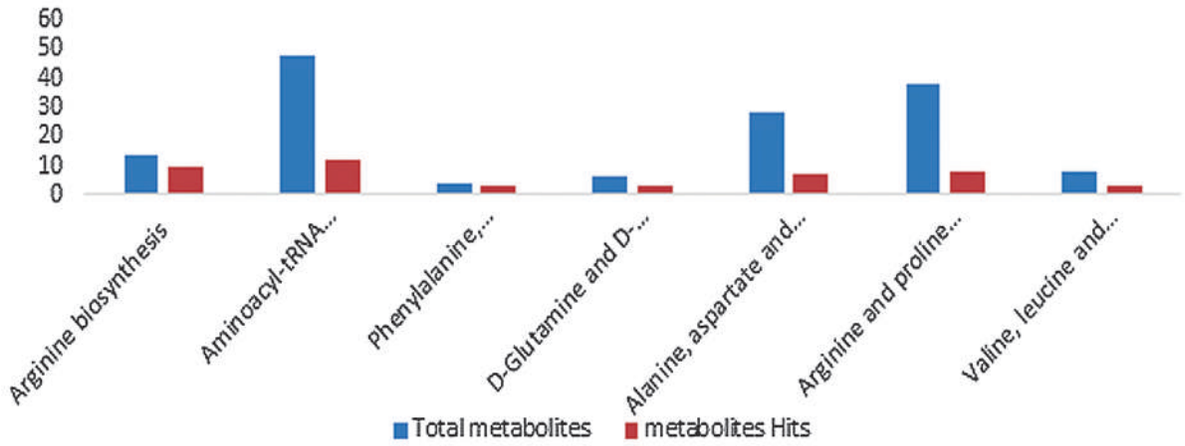


Fig. 2: Significantly altered metabolic pathways with blue bar representing total number of metabolites in the pathway and orange bar represents the total number of metabolites hit in the pathway.

Whole genome sequence analysis of drug sensitive and resistant Leishmania isolates originated from patients of kala-azar and post kala-azar dermal leishmaniasis

Whole-genome sequencing (WGS) data produced from miltefosine resistant *L. donovani* (K133M30) and PKDL isolate from the patient who relapsed to miltefosine treatment (P214R) were compared to decrypt the mechanism involved in drug resistance. A total of 5408 and 5184 gene variants were observed in K133M30 and P214R, respectively, out of which 4180 gene variants were found to be common. 2456 SNPs and 1724 InDels were discovered. Majorly 60.40% of SNPs were upstream, 15.81% downstream, 10.31% intergenic, 6.41% missense, 0.4% disruptive inframe, 0.21% conservative inframe, 0.047% stop lost & splice region and 0.047% stop gained and 4.04% synonymous variants. The highest number of smallnucleotide variants (SNVs) including SNPs and small insertions or deletions (indels)) were present on chromosome no. 34 followed by 31, 36 and 12. In contrast, the least number of SNVs were located on chromosome no. 3 followed by 5, 4, 9 and 1. Amongst all InDels, 1572 nucleotide insertions and 152 deletions of nucleotide were observed. The majority of changes detected in SNVs belong to the transition type, having a transition/ transversion (Ts/Tv) ratio of 1.72. In all, insertion was found to be maximal in the genome, followed by transition, transversion and deletion. The analysis of copy number variations (CNVs) revealed similarities in the genome of K133MIL30 and P214R. The size of gene copy number variants detected was in the range of 2 to 300 kilobase pairs in both K133MIL30 and predominantly maximum CNVs were in the range of 1 to 5kb preceded by 5 to 10 kb which accounts for 52.06 percent and 16.5 percent, respectively in K133MIL30 and P214R. 102 and 141 CNVs were identified to be unique to K133M30 and P214R while 121 CNVs were found to be common in both the genome. The disomic condition was noted in 25 out of 36 chromosomes. Rest eleven chromosome displayed some degree of aneuploidy. Divergence from the normal disomic pattern was observed in chromosome numbers 4, 8, 9, 11, 15, 20, 26 and 29 displayed trisomy state , while chromosome 5 and 31 was found to be tetrasomic followed by chromosome 23 which was in pentasomic condition,uniquely observed in both K133M30 and P214R. Shorter chromosomes have predominantly undergone ploidy alterations which is shown in this box-whisker plot, probably they are more stable in terms of aneuploidy (Fig.3).

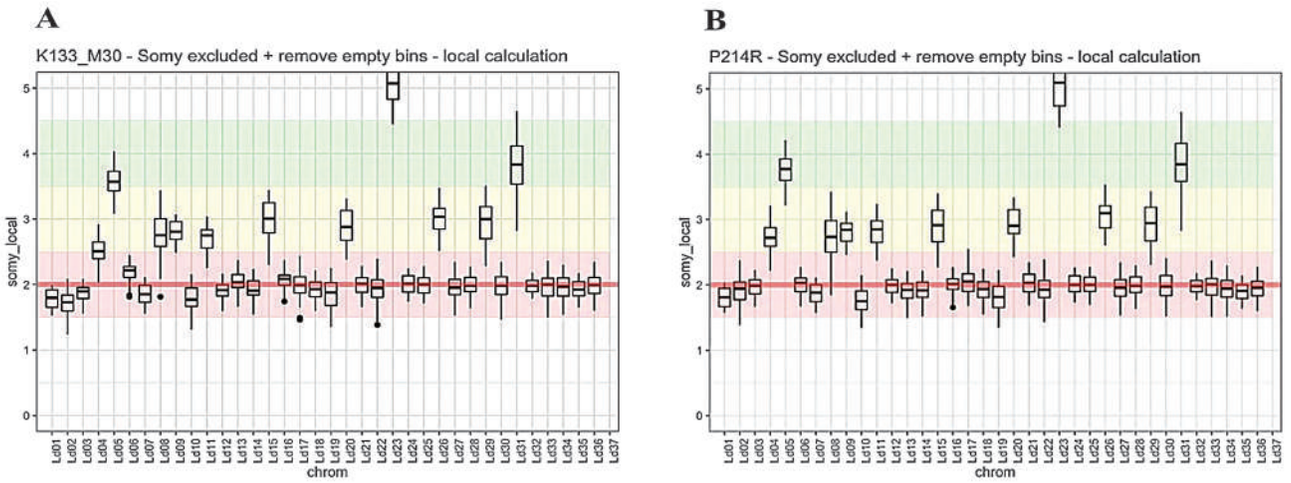


Fig. 3: Computative estimation of chromosome ploidy present in (A) K133M30 and (B) P214R genome. The median coverage of the genome is denoted by a red solid line, which was attributed as 2, taking into consideration that diploid is the most common ploidy condition in *Leishmania*. The coloured region denotes somy, disomic (pink), trisomy (orange), tetrasomic (green) and pentasomic (white).

The role of CRISPR-Cas system in fitness of *Acinetobacter baumannii*

4,977 RefSeq genomes of *A. baumannii* from the NCBI database to comprehend the distribution and association of CRISPR-Cas systems with genomic determinants were investigated. About 13.84% (n=689/4,977) isolates were found to carry the CRSIPR-Cas system, and a small fraction of isolates, 1.49% (n= 74/4977), exhibited degenerated CRISPR-Cas systems. Of these CRISPR-Cas positive (+) isolates, 67.48% (465/689) isolates harboured type I-F1, 28.59% (197/689) had type I-F2, and 3.7% (26/689) had co-existence of both type I-F1 and type I-F2 (Fig.4A). Co-existing type I-F1 and I-F2 systems are located distantly (~1.733 Mb). Isolates with type I-F1+F2 exhibited a significantly high number of mean spacers (n= 164.58 ±46.41) per isolate as compared to isolates with type I-F2 (n=82.87 ±36.14) and type I-F1 (n=54.51 ±26.27) (Fig.4B) with majority targeting the phages. Isolates with type I-F1 (p-value <0.0001) and type I-F2 (p-value <0.0115) displayed significantly larger genome sizes than type I-F1+F2 (Fig.4C). A significantly reduced number of integrated phages in isolates with type I-F1+F2 compared with other counterparts was observed (p-value =0.0041) (Fig. 1D).). In addition, the isolates carrying type I-F1+F2, did not exhibit reduced resistance and virulence genes compared to CRISPR Cas(-) and CRISPR Cas (+) types I-F1 and type I-F2, except for *bap, abaI*, and *abaR*. These observation suggests that the co-existence of type I-F1 and F2 is more effective in constraining the horizontal gene transfer and phage invasion in *A. baumannii* than the isolates exhibiting only type I-F1 and only type I-F2 systems.

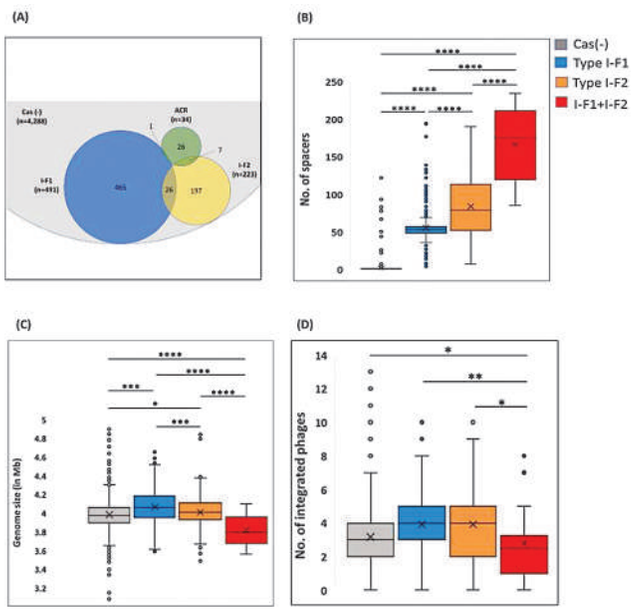


Fig. 4: (A) Distribution of CRISPR-Cas type I-F1, type I-F2,and anti-CRISPR (ACR) in the complete (n=4,977) set of *A. baumannii* genomes. (B) Number of spacers incorporated in CRISPR array/s (C) Genome size comparison of CRISPR-Cas (-) and different categories of CRISPR-Cas (+) isolates (D) Number of incorporated phages in genomes.

Gene expression studies of micro-RNAs in *Chlamydia trachomatis*-associated tubal ectopic pregnancy

Tubal ectopic pregnancy (EP) is associated with considerable morbidity and is responsible for pregnancy-related deaths in the first trimester. Also, a pathogenic link between *Chlamydia trachomatis* and EP has been reported. Prediction of EP and patients' follow-up is an important task in the management of pregnancy. In this regard, miRNAs might have the potential in early detection of EP considering their presence in body fluids such as serum. Present study demonstrated dysregulation of miRNAs as the concentration of miRNA-323-3p, -223 was significantly elevated while miRNA-873, -30a, 517a, 337-3p were significantly lower in the serum and fallopian tube of *C. trachomatis*-positive EP compared to uninfected EP (internal control) and control (tubal ligation) patients. miR-323-3p showed maximum fold-change.

Gene polymorphism and expression study of galectins and microRNAs in women undergoing spontaneous preterm birth with an infectious placental etiology

Spontaneous preterm birth (PTB) is one of the most important issues in current obstetric medicine as it is the leading cause of morbidity/ mortality during the neonatal period in both underdeveloped and developed countries. The etiology of preterm labour leading to PTB is multifactorial, however, localized/ systemic infection and/ or inflammation in the placenta and amniotic fluid are considered as important factors. If women can be identified to be at high risk in early pregnancy, they can be targeted for antenatal surveillance and interventions can be deployed to prevent/ delay birth and to improve subsequent neonatal mortality/ morbidity. Galectins (gals) have been implicated in the regulation of inflammatory response to chorioamniotic infection. The present study showed an altered relative expression of gals in the placental tissue of infected (*Chlamydia trachomatis/ Mycoplasma hominis/ Ureaplasmaurealyticum*-positive) PTB women. The transcript level of gal-1, -3, -7, -8, -13 was significantly upregulated in infected PTB patients *versus* uninfected PTB (internal control) and control (term birth) patients. Gal-13 showed the maximum fold-change in CT/ MH/ UU-infected women undergoing PTB.

ICMR-NATIONAL INSTITUTE OF TRADITIONAL MEDICINE (ICMR-NITM), BELAGAVI

Validation of diabetic wound healing activity of essential oil from NITM-MS-01 flower buds and elucidating its molecular mechanism

The study aimed to estimate the safety and efficacy of one of the traditional practicesfor mitigation of diabetic wounds.Essential oil (EO) from the flower buds of NITM-MS-01was testedusing*in vitro* and *in vivo* diabetic wound models.The yield of the essential oil was 0.58±0.32%, extracted through hydro-distillation. γ-Gurjunene, Copaene, Caryophyllene and Seychellene were identified as the major compounds through GC-MS/MS analysis. The EO Showed significant inhibitory activity (MIC) against *Proteus vulgaris*, *Salmonella typhimurium* and *Staphylococcus aureus*.The EO also showed significant antioxidant potential with IC50 values of 16.40±0.18 and 124.41±2.06 µg/g against DPPH and Nitric oxide free radicals respectively.*In vivo*acute and sub-acute dermal toxicity studiesshowed EO to be safe up to 2000mg/kg in the experimental rats.A significantly higher percentage of wound closure was noticed in the*in vivo* non-diabetic wound healing activity on 16th day in 2.5% and 5% EO treated groups (99.340±0.23% and 99.89±0.10%, $p \leq 0.001$ respectively), compared to standard metronidazole (98.38±0.91%, $p \leq 0.001$). This EO has the potential as an effective treatment for diabetic wounds.

Identification of endophytic fungi and screening for production of Shikimic acid from leaves of *Mammea suriga* and Glaucarubinone from *Simarouba glauca*

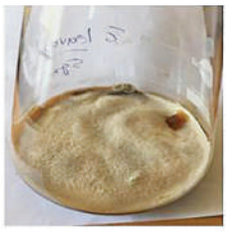
The study was to isolate and identify the endophytic fungal (EF) species from the leaves of *M.suriga* and *S.glauca* and screen them for the production of bioactive compounds, shikimic acid, and glaucarubinone respectively.The plant materialswere collected from various locations in the Western Ghats.The leaves were shade dried and grounded for the extraction process, while surface sterilized, fresh leaves were inoculated into different media for growing endophytic fungi. SDA was found to be the best media for the growth of EF in these cases. From the culture, four fungal strains were isolated and subjected to morphological and molecular identification. The isolated EF were mass cultured in SD broth and incubated at 28^0 C. Both the mycelia and broth were harvested at different time intervals (10, 15, 20, 25, and 30 days) and subjected to quantification of intended compounds. The present results indicated the highest amount of Shikimic acid (664mg/g extract) from the leaf samples of *M.suriga* collected from the Dandeli region.

Investigation of a Possible Mode of Action of Anti-obesity Effect of *Sauropus androgynus*: A Network Pharmacology Study

The objective of the study was to understand the possible mode of action of the *Sauropus androgynus* a medicinal plant claimed to be beneficial for reducing body weight, by using gene set enrichment analysis and network pharmacology. STRING, KEGG pathway, and CYTOSCAPE 3.6.1 were used to perform the study. Further, a molecular docking study was done with three–dimensional structures of quercetin, kaempferol, naringenin, and rosiglitazone (as a PPARG agonist) by using Discovery studio visualizer, and PYRX was used to predict the binding affinity of compounds with PPARG. Compound gene set enrichment analysis predicted different pathways modulated, which are involved in the pathogenesis of obesity. Among them, the PI3K – AKT signaling pathway was identified to score the highest count of genes with the lowest false discovery rate. Among selected phytoconstituents;kaempferol, quercetin, and naringenin, targeting PPARG were predicted to have the binding energy of -7kcal/mol, -7.2kcal/mol, and -7.2kcal/mol respectively, comparable to rosiglitazone which showed -8.5kcal/mol. Two hydrogen bond interactions were found in the ligand-protein complex i.e.MET:329 and ILE: 262. The study suggested kaempferol and quercetin interact with various protein molecules involved in the pathogenesis of obesity viz "PI3K-AKT signalling pathway" as a key pathway regulated by these likely bioactive phyto-constituents.

Unveiling the potential of anti-diabetic activity in the endophytic fungus from the plant NITM-156 along with enhancement of antihyperglycemic metabolites: An in vivo study

The endophytic fungus NITM-156 isolated from the leaf of a plant storedat-80ºC was revived after successive subcultures to achieve its propergrowth. Laboratory scale fermentation was achieved by culturing fungus in Sabouraud Dextrose Broth (SDB) at a static condition for 14 days at 28°C. Initially, it was observed that multiple inoculations of mycelia produced similar secondary metabolites,but the biomass of the mycelia and yield of compounds was found to be low.The experiment was performed to increase fungal biomass andyield secondary metabolite production in fungus by (i) alterationin fungal growth media strength and (ii) alterationin fungal growth media composition (Fig. 1). The endophytic fungus was identified by genomic DNA sequencing and analyzed in BLAST (NCBI) by selecting suitable parameters, and evolutionary analyses wereconductedinMEGA6. Itwas shownthatthe sequence belongs to the *Kalmusia* species. The protocol for fractionation of lyophilized methanol extract of endophytic fungus using column chromatography was standardized and five fractions were obtained. Chromatographic techniques were developed for three fractions. All five fractions were tested on a pilot scale in the streptozotocin-induced diabetic animal model, which showed that a single dose of 25 mg/kg body weight drastically reduces elevated blood glucose. Further, titration at single low doses was carried out, which showed significant antidiabetic activity.



(A) Only SBD media **Biomass – 4.2gm**	(B) SDB + 1% Plant leaves **Biomass-7.2gm**	(C) SDB + 1% Plant leaves water extract **Biomass-7.5gm**

Batch	**Fungal biomass (20x1000ml, Erlenmeyer flask 150 ml SDB**
August (non-supplemented)	85 gm
September (non-supplemented)	90 gm
October (non-supplemented)	60 gm
November (non-supplemented)	70 gm
December (non-supplemented)	69 gm
January (supplemented with 1% parental plant crude extract)	117 gm
February (supplemented with 1% parental plant crude extract)	135 gm
March (supplemented with 1% parental plant crude extract)	132 gm

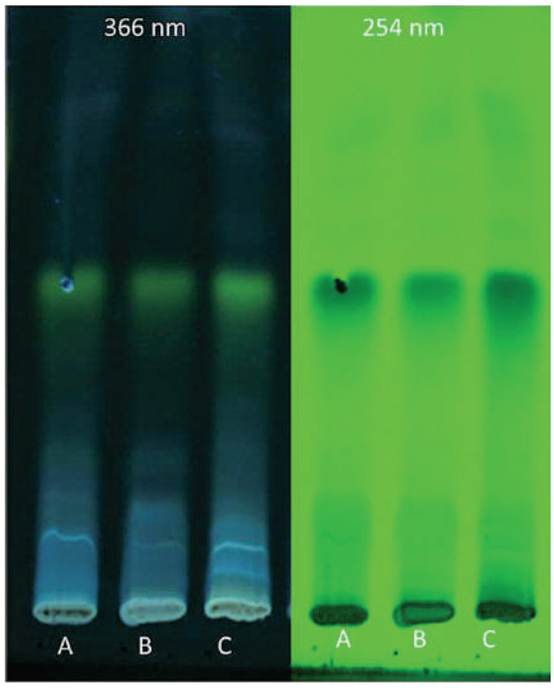


Fig. 5: Effect on fungal growth upon media alteration/Identification of a bioelicitor.Further studies are being undertaken to use this fungus for development management of diabetes.

Identification of Potential Herbal Drug Candidates from Traditional Practices against Viral Hepatitis

The objective of the study was to carry out High-throughput screening of all known phytoconstituents of shortlisted plants against identified targets of hepatitis A-E viruses and map their modes of action by computational studies. Six hundred and ten bioactive phytoconstituents were listed from sixteen plants. The virtual study identified Kaempferol 3-(3'',6''-di-p-coumarylglucoside) and other few phytocompounds as potential drug candidates against Hepatitis B. The flavonoid and the diterpenoid fraction of *Andrographis paniculata* and flavonoid fraction of *Thespesia populnea*were also identified as potent combined therapy against the progression of HBV infection and HBV induced Hepatocellular carcinoma.

Out of 41 selected compounds, 10 (Tannins from *T. chebulla*) were predicted to target HCV NS3/4A and identified to interact with 18 host targets and possess positive drug-like and non-toxic properties. Among 10 compounds, two showed potent HCV NS3/4A inhibitory activity *via* scoring the lowest binding energy (BE) of -8.6 and -7.7kcal/mol and formed 11 and 20 interactions with active site residues respectively. MD studies suggested these two compounds as promising leads *via* exhibiting a very stable RMSD, RMSF, rGyr, and interactions. Further, gene set enrichment and network analysis of 18 protein targets modulated by 10 compounds are found involved in the immune system, hemostasis, cytokine, interleukins signaling pathways, platelet aggregation, etc. This study identified potential compounds for further drug development through*in vitro* and *in vivo* evaluation for efficacy and safety.

Evaluation of selected bioactives from traditional medicinal plants on Olanzapine (OLZ) induced cardiac and metabolic disorders

The objective of the study was to screen the potential bioactives from TM plants against Olanzapine-induced Cardiac and metabolic disorders using a combination of *in silico*, *in vitro*, and *in vivo* studies in olanzapine-induced toxicity models. About 311 targets associated with metabolic syndrome*viz.*, diabetes mellitus, hypertension, obesity, and cardiovascular diseases were identified from the Therapeutic Target Database.

OLZ modulated targets were further identified via SwissTargetPrediction server and cross-varied the modulated targets with the targets listed from the TTD server. About 26 therapeutic targets were potentially modulated by OLZ that cause metabolic syndrome including cardiovascular diseases.From the literature, we shortlisted about 9 plants involving118 phytocompounds. The probable protein targets of these phytocompounds were predicted using BindingDB and about 2095 targets were predicted. These targets were cross verified with the targets of OLZ modulated therapeutic targets. The result showed that, about 21 targets were potentially modulated by 71 phytocompounds.

The enrichment analysis of 26 targets modulated by OLZ were found to be involved in 12 molecular pathways. Also71 compounds targeting 21 protein molecules were found to be involved in 9 pathways. Among them, Fukugcide (*Garcinia indica*), Garcinol (*Garcinia indica*), Capsacian (*Capsicum annuum* L), Dihydocapsacian (*Capsicum annuum* L), Gambogic acid *(Garciniaindica*), and Cyclomahamimbine (*Murrayakoenigii*) phytocompounds and ACHE, OPRK1, ADR1A, OPRM1, OPRD1, CNR1 DRD2, ADRA1B scored the highest edge count. This study helped identify potential molecules from Traditional Medicines and probable mechanisms of their actionagainst metabolic disorders.

PUBLIC HEALTH

- Scientifically validated and developed an essential oil based remedy from the flower buds of NITM-MS-01 for diabetic wounds.
- Provided RT-PCR diagnostic services during the COVID-19 pandemic.

PATENT

Patent on 'Phytopharmaceutical Formulation with natural inhibitors of 3CLpro and spike glycoprotein of SARS-CoV-2' (Indian Pat Appln # 202111034479).

ICMR-NATIONAL ANIMAL RESOURCE FACILITY FOR BIOMEDICAL RESEARCH (ICMR-NARFBR), HYDERABAD

ICMR- NARFBR is currently under establishment and building the state of art facilities with international standards biomedical research. The facilities will be created to develop and provide access to a range of laboratory animals and related technological resources to enable rapid advancement of biomedical research in the country, mainly to facilitate research in medical colleges, research and academic institutions, universities, and biotech, biopharma companies.

The institute will be a platform to acquire specialized skills in designing of animal experiments to scientists and technologists. Besides, it will also provide a strong support for biomedical research using extensive and well-designed physical facilities to provide national information services that promote conservation and well-informed animal research efforts. In a nutshell, it will serve as a nodal point for networking similar facilities for coordinating activities as a "Catalyst for discovery" for all scientific investigations throughout the country.

Once established, this institute will play a very important and crucial role in the coming years with its international standard infrastructural facilities; with its specific objectives to provide the required quality (SPF) biological resources to the needy institutions and by offering the best services for conducting preclinical safety studies for the development of drugs, vaccines, recombinant products, GM foods and medical devices. The institute with its exclusive large animal BSL3 facility in the campus will always have an edge over others to help progress of biotech,bio -pharma and biomedical research in the country. It is envisaged to establish all protocols and standards for testing safety and efficacy of products and intend to become an authorizing and certifying body on behalf of Government of India. Currently, the following buildings are under establishment phase.

Fig. 6: Rodent breeding facility.

Fig. 7. Common containment facility

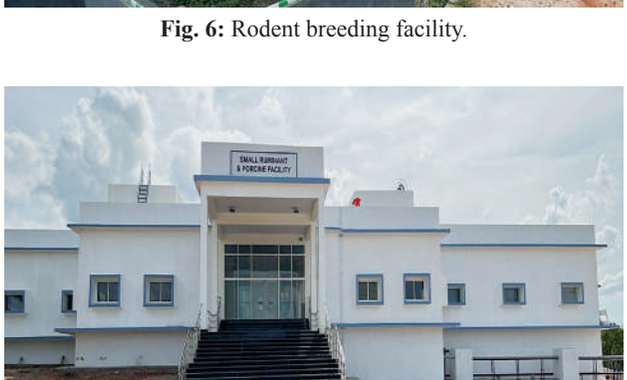


Fig.8. Small ruminant and porcine facility

Fig. 9. Equine experimentation facility

Fig. 10. Equine complex

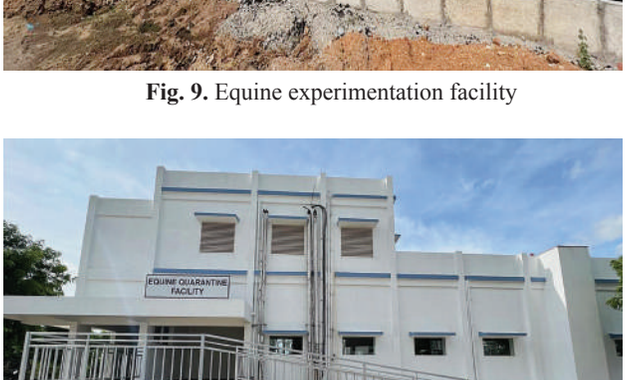


Fig.11. Equine quarantine facility

Fig. 12. Canine experimentation facility

Fig.13. Canine Breeding facility

Fig.14. Primate Breeding facility

Fig.15. Primate corral facility

Fig.16. Primate independent Houses

EXTRAMURAL RESEARCH

Task Force in Gene Therapy & Research

The various projects funded under this task force envisage development of various gene delivery platforms which includes both viral as well as non-viral vectors. Two clinical trials of CAR-T Cell Therapy for relapsed/refractory B-cell malignancies are also underway.

Task Force of Translational Immunological Approaches to Covid-19

The "Immunoprofiling (IP) consortium for COVID-19 Integration of Extended Immune Monitoring (ExImM) and clinical parameters for early prediction of disease trajectory/progression, treatment planning and prophylaxis to improve COVID-19 prognosis" aimed to decipher the unique immune mediated changes that take place in patients of Covid-19. The study displays extensive immunoprofiling with a huge panel of immune markers across the entire clinical spectrum of Covid-19 i.e asymptomatic and symptomatic- mild/ moderate/severe and severe sequelae, which when used in conjunction with various clinical parameters could serve as a useful tool in understanding disease pathogenesis, prediction of disease trajectory, and guidance of treatment.

Task Force of Omics in Health & Disease

Mission mode projects were invited addressing an integrated approach of Genomics (encompassing transcriptomics and epigenomics), Proteomics, Metabolomics and Lipidomics, to gain better understanding of diseases under the following thematic areas: Lifestyle diseases, Neglected Tropical Diseases and Inborn errors of metabolism. Four consortia have been developed as a result focusing on the following objectives:

i. Biomarker identification: multi-omics approaches to differentiate between diabetic and non-diabetic kidney disease and identification of markers of progression in chronic kidney disease

ii. Multicentric and multiomics study to identify novel biomarkers in Dengue fever

iii. Pan-India multicentric study on Neuro CYSTicercosis: Unravelling its metabolOMICs and proteOMICs architecture to enable its diagnosis and understand epilepsy (CYST-OMICS)

iv. Application of Expanded Newborn Screening By Integration Of Metabolomics And Genomics For Second Tier DNA Analysis

National Task Force – Nanomedicine

A total of 13 proposals were finally sanctioned for funding (2019-2022) based on various themes including Nano-drug delivery, Nano-enabled point of care devices, Nano-biosensor, Nano-enabled system for Regenerative Medicine & Wound Healing, Nano-immunotherapeutic & Nano-adjuvant, Imaging & Theragnostic & Nano-enabled emerging technologies like, Photodynamic Therapy (PDT), Nanorobotics etc. A Total of about 16 manuscripts published as activities of the NTF. Total of 2 patents are alsoin process.

National Task Force - Rare Diseases

A total 29 proposals are ongoing on Diagnostic and Functional studies in Primordial Dwarfism (Pd) , Alport Syndrome, Undiagnosed Diseases Program, Bardet Biedl Syndrome, Arthrogryposis Multiplex Congenita, Inborn Errors of Immunity, Primary Immunodeficiency disorders (PID), Hyperinsulinemic Hypoglycemia; Therapeutic Studies on Schwannoma associated with Neurofibromatosis type 2, Infantile Neuronal Ceroid Lipofuscinosis, Fibrodysplasia Ossificans Progressiva (Fop), Neuronopathic Gaucher Disease; Mechanistic Studies on Retinitis Pigmentosa Type 12, Nonsense Suppression Of Atm Mutations, Keratoconus; Animal Models on Pros And Proteus Hemihypertrophy Disorders. Amyloidosis ; Biomarker studies on Seronegative Neuromyelitis Optica (NMO). A total of about 11 manuscripts published as activities of the NTF.

National Task Force – Rational Use of Medicines

The Task Force has 15 intramural and extramural centres working on various projects under the theme of Rational Use of Medicines. Some of these projects include rational use of FDCs, unacceptable deviations from treatment guidelines, prescriptions from NLEM or otherwise, safety in tele-prescription, cost-effectiveness of medicines etc. There are 8 publications that have come out so far and few more in the pipeline.The Task Force has prepared and launched the prescription research software 'PrescReSof' and completed its validation. The task force has analysed more than 15,000 prescriptions across the country.The Task Force is also responsible for the Prescriber Skill Course which is currently in its third cycle, launched on Swayam Portal for which 2492 learners have enrolled so far. The second cycle was utilized by over 8,000 interns and 2000 RMP registered.

Standing National Committee on Medicine (SNCM)

The Standing National Committee on Medicine (SNCM) was constituted by Ministry of Health and Family Welfare with a mandate to revise National List of Essential Medicine (NLEM) 2015. SNCM invited expert suggestions/comments on inclusion and exclusion criteria of NLEM, 2015, invited expert's suggestions on lists of various drugs for inclusion/exclusion/modification of existing list of Essential drugs. Prepared reply after delegation in respective committees of various representations received from different organizations in SNCM Secretariat. Completed deliberations on all the sections of NLEM. Draft report for NLEM, 2021 was submitted to Health Secretary in September, 2021. Thereafter, on the directives from the office of Hon'ble Minister of Health and Family Welfare, the draft report was relooked.

National Consortium for Research and Development on Therapeutics for Rare Diseases (NCRDTRD) in India

Partnering institutes, nodal centres, individual researchers, the rare diseases research groups and patient organizations within the consortium would work together to study rare diseases across the nation towards better diagnosis and therapy.

i. Research and development in the field of Rare diseases for diagnosis and treatment may include:

a. Development/ validation of diagnostic markers.

b. To provide funding for the development of indigenous alternatives for available therapies.

c. In order to reduce the cost of some available therapies, to promote Pharma companies to invest in house production of available treatments e.g- Enzyme replacement therapies.

iii. Integrated Research Platform for the development of –

a. New drugs (synthetic molecules, stem cells, gene therapy etc.)

b. Research on repurposing of drugs

c. Research on biosimilar

ICMR's-National Hospital based Registry on 'Venous Thromboembolic Disorder' (i-RegVeD/ऋग्वेद) launched on 13th June 2022

Fig. 17: (i-RegVeD/ऋग्वेद) launched on 13th June 2022.

There are 16 participating centers along with a data management and analysis unit at ICMR-NIMS along with a coordinating unit in BMS Division, ICMR Headquarters identified to be part of registry. The aim of this activity is to establish a nationwide registry through selected hospitals and collect data for generating evidence on venous thromboembolism (VTE) prevalence for planning response, and strengthening healthcare facilities across different treatment settings.There is a glaring paucity of clinical and basic quality data on VTE and its ramifications among Indians- both in terms of quality of life as well as cost of healthcare. There is a glaring paucity of clinical and basic quality data on VTE and its ramifications among Indians- both in terms of quality of life as well as cost of healthcare. This registry aims to throw light on the disease burden, epidemiology, risk factors, environmental factors, food & nutrition that could play a role in VTE pathophysiology. The registry shall contribute to improving patient management for VTE and related manifestations, and also guide policy and health planning.

The objectives of the study include following:

iv. To develop and establish online registry to record VTE and related manifestation through hospital based Surveillance

v. Clinical, epidemiological, laboratory and outcome characterization of VTE and its manifestation in selected hospitals in India

vi. To observe and identify risk factors for VTE disease.

Evaluation of clinical research proposals for COVID-19 under the National Task Force on COVID-19

There are about 16 completed or ongoing projects with a total budget of INR 23,21,18,061. These are periodically reviewed by the Clinical Research Group of the Task Force. The Task Force has also been responsible for synthesis of evidence available for various treatments in COVID-19 and developing treatment guidelines for COVID-19. Scientists from the division of BMS have been partnering with other divisions of ICMR. There are two trials in collaboration with NIH, USA – ITAC and OTAC (total budget of $89,000 USD), one trial with University of Oxford, UK – RECOVERY (total budget of £6,02,702 GBP).

Review Monographs on Indian Medicinal Plants

The programme aims at consolidation of Indian research contributions (published information) at the various National laboratories/institutions across the country in the area of medicinal plants and present the compiled information in series on Reviews of Indian Medicinal Plants which serve as comprehensive, informative and reliable information on new leads thus helping in systematic and planned evaluation of medicinal plants including drug design, basic and applied research. During the year, the monographs on 169 plant genera and 734 species covered under 24th, 25th, 26th & 27th volumes have been published.

Fig. 18: Reviews of Indian Medicinal Plants Vol. 24th, 25th, 26th & 27th.

Safety Review Monographs on Indian Medicinal Plants

The second volume of this publication covering 75 monographs have been prepared and currently under review by the experts. This monograph documents comprehensive published information on medicinal plants mainly on their historical use, Pharmacopoeial status, preclinical general toxicity/safety, mutagenicity/genotoxicity safety, reproductive safety, adverse effects observed in clinical trials, safety in pregnancy, safety in children, case reports and herb-drug interactions. The 2nd volume of this series will be sent for printing after expert's review.

Development of a Website Exclusively Dealing with Medicinal Plants

A website (https://mpd.icmr.org.in/rm27.php) hyperlinked to ICMR main website has been developed exclusively on the Indian Medicinal Plants activities and is being regularly updated.

Development of a Phytopharmaceutical Drug for Preventing or Delaying the Development of Type-2 Diabetes in Subjects with Pre-Diabetes

The first, second and third stages of the project on development of Phytopharmaceutical drug through chemistry, manufacturing and control (CMC); evaluation of pre-clinical pharmacological efficacy & safety studies and undertaking GLP regulatory toxicity studies on the developed product in the laboratory animals have been completed previously. During the year, the fourth and final stage of the project on clinical assessment of product efficacy and safety has been initiated. For the fourth stage of the project, prepared and submitted IND and phase I clinical trial documents to DCGI, obtained permission to conduct Phase I human trial, selected external agency to conduct Phase I clinical trial through the process of Expression of Interest (EOI), and finally initiated Phase - 1 Randomized, Double-Blind, Placebo-Controlled Single and Multiple Doses of PDP-117 tablet in Healthy Subjects to evaluate Safety, Tolerability, Food effect, Pharmacodynamic and Pharmacokinetic of the developed product. The phase I clinical trial is currently under progress.

Development and clinical validation of a Standardized Ayurvedic Formulation for Treatment of Sleep Disorders

The first, second and third stages of the project on product development through chemistry,

manufacturing and control (CMC); pre-clinical pharmacological efficacy & safety studies; and GLP regulatory toxicity studies on the developed product have been completed previously. During the period, the fourth and final phase of project on clinical evaluation of efficacy and safety of the developed product has been initiated through a well-designed, multicenteric, randomized, double-blind, controlled clinical trial at 4 centers across the country is under progress.

Joint Phytopharmaceutical Drugs Development Programme of CSIR, DBT and ICMR

This is a tripartite Inter-ministerial cooperation and translational research programme of CSIR, DBT and ICMR on development of 'Phytopharmaceuticals'. Under this new initiative, the three organizations will jointly undertake development of Phytopharmaceutical drugs of national need. Under this programme, out of the 9 therapeutic leads identified initially, two leads/ projects have been prioritized.Current status of work on these projects is as described below.

a) Cannabis based Phytopharmaceutical Drug (THC:CBD ratio, 1:1) in Management of Cancer Pain

Under this lead development project, work has been completed with respect to identification, authentication and sourcing including cultivation of the plant (BRM) and has developed revised method for separation of both CBD and THC enriched fractions using single plant material along with completion of standardization work using the chemical markers. The CMC-related quality control studies of raw material, enriched fraction, formulation development studies and in-vivo efficacy validation and regulatory toxicity studies are under progress.

b) Boswellia based Phytopharmaceutical Drug in Treatment of Osteoarthritis

Under this lead development; work has been completed with respect to identification, authentication and sourcing of Botanical Raw Material (BRM) of Gum resin of *Boswellia serrata* and isolation and characterization of four markers, CMC-related quality control studies of BRM and enriched fraction as well as PK of enriched fraction/ marker. The formulation development studies, in-vivo efficacy validation and regulatory toxicity studies are under progress

Establishment of ICMR-National Marrow Donor Registry (NMDR)

ICMR was requested by the Ministry of Health and Family Welfare, to develop a non paper for developing the registry at AIIMS, Jhajjar through extramural programme. Subsequently, Team ICMR from the Division of BMS, sketched a proposal for operationalizing the registry with all granularities which had been circulated to the members of the Working Group for their comments and suggestions. The same is under deliberation and finalization.

Establishment of ICMR-DHR BMT Centres

Bone Marrow Transplantation (BMT)/ Hematopoietic stem-cell transplantation (HSCT) is a curative modality for a number of benign and malignant disorders. The number of patients seeking bone marrow transplant in India has increased over the last five years. However, there is still a critical gap between the patient needs and the available health-care resources, considering the huge burden of hematological cancers and diseases in India. To address this unmet need of providing available, accessible and affordable HSCT/BMT facilities to the patients, ICMR aims to establish State-of-the-art BMT Centers and create a network of all BMT centers in the country. This endeavor aspires to promote operational research related to health and biomedical profession and education through development of infrastructure and capacity building in cutting edge area of BMT/HSCT and management of related information thereto.The Division of BMS is at the forefront of this activity.

National Apex Committee for Stem Cell Research & Therapy (NAC-SCRT) and Gene Therapy Advisory and Evaluation Committee (GTAEC).

a. NAC-SCRT: This Committee was constituted in Oct. 2010 by Department of Health Research, Ministry of Health and Family Welfare as an apex body to oversee the activities in the field of stem cell research in India. It reviews the stem cell research activities through various Institutional Committees for Stem Cell Research registered with it. In compliance with Department of Health Research's notice to reduce compliance burden, an online portal to streamline this process of the registration of IC-SCR with NAC-SCRT has been developed. Till date, of the 179 applications received so far, 57 IC-SCRs have been registered and information from other institutes is awaited.

b. GTAEC: This Committee was constituted and notified by Department of Health Research on 16th January 2020 with secretariat at ICMR. Since inception, the committee has been delivering the mandate of monitoring and oversight in the field of gene therapy research. Four proposals pertaining to clinical trials in gene therapy in the country have been reviewed by the Committee and appropriate recommendations have been communicated to CDSCO.A website along with an online portal for submission of clinical trial applications as well as pre-IND consultations and hand holding of stakeholders involved in gene therapy has been created for promoting ease of business and reducing compliance burden.

National Guidelines for Hematopoietic Cell Transplantation (NGHCT)-2021

These guidelines were released with the aim of providing a template and help transplant physicians and centres formulate their own protocols and policies to conduct HCT. These guidelines in over 12 chapters, highlights the significance of HLA typing in HCT, handling, processing and preservation of stem cells and follow up of patients after transplant. Most importantly, it also enlists the indications for HCT, both in adults and pediatric patients.

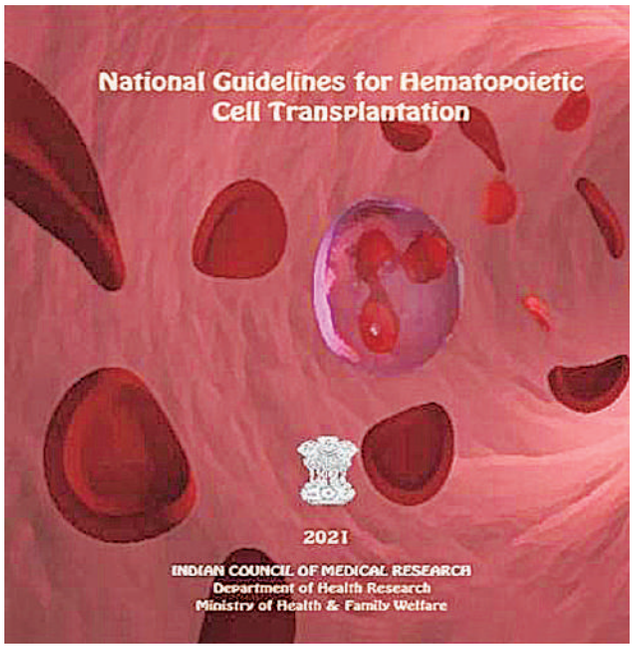


Fig. 19: National Guidelines for Hematopoietic Cell Transplantation

Evidence-Based Use of Stem Cell Therapy in Human Diseases

These statements were also released in public domain to address the experimental use of stem cells and assimilate available evidence in this nascent field. ICMR invited Level I and Level II evidence, writing to professional societies and also through an open call on the ICMR website. Clinical experts for each disease group were invited to review the literature and examine various claims on the use of stem cells. This document is a compilation of these expert reviews.

ICMR-Good Clinical Laboratory Practices (GCLP), 2021

The revised Guidelines for Good Clinical Laboratory Practices 2021 aim to establish minimum criteria which should be followed by clinical and research laboratories involved in examining human samples, in routine healthcare delivery and clinical research, respectively.

Establishing Centres for Advanced Research

Two such centres have been established at NIIH, Mumbai.

Centre of excellence for Research, Diagnosis and Management of Primary Immunodeficiency disorders (PID)

This centre provides advanced facilities for diagnosis, research and management of PID along with genetic counselling and pre-natal diagnosis. The diagnostic services established under COE are being utilized by more than 75 centres across India as well as outside India like Bangladesh, Nepal, Srilanka and UAE. Using the comprehensive diagnostic facilities, the centre has generated large cohorts of patients with specific IEIs over last 4-5 years e. g. LAD1, SCID, CGD, HLH, MSMD, etc. The centre has also generated a large number of trained personnel through workshops and various outreach programs to create awareness and expertise in clinicians.

Centre for Excellence for Advanced Research in Immunohaematology and Transfusion Medicine and create a National Rare Donor Registry

This centre has been established as a reference laboratory for resolving problems in blood grouping and crossmatching. A database of 3425 regular donors for 22 clinically important blood group antigens has been created and 100 rare Oh donors have been registered in the National Rare Donor Registry created under this CAR. A database of 'O' blood group donors for 15 antigens of five blood group system (Rh, Duffy, Kell, Kidd and MNS) has been prepared and will be used to provide antigen matched blood to thalassemic patients. Indigenous red cell panels specific for identifying antibodies have been developed. This screening panel has been distributed to 23 blood banks in western India to identify more patients with antibodies. Next Generation Sequencing (NGS) for genotyping of all the blood group genes in a cost-effective manner has been established so that it can be applied for large-scale genotyping of donors and it is now being used to solve complex serological cases.

PATENT

1. Nano-particulate Form of Genetically Engineered PU.1 Protein (Stem Cell Transcription Factor) as a Priming Agent to Selectively Elicit Myeloid Cell Formation from Hematopoietic Stem Cells. (Patent submitted to DRDO HQ/IPO).
2. Mag-PVA-Statin is a product having the potential of technology transfer and would be done upon filing the patent. This nano-statin-conjugate based assay would be able to track the cellular interactions of statins.

REGIONAL MEDICAL RESEARCH CENTRES

To deal with health problems of the regional and marginalised population, ICMR has established a total of four Regional Medical Research Centres, which are located at Port Blair (Andaman Nicobar), Bhubaneswar (Odisha), Dibrugarh (Assam) and Gorakhpur (UP). The mandate of these institutes is to focus on the regional health problems and find suitable solutions with the help from the respective state governments. The significant outcome of the research activities carried out by these centres during 2021-22 is mentioned below.

INTRAMURAL RESEARCH

ICMR-REGIONAL MEDICAL RESEARCH CENRE (ICMR-RMRCBB), BHUBANESWAR

Establishment of network of laboratories for managing epidemics and natural calamities (COVID-19)

Infrastructure and capacity building for identification and characterization of viruses and emerging infectious etiology

A next generation sequencing (NGS) facility has been established at the regional VRDL in the period 2021-2022. The regional VRDL is one of the laboratories contributing to genomic epidemiology of the SARS CoV2 through the INSACOG consortium in India and one of the only 2 laboratories from the state of Odisha providing information regarding SARS CoV2 variants and sub-variants at the state and national level. The genomic surveillance for tracking SARS CoV2 variants was initiated in February 2022.

Ongoing Surveillance and outbreak investigations

a. Surveillance of Dengue virus disease dynamics, circulating Dengue serotypes and Dengue virus genomic epidemiology.

b. Surveillance of SARS CoV2 variants and sub-variants and genomic epidemiology using NGS as an INSACOG sequencing laboratory.

c. Measles and Rubella laboratory surveillance- The regional VRDL is one of the laboratories which is WHO accredited for MR surveillance. In 2022, the second on-site assessment of the laboratory was performed and the accreditation renewed.

d. Outbreak investigation and laboratory support for Hand Foot and Mouth Disease (HFMD) outbreak in the state of Odisha.

e. The WHO designated the laboratory at ICMR RMRC Bhubaneswar as a DPT surveillance laboratory in February 2022 and DPT laboratory surveillance has been initiated in February 2022.

Providing training support and capacity building

- Training of Trainers for Molecular Testing on COVID-19 held at ICMR-Regional Medical Research Centre, Bhubaneswar, Odisha from 20th to 22nd December 2021 in association with FIND. Participants were from district level and medical college laboratories from Odisha and Goa. Trainers included scientists and research staff from the regional VRDL.
- One of the only 2 virtual classrooms from India coordinating the "SARS CoV2 Bioinformatics Course for Beginners" participating as collaborative classroom with Wellcome Connecting Science, Sanger Institute, UK with ongoing sessions on capacity building for bioinformatics for viruses of public health importance (November 1 to December 1, 2022)

Research for identification of emerging and re-emerging viruses and development of diagnostic assays

- Ongoing intramural study on "Describing the infectious etiology of Aseptic Meningitis and Encephalitis using non-targeted metagenomic sequencing"
- Part of ongoing multicentric study funded by ICMR "Reinfection with Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2) among healthcare workers in India"
- Collaboration with IMGENEX Inc, India for development and clinical validation of indigenous SARS CoV2 Antigen detection kit (Im-CoV-Ag™). Ongoing collaboration for self-antigen test.
- The regional VRDL has provided support for kit verification and validation for 63 different kits/lots of SARS CoV2 real time PCR kits, 56 RNA extraction kits, 15 antigen kits referred by through ICMR and the Odisha state OSMCL.

Quality control and quality assurance activities

- Participation in WHO and CDC coordinated Global proficiency testing for Measles and Rubella serology and molecular testing for 2021 and 2022.
- Coordination and training sessions for ILQC activities for COVID-19 real-time PCR testing for 27 laboratories in the state of Odisha in 2021-2022.
- ILQC and Dengue virus serotyping for NS1 positive samples referred from districts of Odisha.

COVID-19 related activities

a. 1st report from India on use and feasibility of saliva as alternative specimen of NPS for diagnosis of SARS-CoV-2. (https://doi.org/10.1002/jmv.26719)

b. 1st time reported the diagnostic accuracy of three antibody testing platforms ARCHITECT i2000SR (Abbott Laboratories, USA), Cobas e411 (Roche Diagnostics GmbH, Germany) and iFlash 1800 (Shenzhen Yhlo Biotech Co. Ltd., China). (https://doi.org/10.1016/j.jviromet.2021.114121)

c. 1st time reported the feasibility of pooled testing for SARS-COV-2 infection in an automated high 2 throughput platform of Roche Cobas 6800. (http://dx.doi.org/10.2139/ssrn.3685635)

d. 1st time documented that the lower persistence of anti-nucleocapsid SARS-CoV-2 antibody may not be the exact phenomenon as those cases were still seropositive against spike protein and help in neutralizing the virus. (https://doi.org/10.1007/s15010-021-01651-4)

e. Ct value associated with the antibody response among the SARS-CoV-2 infected individual. (https://doi.org/10.1101/2020.11.13.2022971)

f. The centre 1st time documented that a single dose of BBV-152 and AZD1222 induced a high concentration of neutralizing IgG

antibody in HCWs having a recovery history from COVID-19. (https://doi.org/10.1016/j.tmaid.2021.102170)

g. Currently working on dynamics and persistence of the quantitative Antibody against Spike protein of SARS-CoV-2 virus in the vaccinated individual and follow up of Ab persistence in COVID-19 infected individual.

h. The findings on the persistence of Ab against Spike protein of SARS-CoV-2 virus in the vaccinated individual and Ab persistence in COVID-19 infected individual over a period of 1 year are published in various journals of repute and high impact.

TUBERCULOSIS RELATED ACTIVITIES

National Reference Laboratory for Tuberculosis (NRL)

During the period, NRL carried out the third round of proficiency testing for IRL Cuttack, IRL Kolkata, IRL Guwahati, NBMC-Silliguri, Nazerath Hospital and SRL Kolkata. The NABL assessment was completed successfully and the certificate was renewed. The 13th round panel testing under SNRL ICMR-NIRT Chennai was completed successfully. During this period, consultants visited IRL Kolkata, NBMC Siliguri, IRL Guwahati and IRL Cuttack for the assessment of renovation of these laboratories in collaboration with FIND. Two Senior LTs and One Biotechnologist had undertaken training on "Quality Management systems and Internal audit in Medical Laboratories as per ISO 15189:2012" from 28th July to 31st July 2021. One scientist along with one consultant microbiologist had attended a workshop on Genomic sequencing of *Mycobacterium tuberculosis* at NIRT, Chennai in December 2021.

Assessment of comparative performance (efficacy & safety) of C-TB with QuantiFERON-TB Gold Plus & 2 T.U. Tuberculin PPD RT23 SSI in Tube for detection of TB infection in general & key population [Multi-centric]: Odisha, Gujarat, Kerala, New Delhi, Sikkim & Telangana

- C-TB has shown similar safety profile as that of PPD and is safe in Indian population at 48-72 hrs and at 28 days.
- C-TB has shown overall better sensitivity in general population and Household contacts/ high risk population of TB patients as compared to PPD while specificity was comparable in both the groups in detecting latent TB taking IGRA as the reference standard.
- C-TB can be used for detection of latent- TB under the NTEP for population of age 18 years and above.
- More data need to be generated in population less than 18 years of age.
- Lack of availability of PPD necessitates use of C-TB which is more sensitive than PPD from programmatic point of view.

A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac (M*w*) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly Diagnosed Sputum Positive Pulmonary TB Patients

The study is carried out to evaluate the efficacy of VPM1002 and Immuvac by comparing reduction in the incidence of TB over 3-year period among Indian healthy household contacts of newly diagnosed sputum positive PTB patients vaccinated with VPM1002 and Immuvac in comparison to placebo. The study is designed as a multicentre, double-blinded, randomized, placebo-controlled trial with three groups of healthy household contacts of new index cases of sputum positive PTB, receiving either VPM1002/Immuvac/Placebo (three arm study). The study was started after the approval from the Drug Controller General of India (DCGI) and the Institutional Ethics Committee

(IEC) from the respective study sites. The details of the sputum positive PTB cases presenting to the DOTS centres/clinics/OPDs of the implementing institute in the last 4 weeks before initiation was obtained. The index cases were contacted and a list of household contacts was obtained from the index case. Household contacts who were willing to be screened were registered. After obtaining the informed consent from the contacts, screening was performed. Eligible and willing participants were enrolled in the study. After injecting the participants with the investigational vaccines as per the protocol, they are being followed up at periodic intervals. A total of 1742 participants enrolled at the 3 study sites - RMRC, Bhubaneswar site, AIIMS, Bhubaneswar site and SCBMCH, Cuttack site are being followed up clinically, and with X-ray and sputum examinations at regular intervals. The follow ups are expected to be completed by February, 2024. If the results of the trial are found to be encouraging, the vaccines may prove to be effective stepping stones towards TB elimination.

A study to assess Silicosis, TB & their possible risk factors among glass industry, coal mines & mica-scavengers silica dust exposed workers: an interventional study

The study has been initiated in the mining regions of Odisha, namely Anugul, Jajpur, Keonjhar & Sundargarh. Necessary approvals from IHEC, State Research & Ethics Committee, STO, DTO, etc. have been obtained.

A feasibility study for implementation of innovative RBSK-NTEP collaboration module for active case finding of Tuberculosis among school students: a Multi-centric Study

The study has been initiated to identify presumptive Pediatric TB cases in school going children by using RBSK infrastructure. Till now, 1000 children attending primary, secondary & Higher secondary classes in the private schools of Bhubaneswar have been screened for TB.

TRIBAL HEALTH & SICKLE CELL DISEASE

Odisha Tribal Family Health Survey (OTFHS)

Initiated by the tribal department of Government of Odisha and in collaboration with the SCST Research and Training Institute, Odisha, the centre has carried out a mapping of sickle cell anemia in the state of Odisha along with developing a compendium of evidence of all research outputs in India related to sickle cell disease. Following this, the same partnership has led to a state of Odisha supported project, the Odisha Tribal Family Health Survey (OTFHS). OTFHS is a first of its kind comprehensive and multidimensional survey exclusively among tribal population of Odisha. The aim is to provide high quality data that can help the state health and tribal affairs departments to design and target interventions for improving the health and social status of tribals. The survey has been designed to provide comparable estimates on over 140 social and health indicators for each of the 62 tribes and 13 primitive vulnerable tribal groups in the state. Data is being collected digitally from over 10000 households with an estimated 42000 participants in total. Household level tests such as RBS, Hb, BP, Anthropometrics, grip strength and hemoglobinopathies are being conducted along with collection of serum samples for a battery of investigations to be performed at RMRC. OTFHS would form the baseline for future need-based surveillance rounds and for the Tribal Health Observatory for real-time decision-making support to the health system of the state.

Sickle cell Disease

ICMR- National task force, intervention research project, was undertaken with the aim to develop effective intervention model for the SCD patients in tribal areas for accessing government health care system and capacity building in terms of knowledge, skill and training of the health care workers at different levels of health system for prevention and management of SCD. In Odisha, the study was conducted in the tribal dominated,

Kandhamal District. A rapid screening of Sickle cell anaemia was done to assess the disease burden in Kandhamal, one of the tribal dominated (>50%) districts of the state of Odisha. Around 237 under-five children belonging to Kandha tribe were screened from four selected PHCs and amongst them 33 (13.92%) were found to be sickling positive indicating a high prevalence of sickle cell anaemia in the tribal community of the selected study area. ASHA identified a total of 1424 individuals with SCD related symptoms. Solubility test performed by ANM/MHW found 554 positives suspects for sickling trait or disease out of the 1424 individuals. These 554 patients were sent to PHCs for confirmatory test and identified patients received medication from PHC. During the evaluation phase it was observed that the patients identified from the area, now could take their medication from the PHCs itself instead of going to DHH for the same. This saved them from out-of-pocket expenditure incurred while getting the medication. The nearby location of medication motivated them to continue with the treatment. Given the success of the project, a follow-up will be undertaken scaled up the intervention to the entire CHCs of Kandhamal district. This will be done with support from the state NHM department.

Out of 75 Particularly Vulnerable Tribal Groups (PVTGs) identified by Govt. of India, 13 PVTGs are found to be distributed in 12 districts of Odisha. The ICMR-Regional Medical Research Centre (RMRC), Bhubaneswar had undertaken a study during 2018-19 to assess the disease profile of all the PVTGs living in 17 micro project areas (MPA). During July 2018 to February 2019, a total of 1461 individuals belonging to 13 PVTGS were screened for hemoglobinopathies, out of which around 6 % were found to be sickle cell disorder. Cord blood screening for Sickle cell anaemia was carried out on 761 newborn samples of tribal district i.e Kalahandi from March 2013 to June 2013. Out of 761 cases, 83.44 % (n=635) found to be normal, 14.71 % (n=112) heterozygous and 1.7 % (n=13) homozygous for sickle cell gene. Only one (0.13 %) was heterozygous for Hb D. Prevalence of sickle cell disorder varies from 1.71 to 10.52 % in different areas of Kalahandi district and the prevalence was highest in M. Rampur (10.52 %).

ONE HEALTH RESEARCH

"One Health" strategy for elimination of human anthrax from an endemic district of Odisha: a demonstration project

Advocacy with district administration for waiver of livestock vaccination fee: Observations from the field work during the quantitative and qualitative baseline surveys we have noted that the coverage of livestock vaccination against anthrax is very minimal in the district.

Livestock Vaccination in Mission Mode: This drive was led by the district veterinary department with the support of health department and panchayat officials at the grassroot level. During the period of six months (August 2021 to January 2022) the department was able to vaccinate about 1.46 lakhs large animals across the district.

Development of Training Modules & Brochures: We have developed three capacity building and training modules for different stakeholders (health, veterinary and forest) and undertook various rounds of capacity-building trainings. We have developed and distributed brochures for creating knowledge among the ground-level workers from the health, veterinary, forest, education, ICSD and PRI department and community people.

Capacity Building Training: We have trained about 450 participants across all the departments at the district level. Participants in the training were Medical Officers, Veterinary and Forest departments.

IEC/BCC Activities: Currently IEC/BCC activities and campaigns are being carried out through different mediums such print media, social media, radio (All India Radio) through local destination at Jeypore, Koraput, posters and banners (Sun Boards) at CHCs, PHCs, Sub-Health Centre's, Gram Panchayats, Community Halls, Livestock Aid Centre, direct communication in community meetings, panchayat meetings etc.

Online certificate course on One Health

The centre has developed the 1st course of its kind on One Health in India. In view of the rapid emergence and re-emergence of various pathogens of public health importance, the course is designed to develop a basic understanding of the One Health approach in management and control of various outbreaks and diseases. The course will be launched by NPTEL and is a AICTE approved FDP course. The course will be launched on 23rd January, 2023 and the last phase of recording of lectures by various experts is underway. The enrollment for the course has already been initiated.

ACTIVITIES OF RESEARCH UNITS

Model Rural Health Research Unit, Tigiria

Demography Integrated Surveillance for Health Assessment (DISHA) on Dengue and Chikungunya in Tigiria block of Cuttack district, Odisha

Project DISHA aims to establish a rural health and demographic surveillance system HDSS to provide a platform for research on dengue, chikungunya and their determinants. A population cohort of about 80,000 participants has been developed and all relevant data is collected before initiating the trial.

Laboratory surveillance system for antimicrobial resistance in community settings and understanding the perception and determinants leading to antimicrobial (mis) use in rural settings of Odisha & Chhattisgarh

The study is being carried out at MRHRU catchment area to study the patterns of AMR, practices & perceptions related to antibiotic use in rural communities to strengthen rational antibiotic usage policy. A total of 1340 clinical specimens were collected from UTI (970), bacteremia (342) and diarrhoea (28) cases of hospital outdoor patients having clinically evident infection during the period of January to October 2022. Organisms including *S. aureus, Enterococcus facium*, *E. coli, Klebseilla, Pseudomonas* and *Proteus, Streptococcus, Vibrio cholera* were isolated from 301 culture positive samples. Gram positives were resistant to erythromycin, ofloxacin, ciprofloxacin and cefoxitin. Gram negatives were resistant to cefoxitin, ciprofloxacin, levofloxacin, imipenem and cefepime. In Gram negatives, most of *E. coli* isolates produced extended spectrum ß-lactamase.

COVID-19 sero-survey

A COVID-19 sero- survey was conducted in the rural catchment area of Model Rural Health Research Unit in Odisha, India during Mar-April 2021, the initial phase of COVID vaccination. Among 3622 participants, the overall seroprevalence after adjusting for test performance was 54.21% with an infection to case ratio of 96.89 along with 4.25 % partial and 6.79 % full immunization coverage. Highest sero-prevalence was observed in the age group of 19-44 yrs and female had both higher sero-prevalence as well as vaccine coverage. People of other backward caste also had higher sero-positivity than other caste categories. The study emphasizes on continuing surveillance for COVID-19 cases and prioritizing COVID-19 vaccination for susceptible groups for better disease management.

Survey of chronic kidney disease patients and analysis of their socio-demographic and biochemical characteristics

The rural catchment area of MRHRU, Tigiria is known to harbor a large no. of chronic kidney disease (CKD) patients. Monitoring the biochemical parameters like liver function test, kidney function test and lipid profile is crucial for early identification of health complication, it's prevention and prompt management in CKD patients. A cross-sectional study was carried with 530 participants who are registered CKD patients, their Socio-demographic data and blood samples were collected for lipid profile, kidney and liver function analysis. The abnormal eGFR was found to be more among older age group (> 45 years),

literate and those in private job compared to their counterparts. Both lipid profile and liver function abnormalities were significantly associated with those having normal eGFR.

Regional Hub for Health Technology Assessment

- The Health Technology Assessment of Telemedicine-enabled Otoscope for Prevention of Ear Diseases was completed and the report was submitted to DHR and approved by HTA Board to assess the cost-effectiveness and operational feasibility of implementing a telemedicine enabled otoscope (TEO) ear disease prevention.
- The studies on Assessment of cost-effectiveness of 'Durgama Anchalare Malaria Nirakarana (DAMaN) – Malaria Control in Inaccessible Areas in India and Cost Effectiveness of Hearing aid devices among older adults in India are ongoing.

Fig. 1: Field & laboratory related activities.

Fig. 2: 1st Make in Odisha Rapid Antigen test kit, ImCOV-Ag developed in collaboration with Imgenex, India.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE (ICMR-RMRCGKP), GORAKHPUR

ONGOING STUDIES

Studies on SARS-CoV 2

The ICMR-RMRC GKP conducted various studies on different dimensions of SARS-CoV-2 including its diagnosis, epidemiology, molecular characteristics and impact on health care services.

- **Testing:** Since 23 March 2020, COVID cell at centre has tested more than 10.1 Lac samples.
- **The comparative analysis** of patients' characteristics, tested during first and second wave of COVID 19, found higher positivity rates among older age groups, with a shift of 11 years in the mean age of positivity in the second wave compared to the first
- **Vaccine efficacy study:** The vaccine interchangeability (after heterologous vaccination by Covishield followed by Covaxin) study was conducted to determine the vaccine effectiveness, immunogenicity and reactogenicity. The centre also conducted a study to characterize the immune response to precautionary third dose of COVISHIELD/ COVAXIN among healthy adult population.

Studies on JE/AES

- **JE/AES Testing and etiological investigations**: Since 2008, the centre is providing diagnostic services for AES cases. During the year, 563 CSF and serum samples were tested for different etiologies of AES including Japanese Encephalitis virus (JEV; 5.1% anti-JE IgM CSF positive & 8.4% serum positive), Scrub Typhus (ST; 62%), Dengue (DEN; 0.7%), Leptospira (2.6%) and samples negative for these etiologies were further tested for HSV (2.8%; 3/106), CMV (0.94%; 1/106), VZV (0.94%; 1/106), enterovirus (0%), Chandipura Virus (0%), H. influenza (0%) and S. pneumonia (0%).

- **Point of Care Testing of AES etiologies:** Centre is promoting development of rapid testing kits and working on two project entitled "To develop and validate the nucleic acid based RDT kit to detect Orientia tsutsugamushi" and "to develop and validate the CRISPR/Cas based nucleic acid detection RDT kit to detect Orientiatsutsugamushi" to develop point of care testing for scrub typhus.
- **Study on geo-spatial distribution of AES** cases and associated environmental factors to identify disease hotspots.
- Molecular and serological detection of Spotted Fever group (SFG) and typhus group (TG) among AFI and AES cases in the Gorakhpur region.
- **Socio-behavioural studies:** Two ongoing studies entitled "a study of psycho-neurotic disorders and socio - behavioral changes among AES/JE cases recovered in Gorakhpur" and "A study of cognitive awareness level about Japanese Encephalitis and behaviour Patterns among people belonging to north east districts of UP" are investigating the functional outcome of JE/AES and relation of JE/AES incidence with socio-behavioral pattern of general population.

Other Important Studies

- **Establishment of a Health and Demographic Surveillance System [HDSS], Gorakhpur, Uttar Pradesh:** The HDSS coupled with GIS mapping identified morbidity and mortality pattern, data on prevalent communicable and non- communicable diseases, socio-economic and nutritional status of one lac population from HDSS villages.
- **Establishment of a Consortium for One Health to address Zoonotic and Transboundary Diseases in India, including the Northeast Region. (Multi-Institutional DBT Project):** The centre is a collaborative partner for establishment of One Health Consortium in India and will help in estimating prevalence of zoonotic diseases and associated risk factors.
- **Surveillance of scrub typhus infection by serological and molecular testing by DHR- virus diagnostic laboratories across the country:** To determine the prevalence of scrub typhus infection among cases of Acute Encephalitis Syndrome (AES) and Fever Rash Syndrome (FRS).
- **Gap in Spatial distribution of disease density and health facilities in rural Gorakhpur:** This study was conducted to map the prevailing disease in the region and available healthcare facilities in the region and to estimate the out of the pocket expenditure of the healthcare facilities.
- **ARI/SARI surveillance study:** Hospital based surveillance to identify the circulating strains of respiratory pathogens among paediatric population in the region.
- **Vector Biology studies:** The centre is conducting studies on *Lymphatic filariasis* transmission, bionomics of vector for Kala-azar and insecticide susceptibility, *Brucelliosis* and *Leptospirosis* in AFI cases.

COMPLETED STUDIES

SARS-CoV2 Studies

Molecular surveillance and assessment of genomic diversity of SARS CoV-2 in Eastern Uttar Pradesh

The study revealed circulation of GR, O, GH, G and S clade during the first wave of pandemic whereas only G clade variants were detected as the predominant strain during the second wave of infection.

Impact assessment of COVID-19 pandemic on Maternal and Child health services in India

In this study, 245 beneficiaries were interviewed and data were sent to ICMR-NIMS for further analysis.

A qualitative study on psycho-social issues and challenges of individuals diagnosed with Covid-19 in eastern Uttar Pradesh

This study was conducted in which 58% non-migrants reported the experience of social stigma and 86% migrants reported the experience of social stigma. Due to COVID-19 infection people reported inducement of irritation (6%), fear (12%), change of attitude towards society and other people and learnt lesson with the infection (24%)

A study to determine the factors Related to Covid-19 Stigma (A Mixed Method Study)

In this study, it was found that the majority of respondents reported of television being the major source of information about COVID-19 infection and also referred to TV being the most reliable source of information on COVID-19.

Population-based serosurvey to estimate prevalence of SARS-CoV-2 antibodies in India: Fourth survey, June - July 2021

Serosurvey findings indicate that nearly two of the three individuals aged ≥6 years from the general population and 85% heath care workers had antibodies against SARSCoV- 2 by June 2020 in India.

OTHER STUDIES

A multi-centric study to understand the clinical spectrum and course of disease caused by Omicron VOC

In this study, clinical details of 34 cases were submitted in NCRC registry portal and samples were shipped to NIV Pune for sequencing and analysis.

National Survey for State Wise Prevalence of Microbiologically Confirmed Pulmonary Tuberculosis in India

Survey of 25000 population was done, among which 48 persons were found TB positive (41 Rifampicin sensitive, four rifampicin resistant and three intermediate).

Study on still birth and under 5 mortality

The centre was a site for project entitled "Family and community perceptions and practices related to stillbirth and under-five child death and feasibility of conducting minimally invasive tissue sampling in Gorakhpur District" and assisted INCLEN in conducting the study. A total of 76 interviews (parents of deceased children, neonates or stillbirths, n=36; community members, n=4, community health functionaries, n=8, and religious leaders, n=7), healthcare providers, n=21), and 8 FGDs (n=72) were conducted. The parents were positive and expressed willingness to accept MITS. The key determinants for acceptance of MITS were: (1) understanding and willingness to know the cause of death or stillbirth, (2) experience of the healthcare received and trust, (3) the religious and sociocultural norms.

HRD support

Two DHR Young Scientists joined the centre and one MSc and one MD dissertation was completed during the year.

- **DHR projects under young scientist scheme (YSS) includes:** Development of CRISPR/ Cas based isothermal detection platform for rapid and accurate diagnosis of Dengue and Chikungunya" and "To study the pattern of long term disability and poor prognostic factors for disability among children with Acute Encephalitis Syndrome (AES)"
- **MD dissertation project:** Etiological investigation of the bacterial and viral causes of acute respiratory infection in 1-5 years children: The most frequently detected virus RV (7.2%), followed by HMPV, PIV-4, and SARS CoV-2 with detection rate 4.8%%, 2.4% and 0.6% respectively from all ARI cases
- **MSc dissertation project:** Understanding the key mechanism of multidrug resistance in

clinical isolate and isoquinoline derivatives as drug resistance reversal agent: isoquinoline derivatives are being reported as antibacterial agent against clinical isolate of *Klebsiella pneumoniae* (RMRC-KN-1).

ICMR-REGIONAL MEDICAL RESEARCH CENRE (ICMR-RMRCNE), DIBRUGARH

COMMUNICABLE DISEASES

Human pulmonary paragonimiasis in crab-eating communities and smear-negative suspected TB cases from some states of India

Pulmonary paragonimiasis is often misdiagnosed with smear-negative pulmonary tuberculosis due to overlapping clinical manifestations and radiological pictures. Studies have revealed that pulmonary paragonimiasis is one of the important public health concerns in the northeastern (NE) region of India. However, in other states of India, the public health importance of paragonimiasis is not known. ICMR-RMRCNE is leading this Multi-centric task-force study on pulmonary paragonimiasis. New foci of paragonimiasis were detected for the first time in Kerala, Karnataka, Madhya Pradesh and Odisha. *Paragonimus* metacercariae were also detected in Kerala, Karnataka, Madhya Pradesh, Arunachal Pradesh and Manipur. Identified new intermediate crab host *Travancoriasp***.** harbouring lung fluke metacercariae in Kerala.

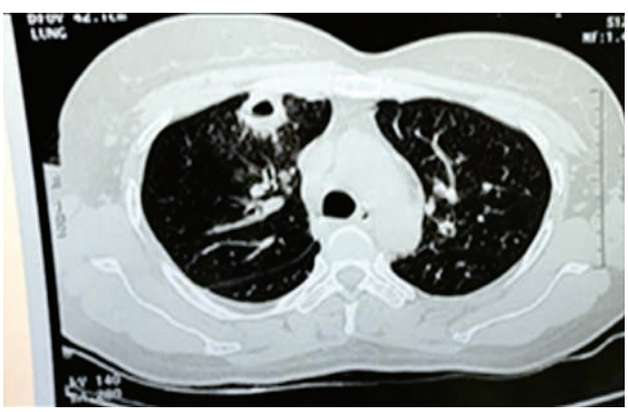


Fig. 3: High-resolution CT-scan (HRCT) thorax view of Paragonimiasis positive-patient from Manipur.

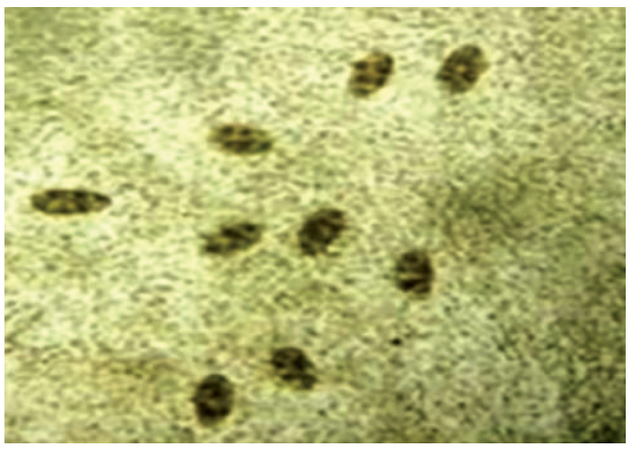


Fig. 4: Eggs of *Paragonimus* species found in sputum of Manipur patient.

Molecular investigations including NGS-sequencing of *M. tuberculosis* isolates from the NE region

About 3023 sputum samples from suspected TB patients from Assam, Meghalaya, and Tripura were collected out of which 684 were culture-positive for MTB. Out of the 684 MTB cultures, 535 samples were tested for drug sensitivity, and nearly 8.22% showed MDR. We have sequenced by NGS more than 200 samples. The team has deciphered novel mutations and identified the protein families showing maximum variants. SNPs present in MTB samples from the NE region showed that variants belong to genes related to cell wall synthesis, transcriptional regulation, and secretory protein belonging to Type VII and ESX-1 secretion system protein, ABC transporter protein, and copper transporter protein. Molecular diversity of the *Mycobacterium tuberculosis* complex (MTBC) from Sikkim was revealed for the first time. Artificial intelligence-based machine learning (ML) methods such as Random Forests (RF), Support Vector Machines (SVM) and Artificial Neural Networks (ANN) were used to predict dominant spoligotypes of MTBC using MIRU-VNTR data.

Expression profiling of inflammatory gene Angiotensin-converting enzyme 2 (ACE2) and high sensitive C reactive protein (hsCRP) among SARS-COV2 patients and clinical outcome: A prospective follow up study in Assam

The study primarily aims to correlate the differential expression of ACE2 and hsCRP and disease severity among COVID-19 cases. The physiological and pathological processes of SARS-CoV2 are still in the investigative stage. The study hypothesis is that in the early stage of COVID-19, monitoring inflammatory gene levels could reflect the possibility of a patient going into severity. This could identify prognostic markers, which may give time for better preparedness for managing COVID-19 patients.

Regional Viral Research and Diagnostic Laboratory (Regional-VRDL)

SARS-CoV-2 testing

During the reporting period, a total of 1,39,201 cases have been screened for SARS-CoV-2 using real-time PCR assay. Further, Inter Laboratory QA/QC (ILQC)testing services were offered to designated labs from northeast India for COVID-19 diagnosis. Further, Omicron variant of SARS-CoV-2 was successfully isolated in BSL-3 laboratory.

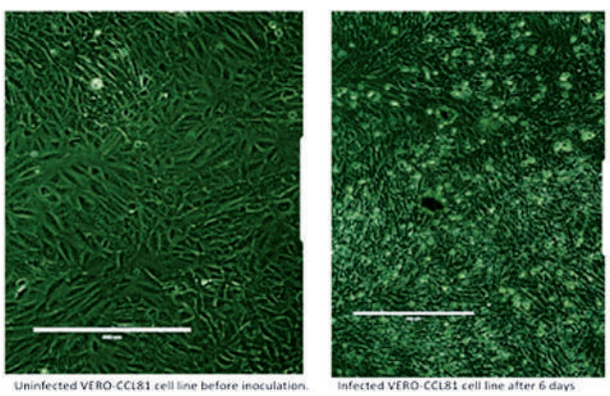


Fig. 5: Omicron variant isolation.

Development of kit

Developed a real-time PCR based kit for the detection of the Omicron Variant of SARS-CoV-2 and to distinguish its sub-lineage BA.1 and BA.2. This kit is under the process of external validation.

Comparison of positivity rate among Un-vaccinated, partially vaccinated, and fully vaccinated for SARS-CoV2 individuals (n= 159,268)

It was found that positivity rates were found to be higher among fully vaccinated individuals (34.73%) compared to un-vaccinated individual (16.54%) during the third wave of Covid-19.

Establishment of ten ICMR biorepositories for COVID-19

Except for age of patients, no factors such as hypertension, alcohol consumption, and smoking were found significantly associated with the symptomatic outcome of Covid19.

Evaluating SARS-CoV-2 IgG antibody titre after vaccination by the COVISHIELD vaccine

A single dose of recommended vaccine (Covishield vaccine) had a better antibody response against SARS-CoV-2 with prior naturally infected people compared to naïve cases.

Work related to other viruses

Among the 139 referred samples, 49.6% (69/139) were found to be positive for Dengue by Dengue NS1 ELISA. JE and Chikungunya was detected 47.22% (17/72), and 32.69% (34/104) respectively by IgM ELISA. Scrub Typhus was the major health burden caused by non-viral pathogens with a 29.16% (21/72) positive test rate in the state of Tripura during this period. HPV DNA from dry cervical swab in filter papers was extracted by in-house developed heat and Snap-chill methods and subjected to do nested-PCR. Out of 80 samples tested, 15 (PTR: 18.75%) were found positive for HPV. Surveillance of Influenza A & B in Dibrugarh district among SARI and RTI cases found influenza A & B prevalence of 14.7% (158/1116) and 200 (17.92%) samples positive for SARS-CoV-2 infection.

Mobile Application for Immunization Data in India-MAIDI (PILOTING PHASE I & II Target age– 0 to 1 yr.)

The Phase-I pilot study of the MAIDI m-Health application completed in four health sub-

centres under Lahoal Block PHC of Dibrugarh. Acceptability and feasibility of the MAIDI application among beneficiaries as well as health care workers demonstrated.

Surveillance of food borne pathogens from North east India

This task force project is running in four states of northeast India namely Assam, Arunachal Pradesh, Sikkim and Tripura. The aim of the project is to isolate circulating food-borne pathogens from market surveys, clinical surveys and during outbreak investigations.

To study the bacterial aetiology, antimicrobial sensitivity pattern resistance determinants and associated risk factors of neonatal sepsis in 4 different districts of Assam

A total of 1711 clinically suspected neonatal septicaemia cases were recruited from all study sites along with socio-demographic, clinical and about 1 ml of blood after obtaining consent of guardians. Overall culture positivity of the recruited samples was 27.9 % (478/1711). Gram positive organisms was found at a rate of 43.1 % (206/478) and gram negative to be 48.3% (231/478) while yeast to be 8.6% (41/ 478). Common sepsis signs found amongst the suspected neonates were- respiratory distress, poor cry and refusal to suck. Amongst clinically suspected neonatal cases, it was found out that males had higher rate of sepsis than females in all the four sites.

Development of rapid, point of care diagnostics and drug resistance monitoring technologies for malaria in N.E India using highly sensitive CRISPR based molecular tools

Proof of concept for rapid (45 minutes), point of care, visual detection one pot assays using isothermal methods (RPA) and CRISPR technology has been developed for *P. knowlesi* and *P. falciparum* k13 C580Y mutation using plasmid controls. An in-house low-cost incubator was designed for performing the assay and mimics a point-of-care assay using blue-LED lights for field settings.

Field deployable CRISPR technologies for rapid, ultra-sensitive detection of malaria transmission biomarkers and sub-microscopic asymptomatic cases

Successfully amplified and cloned known *Plasmodium falciparum* transmission biomarker gene Pfg17 into TA vector for use as controls for CRISPR based detection and confirmed by Sanger sequencing.

Microbial detection within minutes: Development of rapid, low-cost, ultra-sensitive, mobile-app-based CRISPR technologies for detection of clinically important bacterial infections and drug resistance

Five targets of clinical importance, including antibiotic resistance, have been identified, amplified, cloned and being processed for sequencing. Robust bioinformatic algorithms were used to design the RPA, qPCR primers and gRNAs for CRISPR.

Operational feasibility of additional intervention package for accelerated malaria control in areas with Jhum Cultivators in Tripura

This project focuses on malaria reduction strategies in Dhalai district. The presence of asymptomatic and sub-microscopic malaria helps in maintaining the chain of transmission and project aims to identify pockets and look for sustainable model to effectively control the problem.

Assessment of the malaria situation, and the role of Anopheles species in its transmission in selected International border areas adjoining the Districts of the North-Eastern States and the North-East corridor

In this first year of the project, primary aim is to establish units in border areas, often difficult terrains, for surveillance of malarial. This is spread over seven states of north east and West Bengal. It will be mix of qualitative and quantitative design

along with collection of samples from both human and vector population.

A study of low-density malaria parasite infection in the community and its transmission potential in Udalguri, Kokrajhar Districts of Assam and South Tripura District of Tripura

The project aims to map low-density malaria in identified districts of Assam and Tripura. It will involve collection of both human and vector samples.

A Systematic assessment of acute viral hepatitis and chronic liver diseases in Northeast India with special reference to strengthening of laboratories in the region

A total of 2004 subjects were enrolled in a hospital-based study with sites across 8 northeastern states. It was found that the prevalence of chronic hepatitis (36.3%; 728/2004) was highest, followed by acute viral hepatitis (33.8%; 673/2004), liver cirrhosis (26.4%; 529/2004), acute liver failure (2.2%; 44/2004) and hepatocellular carcinoma (HCC) (1.2%; 25/2004).

Study on impact of climate change on seasonality and distribution of insect vector borne viral and Rickettsial diseases in Northeast India

A Remote sensing and Geographical Information system approach(completed). The project identified hotspots for Dengue, Scrub Typhus and association with environmental factors like rainfall, mean temperature and factors like grass land/paddy fields etc.

Comprehensive analysis of the follicular helper T cell repertoire in flavivirus infection and vaccination (completed)

The completed project on comprehensive assessment of immunological aspects of the JE vaccine SA-14-14-2 were carried out with special reference to the role of follicular helper T-cells. Comparison of baseline and end line results identified the trajectory of immune response following vaccination.

Prevalence and drivers of select zoonotic pathogen and use of antimicrobials in livestock farms in NE region: A mixed methods study

Seven bacterial zoonotic pathogens including *Brucella, Klebsiella, Campylobacter, Escherichia coli, Leptospira, Staphylococcus* and *Salmonella* were screened among 798 animal handlers from 387 back-yard farms of Assam and Meghalaya.

Integrative functional analysis of the human immune response to a flavivirus vaccine

Integrative functional analysis of the immune responses against live attenuated JE vaccine, SA-14-14-2 was performed in humans on day-7, day-14 and day-28 post vaccination and followed up at Year 2 and Year 3 post immunization.

Rickettsial diseases in the states of Manipur, Tripura and Sikkim in Northeast India: Epidemiology, disease burden and vectors

Blood Samples were collected to screen for three diseases; 55% were positive for various rickettsial infections. Commonest was scrub typhus, followed by spotted fever group rickettsia and typhus group rickettsia.

A prospective facility-based study of arthropod borne viral and bacterial aetiologies of non-malarial fever cases in Tripura

Overall, 708 serum samples were collected from pre-designated civil hospitals of four districts of Tripura. 21.9% samples were seropositive for ST, and less than 1% for JE or Dengue. None of the sample was positive for Chikungunya or Leptospira.

Clinical and Epidemiological study of Lyme disease: A Multi-centric taskforce study in India

Overall, 327 human sera samples were collected from suspected patients from three hospitals of

Assam, Meghalaya and Mizoram. Entomological surveys conducted in case reporting areas and 46 ectoparasites (ticks) were collected from domestic pets *viz*. dog, goat, cattle. *Borrelia* IgM positivity was reported in 10.09% of the cases followed by *Borrelia* IgG (8.25%) and both in 1.22 % of the cases. Two ectoparasites have been identified as *Ixodesspp*.

Sero-prevalence and clinico-epidemiological and molecular aspects of Leptospirosis in Assam, India

A total of 1050 individuals including 436 (41.52%) males and 614 (58.48%) females were enrolled using cluster sampling. Leptospiral IgG antibodies was detected in 75 (7.14%) individuals.

Studies on the prevalence, distribution and biology of *An. culicifacies* in relation to malaria transmission and control in three states of North-east India

Total 101 anopheline mosquito was conducted in Changlang and Namsai districts of Arunachal Pradesh and 936 from Goalpara and Kamrup (Rural) districts of Assam. *An. culicifacies* species were found in Goalpara, Assam but not in other areas; however, none was found positive for plasmodium.

Establishment of a consortium for One health to address zoonotic and transboundary diseases in India including North-East region

As part of nationwide study on One-Health, 598 serum samples were collected from patients with suggestive symptoms and also asymptomatic contacts, from states of Assam, Meghalaya & Arunachal Pradesh. Brucella seropositivity was detected in 6.02% of the cases followed by JE in 3.84 % and ST in 2.5%.

Design, Microwave assisted synthesis and antimalarial evaluation of hybrid para-amino-benzoic acid- 1,3,5-triazine derivatives

Five hybrid Para-Amino- Benzoic Acid-1,3,5-triazine derivatives were found to show good anti-malarial property.

Role of Merozoite surface protein antigens on immunological profile of cultured peripheral blood mononuclear cells of pregnant women with malaria

In case of TNF-α, IL-12 and CCL-5, the serum values observed in malaria cases were lower than those in healthy controls and the differences were significant. In case of IL-12, following stimulation with antigens A1 and A2, the cases showed higher values as compared to controls and the differences were statistically significant.

NON-COMMUNICABLE DISEASES

Establishment of population-based Stroke Registry and Clinical Stroke Care Pathway using Mobile Stroke Unit in Dibrugarh, Assam

A total of 4654 cases (Male: 3005 and Female: 1649) cases have been registered from Assam Medical College and Hospital [3542 (76.1%)], Private Hospitals [717(15.4%)] and community [395(8.5%)]. Of the total stroke cases, major stroke type was hemorrhagic [2890(62.1%)] followed by ischemic [1457(31.3%)] and CVA [307(6.6%)].out of registered cases 1137(24.4%) were from study sites and 3517(75.6%) were from outside the study area.

Screening, Screening, awareness and counselling for prevention of sickle cell haemoglobinopathies among tea garden labour communities of Upper Assam

In consultation with the Tea Garden management, we conducted various webinars / Video Conferences to sensitize the tea-garden community about Sickle Cell haemoglobinopathy by showing animated videos that were developed in-house. These were shared through social media and digital platforms to create awareness. We collected 1082 blood samples from unmarried adult individuals from tea gardens in upper Assam. Analysis of these samples indicated the following results.

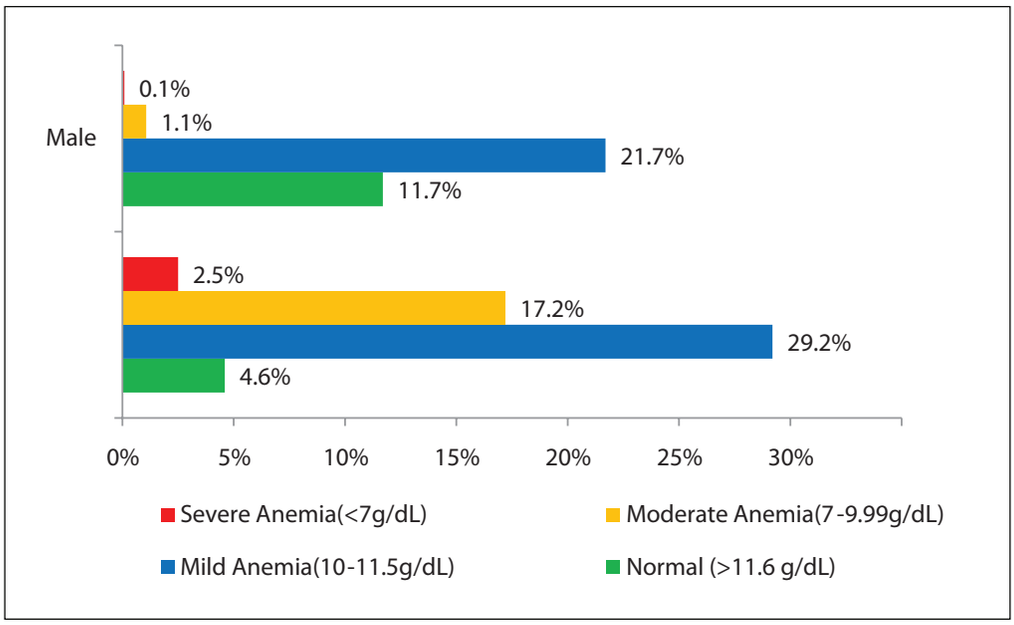


Fig. 6: Haemoglobin status among unmarried young adults of Tea Gardens.

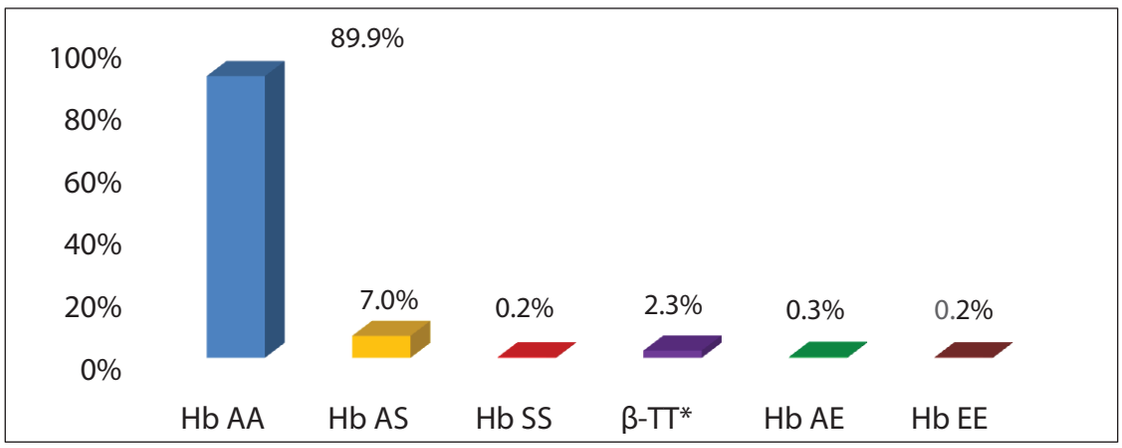


Fig. 7: The Prevalence of Sickle cell & other haemoglobinopathies in young adults of Tea Gardens.

Biochemical and haematological characterization of haemostatic derangements with special reference to role of Factor IX in subjects with β-thalassemia syndromes in Upper Assam

The project aimed to evaluate and characterize the haemostatic abnormalities in patients with β-thalassemia syndromes. Among samples collected in reporting period, it was observed that nearly 75% of the β-thalassemia individuals had derangements in one or more of these haemostasis screening tests. Of these, prolongation of APTT was found to be the most common derangement; present in nearly 70% cases. There were significant differences noticed in platelet count, clotting time, aPTT, D-Dimer, and Factor IX values between the two groups of subjects, during interim analysis.

Self-Monitoring of Blood Pressure and Decision Support with Lifestyle Intervention through Mobile Phone Application to Control Blood Pressure

A mobile-based application named "MyHeart" to facilitate self-monitoring and enabled with decision support facility developed for prevention and control of hypertension. Cluster-randomized trial in two districts covering 12 clusters (6 intervention and 6 control). There is a significant reduction of the blood pressure among the participants from the intervention arm.

Progression of blood pressure of prehypertensive subjects from native rural Assamese and tea garden community: A two years prospective follow-up study in a health and demographic surveillance cohort from Dibrugarh, Assam

Distribution of hypertension categories in the baseline (n=53,763) showed that 16,887(31.4%) were normotensive, 22,283(41.4%) were prehypertensive and 14,593 (27.1%) were hypertensive subjects.

Assessment of hematological and biochemical parameters of the population under Dibrugarh- HDSS

This study has been started recently. Field activities including sensitization of community, IEC activity have been initiated. Purchasing of the equipment including the lab bike is in progress.

OTHER PROJECTS

Model Rural Health Research Units (MRHRUs) in the North Eastern Region

Under the initiative of Department of Health Research (DHR), Model Rural Health Research Units (MRHRUs) have been set-up for empowering remote and rural areas of the country by promoting biomedical research. In the North Eastern Region, ICMR-RMRCNE Region Dibrugarh acts as the nodal agency and mentor institute for these MRHRUs in close collaboration with the link medical colleges and health departments.

Table 1: The state-wise list of MRHRUs is as follows:

Sl. No.	State	CHC/PHC	Linked Medical colleges
1	Arunachal Pradesh	CHC Sagelee	Director Medical Education & Research, Govt of Arunachal Pradesh, Naharlagun
2	Assam	RHTC Chabua	Assam Medical College and Hospital, Dibrugarh.
3	Meghalaya	CHC Sohra	Director Medical Education & Research, Govt of Meghalaya, Shillong
4	Mizoram	PHC Aibawk	Zoram Medical College, Falkawn, Mizoram
5	Nagaland	PHC Niuland	Directorate of Health & Family Welfare, Govt. of Nagaland, Kohima
6	Tripura	CHC Khumulwng	Agartala Govt. Medical College, Agartala

Establishment of Health and Demographic Surveillance System in Dibrugarh District, Assam (Dibrugarh-HDSS)

HDSS was successfully established in Dibrugarh district of Assam covering 60 villages and 20 Tea gardens. A total of 1,06,769 (Village: 46,762 Tea Garden: 60,007) participants were included in the baseline survey consisting of 52,934(49.6%) male and 53,835(50.4%) female subjects. A total of 75,686 individuals (Village: 40,726 Tea Garden: 34,960) from 16,292 households were followed up.

DBT-Animal house facility for Biotechnology Research in North-eastern Region

This is a DBT funded infrastructure development project at ICMR-RMRC, Dibrugarh for Northeast region. The objective of the project is to develop an advanced animal facility for housing small laboratory animals, accessible to all the Northeastern states of India for biomedical / biotechnology research and creating a pool of skilled and competent manpower for animal experimentation in biomedical sciences.

Patents

- Developed a real-time PCR-based kit for the detection of the Omicron Variant of SARS-CoV-2 and its sub-lineage BA.1 and BA.2 in December 2021. [Preliminary patent application no. 202111058937].
- Patent has been filed and copyright has been registered for “Fever Tracker app for Health workers”

ICMR-REGIONAL MEDICAL RESEARCH CENTRE (ICMR-RMRCPB), PORT BLAIR

RISK REDUCTION / ELIMINATION OF INFECTIOUS DISEASES

Mass distribution of double fortified salt (DEC + iodine), as novel strategy supplementary measure to the ongoing Mass Drug Administration (MDA) for eliminating a persistent focus of diurnally sub-periodic *Wuchereriabancrofti* towards accomplishing elimination of the disease in the entire Nancowry group of islands, Andaman and Nicobar Archipelago, a lone focus in India among Nicobarese tribe

Diurnally sub periodic form of *Wuchereriabancrofti* filariasis is endemic in five remotely located islands of Nancowry. Even after six annual rounds, annual MDA plus Albendazole, persistence of infection with microfilaremia (*Mf)* prevalence was 3.3%. Therefore, in order to hasten the process of elimination, Distribution of DEC double fortified salt (Diethylcarbamazine (DEC) at 0.2% w/w and iodine) was implemented in collaboration with NVBDCP, under the Directorate of Health Services, A & N administration. Port Blair. The study was conducted in two phases(phase I 2015-2017 & phase II 2019-2022). A total of 60 metric tons of DEC double fortified salt (DEC at 0.2% w/w and iodine) was distributed in all four endemic islands (*Nancowry, Teressa*, *Kamorta and Chowra*). The efforts made (during phase I and Phase II studies) resulted in elimination of persistent foci of diurnally sub-periodic Wuchereriabancrofti among Nicobarese tribe in the entire group of Nancowry group of islands, a lone focus in India. (Mf less than 1% and antigenemia among children nil in all villages of four islands)

Control of Tuberculosis among the Nicobarese of Car Nicobar: Consolidating the gains of a strengthened public health system and the recent socio-economic progress

Tuberculosis both pulmonary and extrapulmonary is one of the major public health problems among Nicobarese of Car Nicobar islands where more than 80% of Nicobarese reside. For the effective control of TB, ICMR RMRC initiated control programmes. The present study is series one and initiated during 2019 – 2020**,** which involved the following steps.

Sensitization meetings : Meetings were conducted with Director, Directorate of Health Services (DHS), State TB officer, A&N Islands, District TB Officer, Nicobar and Deputy commissioner Car Nicobar for logistic support. **Focal group discussions**: Meetings were conducted with the representatives of tribal council. **Meetings with Traditional knowledge practitioner (TKPs), Car Nicobar Island:** TKPs are crucial persons in effective implementation of the projects as a major proportion of patients during initial stage of TB consult TKPs, for the treatment. **During 2021-2022 active surveillance was continued in collaboration with BJR district hospital** :Sputum sample were collected from each chest symptomatic patients which were processed using Microscopy and CBNAAT and Line -Prob assay. **Screening of pulmonary tuberculosis patients for *hepatitis B viral* infections *(*HBV) during the treatment** : Since high rate of the seroprevalence of Hepatitis B, all TB patients were screened for hepatitis B virus infections towards adaptation of the treatment strategy based on levels of liver enzymes. **Follow-up of the children who were on chemoprophylaxis and counseling of parents on importance of chemoprophylaxis** :During the 2nd and 3rd year (2020 -21 & 2021-22), the children who were on chemoprophylaxis in the households of sputum positive cases were counselled. **Detection of Latent TB infection among household contacts and close contacts using Interferon Gamma Release Assay (IGRA) -A follow up of study :** During 2nd year and 3rd year, house hold contacts and close contacts were followed and household contacts were screened for latent TB infection and treated. The efforts resulted in the decline of occurrence of new cases per year and mortality was reduced due to pulmonary

Tuberculosis during 2021 -2022 when compared to that of during (2019 – 2020). A total of 57 new cases of pulmonary tuberculosis (MTB) were detected and 4 deaths reported due to Pulmonary tuberculosis during 2019 – 2020 whereas a total of 32 new cases MTB detected and one death reported due to Pulmonary Tuberculosis during 2021to 2022. However, occurrence of MDR TB increased. The program is in continuation.

Surveillance of long term Sequelae of Chronic Hepatitis B infection and Risk reduction among the Nicobarese of Car Nicobar

A total of 4,405 individuals have been recruited into the study. Among them 2,412 (54.8%) were females and 1,993 (45.2%) were males. The study included individuals of all age groups starting from 4-9 years age group. A total of 184 (4.2%) individuals reported that they had jaundice in the past. A total of 63 (1.4%) individuals reported family history of jaundice and 5 individuals reported that there had been death in their family due to jaundice. Among the 4,405 surveyed population, 3,474 (78.9%) had history of injections, 1,415 (32.1%) had IV infusions, 138 (3.1%) had blood transfusions and 749 (17.0%) had undergone surgical procedures (most of them for female sterilization) in the past. Out of these, 108 (57 females and 51 males) were positive giving an overall HBsAg prevalence of 17.3% (95% CI: 14.4, 20.5). The prevalence in females was 16.4% (95% CI: 12.6, 20.7) and that in males was 18.5% (95% C: 14.1, 23.6). The association of a few healthcare related events with HBsAg positivity was assessed with the HBsAg positives taken as cases and HBsAg negatives as controls in univariate analysis. IV infusion was found to have an association with HBsAg positivity in the univariate analysis, but the other three factors tested did not have any association. The observed association between IV infusion and HBV infection needs to be confirmed by assessing the independent association by multivariable analysis.

Establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities: State Level Viral Research and Diagnostic Laboratory

The centre is providing diagnostic and referral services to Whole Andaman Nicobar Islands - All the three districts –1) South Andaman 2) North & Middle Andaman and 3) Nicobar – mainly populated by indigenous tribes. The diagnostic and referral services extended to viral diseases viz. Dengue, Chikungunya, HSV-1, HSV-2, Rotavirus, Measles, Enteroviruses, Influenza A, Influenza A (H1N1 pdm09), Influenza B, Parainfluenza, RSVHuman Meta-pneumovirus, Rhinovirus, Parvo B-19, Astrovirus, Sapovirus, Norovirus, HPV, Adenovirus and SARS CoV 2 (COVID 19)

Study on Primary and secondary Dengue infection

Clinical presentations of dengue Infection were seen with any of the four dengue serotypes in the range of mild uncomplicated febrile illness to severe syndromes such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS). Infection with one of the serotype confers lifelong immunity to that serotype. However, secondary infections with another serotype of dengue may commonly lead severe syndromes associated with high morbidity and mortality.The present study was conducted to determine the proportion of primary and secondary dengue infections among the suspected cases of dengue fever.

A patient positive for Dengue NS1 Ag and/or IgM ELISA is considered as confirmed case of dengue. Primary dengue infection is classified as those cases which are positive for Dengue NS1Ag and/ or IgM ELISA where as a secondary infection refers to those positive for DengueNS1 Ag and/ or IgM ELISA with Dengue IgG ELISA positive. A total of 140 samples were tested to estimate the secondary infection, out of which, 23 were found positive giving rise to 16% indicating importance of the present study in case management of secondary infection which commonly leads to severe syndromes.

Chikungunya

During the reporting period, fever cases with joint pain at GB Pant hospital, (referral hospital), Port Blair, district hospital Garacharma and primary health centres *viz.,*Manglutan, Tushnabad, Couldhari, Ferrargunj, Wimberlygunj in South Andaman were screened for CHIKV infection. In addition, samples sent from Middle Andaman and Nicobar districts were also screened. A total of 100 blood samples were obtained during April 2021- March 2022. Serum samples were processed for detection of anti–chikungunya virus IgM antibodies using Chikungunya IgM capture ELISA kits obtained from NIV, Pune. Out of the 100 samples, 2 (2.00%) were positive.

Respiratory Tract Infections

Throat/nasal swab specimens of the subjects suffering with respiratory infections with ILI were referred to this centre for diagnosis of respiratory tract infection from GB Pant hospital, (referral hospital), Port Blair, district hospital Garacharma and primary health centres *viz.,*Manglutan, Tushnabad, Couldhari, Ferrargunj, Wimberlygunj and Chirayu child care centre in South Andaman. In all, a total of 134 throat/nasal swabs were received, during the study period. All the samples were tested by real time RT-PCR assay using a panel of 12 viruses which includes Inf-A (H1N1pdm09, H3N2), Inf-B, RSV A&B, HMPV, PIV-1, 2, 3 &4, Rhinovirus and Adenovirus.

During 1 April 2021 to 31 March 2022, a total of 134 throat/nasal swabs samples were received from suspected cases of influenza like illness. Out of the 134 samples tested, 23 (17.16%) were found positive for influenza infection.

DIARRHOEAL DISEASES

Rotavirus diarrhoea

Diarrhoea cases which reported at GB Pant hospital, (referral hospital), Port Blair, district hospital Garacharma and primary health centres *viz.,*Manglutan, Tushnabad, Couldhari, Ferrargunj, Wimberlygunj in South Andaman were screened for *Rotavirus* infection. During 1st April 2021 to 31st March 2021, a total of 100 *Rotaviral* suspected cases which were admitted to the wards of the selected hospitals/CHCs/PHCs, were enrolled in the study. Stool samples were obtained from patients and tested by using antigen detection method. Viral pathogens were detected in stool specimens of 13 of 27 (48.14%) patients.

INVESTIGATION OF PANDEMICS AND EPIDEMICS

Outbreak of influenza among children

An upsurge influenza like illness associated with diarrhoea reported at Port Blair, South Andaman During December 2021. Patients reported at Chirayu Children Hospital, Port Blair were investigated. Throat and Nasal swabs were collected from nine children and tested by real time RT-PCR assay using a panel of 12 viruses which includes Inf-A (H1N1pdm09, H3N2), Inf-B, RSV A&B, HMPV, PIV-1, 2, 3 & 4, Rhinovirus and Adenovirus. The samples were also tested for SARS CoV 2 using RT -PCR. Out of nine samples, one sample collected from female child aged 18 months was found positive for influenza B subtype Victoria. All 11 samples tested negative for SARS CoV 2/ COVID 19.

Investigation of SARSCoV 2/ COVID 19

The centre was designated as nodal COVID-19 laboratory in March 2020, Andaman and Nicobar Islands. Since then, the centre is providing diagnostic services and advocacy to DHS, Andaman Nicobar Administration for undertaking the interventions. BSL3 / 2 complex laboratories were further strengthened and made operational. The centre has been providing diagnosis in time for initiation of specific treatment. Besides, the centre played a crucial role in screening of tourists from whole India and abroad.

MOLECULAR CHARACTERIZATION OF VIRUSES - SARS-COV-2

During the second upsurge of COVID 19, a total of 136 SARS-CoV-2 / COVID 19 positive samples were sent to NIV for sequencing on regular intervals to identify the prevailing genomic variants circulating in the Islands for effective implementation of control strategies. Out of 136 sample sequenced, significant mutations were detected in 98 samples. The details are Alpha B.1.1.7 (2), Delta B1.617.2(42), Delta sub lineages (14), Omicron B.1.1.529.(1), Omicron BA.2(26), Omicron other lineages (13).

During the first- upsurge of COVID-19 pandemic, 59 of the positive samples were sequenced to characterize the SARS-CoV-2 genome and to identify the prevailing genomic variants in the Islands. No variants were observed. In the context of morbidity, all of the strains in GR clade and GH clade are similar to those belonging to high morbid regions like Peru, Ecuador, USA. Overall, 27% (16 out of 59) of the genomes were related to those identified in the high morbid regions.

ONE HEALTH APPROACH

NCDC - National one Health Program - prevention and control of zoonoses

HANDS ON WORKSHOP

Hands on Training Workshop on Leptospirosis diagnosis and tracking of Animal Vectors with the Theme "Leptospirosis Control-(26th - 29th April, 2022) Opportunities opened by new insights-one Health vision Approach"

Ministry of Health and Family Welfare, Govt. of India launched a scheme "Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases with an objective to strengthen Intersectoral coordination between the different sectors. Development of Regional Coordinator (RC) is the key strategy of the program for strengthening Intersectoral Coordination at the regional and state levels between different sectors for prevention and control of Zoonotic Diseases. RMRC Port Blair is identified as one of regional coordinator for strengthening Intersectoral Coordination between different sectors at four states / UTs i.e. Andhra Pradesh, Tamil Nadu, Puducherry and Andaman & Nicobar Islands.

Regional Medical Research Centre (RMRC) Port Blair organized workshop on Leptospirosis diagnosis and tracking of animal vectors with the theme 'Leptospirosis control – Opportunities opened by the new insights – One Health Vision Approach' during 26th – 29th April, 2022. The states represented include Andaman & Nicobar Islands, Andhra Pradesh, Assam, Dadra Nagar and Haveli, Himachal Pradesh, Maharashtra, New Delhi, Rajasthan, West Bengal.

Fig. 8: Panel discussion during the workshop.

A Symposium on Zoonosis with Special Reference to Leptospirosis, Crimean Congo Haemorrhagic Fever & Scrub typhus (World Zoonosis Day 2022-06/07/2022)

Dr. P Vijaychari, Director, RMRC, welcomed participants with opening remarks that emerging and re-emerging zoonotic diseases is a huge challenge. The reasons are probably due to global warming, climatic change and extreme weather that facilitates high risk at human-animal-environmental interface. He explained the targets of inter sectoral collaboration in tackling the vectors of zoonotic diseases through National One Health Program.

Study on the prevalence of oral premalignant and malignant lesions and the associated viral etiological agents among the tribal population of Car Nicobar Island

A total of 1239 individuals, who gave informed consent, were screened for oral premalignant and malignant lesions. Among the individuals screened, the mean age of participants was 44 years and among them, 529 (43%) were males and 710 (57%) were females. The Nicobarese largely belonged to lower socio-economic class (60%) followed by lower middle (18%) and upper middle class (16%). The study showed that the usage of tobacco and alcohol were high among all of them. It was found that 10% (121) of the Nicobarese smoked cigarette and *beedi* and 86% (1062) of them used smokeless form of tobacco. The most common form of smokeless tobacco used were the combination of *Zarda* with betel nut and slaked lime (46%)/ *Zarda* with betel leaves, betel nut and slaked lime (26%) which were chewed by 67% of them every day. The use of *sukka*, a preparation with tobacco and lime which is placed in the buccal/labial vestibule is also predominant among Nicobarese, either used alone or in adjunct with other smokeless tobacco.

PUBLIC HEALTH

1. Demonstrated the advantage of novel strategy of supplementing MDA with mass distribution of double fortified salt (DEC+iodine). The efforts made resulted in elimination of persistent foci of diurnally sub-periodic Wuchereriabancrofti among Nicobarese tribe in the entire group of Nancowry group of islands, a lone focus in India. (Mf less than 1% and antigenemia among children nil in all villages of four islands)
2. The efforts made during 2020 - 2022 resulted in the decline of occurrence of new cases per year and reduced mortality due to pulmonary Tuberculosis during 2021 - 2022 when compared to that during 2019 - 2020.
3. SARS CoV2 laboratory with BSL 3 facility is operational 24X7 and extended diagnostic support to whole islands since March 2020 to April 2022 and continued and providing diagnostic support to DHS and Indian Naval Hospital.
4. Established leptospirosis diagnostic laboratories and conducted quality assurance for both serological and molecular diagnosis in Leptospirosis for 30 DHR- virus diagnostic laboratories across the 14 states in view of emerging of leptospirosis in the country.
5. National Hands-on training workshop on diagnosis of Leptospirosis and tracking of animal vectors organized during April 2022. The states represented include Andaman & Nicobar Islands, Andhra Pradesh, Assam, Dadra Nagar and Haveli, Himachal Pradesh, Maharashtra, New Delhi, Rajasthan, West Bengal.
6. ICMR - RMRC Port Blair is identified as a regional coordinator for strengthening Intersectoral Coordination between different sectors at four states / UTs, Andhra Pradesh, Tamil Nadu, Puducherry and Andaman & Nicobar Islands. Ministry of Health and Family Welfare, Govt. of India launched a scheme “Strengthening of Intersectoral Coordination for Prevention and Control of Zoonotic Diseases” with an objective to strengthen Intersectoral coordination between the different sectors.
7. Lieutenant Governors commendation certificate was awarded to two RMRC scientists in view of exceptional contributions in 2022 and one scientist was elected as fellow of Indian National Science Academy in 2022.

SUPPORTING FACILITIES

During the period under report, Health systems research (HSR) and social and behavioural research (SBR) were intensified by starting new projects and with the completion of previous projects. Various new agreements and letters of intent were signed with different national and international organizations. Publication and information Division showcased the achievements of ICMR organization in various significant exhibitions throughout the country. The ISRM Division strived to move the organization towards new goals of technology and digitization.

EXTRAMURAL RESEARCH

SOCIO-BEHAVIOURAL & HEALTH SYSTEMS RESEARCH (SBHSR), DIVISION

Studies on healthcare access to the tribal population

Sickle cell disease in Tribal population

The ongoing national task force projects addressed three important health issues of the tribal population. The first national task force project is to develop an effective care model for sickle cell disease (SCD) patients, which will be available at the primary health centre (PHC) level. This model aims to access the government health care system by the tribal population and for the capacity building in terms of knowledge and skill of the health care workers and infrastructure at different levels of the health system for screening and management of SCD. This study was implemented in the six tribal districts spread in six states. The screening system has been developed under this project, which will be carried out in three levels. At the first level in the community, the accredited social health activists (ASHAs) and health workers have identified the patients based on the symptoms. A list of SCD related symptoms has been provided during the orientation of ASHA and health workers. These probable SCD patients are screened at the sub-health centre by the health worker. For this, sickle cell solubility test kit (Kruise Pathline Private Limited) is used. This is the first tier of screening for SCD. Those who are positive in the solubility test are screened at PHC through haemoglobin electrophoresis. Through this technique, the solubility positive people are diagnosed as SCD patients (Hb SS), carriers (Hb AS) and normal (Hb AA). Before initiating it, a rapid survey was conducted, and the total prevalence of SCD and carriers, respectively, was 1.52 (95% CI: 0.92-2.36) and 7.74 (95% CI: 6.32-9.36). The Hb S gene had a frequency of 0.0539. A registry has been developed to record the details of patients and treatment.

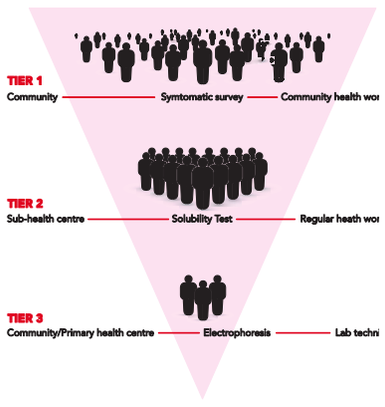


Fig. 1: Three tier screening system

The screening programme was initiated in March 2021. Half of the study population (110,752) was covered in the first six months. Of this population, 8418 (7.6%) were identified by ASHAs based on symptoms. Additionally, in some places, regular health workers identified individuals who had symptoms of SCD, during immunisation and other routine activities. Also, some people self-reported to SHCs after seeing pamphlets/posters, etc. As a result, 9416 people were tested by regular health workers at SHCs, and out of them 2607 (27.7%) were positive for the solubility test. Of the people who were positive, 1978 (78.9%) underwent haemoglobin electrophoresis. A total of 1269 (64.2%) were found to be positive from this confirmatory test. Of these, 233 (18.4%) had SCD and were added to the registry, and the remaining people (81.6%) were of SCD trait.

All the doctors of these PHCs were given orientation in treatment by a clinical haematologist and treatment guidelines were provided. The PHCs were provided with the required medicines including hydroxyurea from states after advocacy. It is found during the formative phase that the communities' awareness of SCD is very poor.

A clinical haematologist provided orientation in therapy to all of the PHC doctors. Guidelines for treatment are also given. The necessary medications are given to the PHCs. Hydroxyurea is supplied to PHCs from states. During the formative phase, it is discovered that the communities have very little knowledge of SCD. Only 32.1% (CI 31.2 to 33.1%) of participants had heard of SCD, 7.9% (CI: 7.3 to 8.4%) knew that SCD is hereditary, 19.4% (CI: 18.7 to 20.3%) knew that a blood test could diagnose SCD and 23.9% (CI: 23.1 to 24.8%) knew that SCD is treatable. Only 13.1% (CI: 12.4 to 13.8%) knew that SCD could be prevented. Only 16% were aware of any SCD symptoms. Hence, there were numerous information, education, and communication (IEC) and awareness programmes conducted in the community. Similar orientation programmes have been developed for health system staff.

Fig. 2: Community Awareness.

Fig. 3: Community Awareness through IEC

These interventions are all carried out through broad community engagement and inclusive collaboration. One of the most crucial phases in putting the intervention into action is creating partnerships with a variety of health and non-health partners as well as the community. Building and improving capacity is a crucial step in enabling basic healthcare facilities to screen and manage SCD patients. Post-intervention Assessment is going on.

Fig. 4: Community Awareness through traditional methods of the Disease

Universal health coverage among Tribal population

The second national task force project is to develop implementation strategies towards achieving universal health coverage by identifying and addressing the implementation barriers to improving access to health care services of assured quality without suffering financial hardship to the tribal community through the existing health care systems.This implementation research is going on in nine tribal districts.The formative phase of the research has been completed with the collection of both quantitative and qualitative data. The formative reis going on. Several access related issues from both the health system and the community are being studied. The focus is on the newly initiated Ayushman Bharat, and hence the issues related to access to newly established Health and Wellness Centres (HWCs) will be examined. These details will be used to develop an implementation research framework and plan to improve access and optimise the utilization of services of HWCs.

The formative phase of the research is completed with the collection of both quantitative and qualitative data. Data analysis of the formative phase was done and the major findings were presented here. The findings of the present study show that more than half of the households (57.80%) of the tribal population reported at least one episodic illness in the past 12 months. Higher proportions of the tribal community (98.64%) sought some treatment for the recent episodic illness, while 90.23% of them sought treatment with expenditure. Tribal community sought treatment more from private hospital (37%) than government hospitals (34%). Some of the tribal people (32%) sought treatment from other sources like medical shop, traditional healers, unqualified practitioner etc. Most of the tribal people (26%) suffered from skeleton-muscular problems. Higher proportions of the tribal people (40%) used saving and current income as the mode of money arrangement for seeking treatment from the healthcare facility. Intervention phase started with the broad approach initiatives including advocacy, community mobilization, and inclusive partnership to minimize the barriers and gaps identified in the formative phase and to increase the utilization of the services of public health facilities (SHC/PHC/CHC).

Through intervention development and implementation research, up-gradation of existing SHC and PHC to HWCs were done along with the optimization of utilization of HWCs services. Capacity building of the health workers/staff was ensured through various training and health education program. Tribal communities were motivated to seek treatment from government health facilities through health camp, Health mela and community and health workers meetings. Maternal and child health (MCH), non-communicable diseases (NCDs) like hypertension and diabetes, vector borne disease like malaria, Tuberculosis, Telemedicine, Mental health, and Referral services were other major site specific health issues focused as the targets of achieving universal health coverage among the tribes of India.

Findings of the second year show increased awareness about the existing HWCs, increased utilization of HWC/SHC/PHC services for health needs, improved supply of medicines and equipment (health system services improvement as indicators) through advocacy, manpower supply, logistic support, equipment, medicines and consumables availability. Evaluation phase is initiated and the data collection of both quantitative and qualitative is going on in the intervention area. The findings of the first and third year (pre intervention versus post intervention) will be compared and evaluated for the changes observed in achieving the utilization of health care access at public health facilities and the quality of care achieved after the intervention and implementation research of the NTF- UHC Project.

Fig. 5: Food mela to ensure healthy diet practice

Fig. 6: Activities showing Screening of Hypertention and Diabeties

Non-communicable Diseases among Tribal population

The third study is to develop implementation strategies for strengthening selected non-communicable diseases (NCDs) (hypertension and diabetes and chronic obstructive pulmonary disease (COPD)) related continuum of care under the National Programme for Prevention & Control of Cancer, Diabetes, Cardiovascular Diseases &Stroke (NPCDCS) among scheduled tribe population. Also, implementation strategies for optimising the NCDs-related services of HWCs are being developed and implemented. This implementation research is going on in six tribal districts.This implementation research with quasi-experimental design is being carried out in three phases –(i) formative research (pre-implementation phase), (ii) implementation research, and (iii) evaluation and dissemination for scaling-up of strategies.This study focuses on the activities of newly established HWCs and their activities related to the management of NCDs. The formative research is going on, and the findings of the formative research are helpful in developing the implementation research to avail the services of HWCs in promoting diagnosis and continuum of care of selected NCDs.

Prevalence of hypertension is 30.52% of which 34.72% in men and 27.81% in women is found from the survey done in the Phase-I. State-wise data is as follows- Himachal Pradesh 4.34%; Jammu & Kashmir 5.28%; Karnataka 3.44%; Meghalaya 4.55%; Odisha 3.37% and Tamil Nadu= 9.05%. Prevalence of diabetes is found to be 4.77% (4.33-5.25) by measuring random blood sugar levels and 6.80% (5.95-7.74) hyperglycemia by measuring fasting blood sugar levels. Focusing the components of the implementation research in the second year, optimization of health and wellness centers (HWC) services at all levels of health care delivery system along with diagnosis and treatment, outreach services, monitoring and evaluation is in progress.

Health promotion, awareness generation and improving treatment seeking behaviour is going on through street plays, dramas etc. Availability of equipment, medicines and health personnel is ensured. Technical assistance and hands on training was provided to ASHA workers in handling NCD

app and Ayushman Bharat app in collaboration with district NCD cell. A uniform NCD registry was created using a participatory workshop method. Print and electronic IEC/BCC materials were prepared and were used in health centers and in community during street play. Educational tools such as pamphlets on healthy lifestyles and early detection were used both in health facility and community levels. Referral of complicated cases to tertiary level health facilities is also initiated wherever necessary.

Fig .7: Screening activities at sub centers

Fig. 8: Screening and follow up activities

Fig. 9: Health camp on NCD awareness

Ad-hoc Studies on healthcare access to the tribal population

In addition to these three national task force projects, the Division has supported fourteen ad-hoc projects that addressed various tribal health and healthcare challenges. By organising ethnomedical practitioners in the Savara tribal group to engage with public health officials, an action research project in Andhra Pradesh is building models for effective preventive and curative care. It advocated a collaborative approach to healthcare for the tribal people, which is culture-sensitive and emotionally relatable to them because of the presence of their local healers in the care matrix. Mapping traditional medical practitioners (TMPs) in the study, PHCs reported that the patient load per month per TMP is 9.70. About 85% of the TMPs reported an experience of more than 20 years, and a little above 17% reported more than 35 years of experience. The most commonly treated illnesses by the TMPs are jaundice, 'gastric' and stomach disorders, muscle and bone problems, and illnesses due to witchcraft/ ancestral spirits/supernatural beings.

Another study looked at the health-seeking behaviours of tribal elders in Kerala and challenges related to healthcare service access and utilisation. It highlighted barriers to tribal elders' access to and utilisation of healthcare services, allowing policymakers to strategy for optimal healthcare system responsiveness. After adjusting for socio-demographic indicators and general household standard of living scores, the study determined the factors determining tribal older people's reliance on family members for healthcare service access throughout the project's first year. The functional ability of older persons as measured by instrumental activities of daily living (IADL)scale and activities of daily living (ADL) scale significantly and positively influenced their self-rated health. At the same time, perceived difficulties in accessing healthcare alongside multi-morbidity significantly reduced self-rated health. Another ethnographic study intended to examine the malaria prevention practices and treatment-seeking behaviour related

to the tribal population of Chhattisgarh. Preventive, promotive and therapeutic care aspects will be designed in a participatory way with the local community and health care providers as part of the integrated intervention package.

The prevalence of urinary tract infections (UTI) among tribal women of Tamil Nadu was investigated. Preventive interventions, such as raising knowledge about UTI and using a foldscope to screen for bacterial infection, were introduced among tribal women. Foldscope was used to identify a few gram-negative microbes, pus cells, and RBCs within the first year. Foldscope would be utilised in the next step of the project to identify the organisms in the infected urine samples.

A study is being carried out to understand health-seeking behaviour and to examine facilitators and barriers both from peoples' and providers' perspectives, which influence the delivery and utilization of maternal and child health services. Another study evaluated the effectiveness of health promotion intervention through community mobilization with women groups facilitated by ASHAs to improve maternal and child health status in the tribal population of Chittoor district.A model programme, Model for Oral Cancer Eradication, is conducted among the Narikurava tribal population in Puducherry to prevent, screen, and treat oral pre-cancer and cancer. During this investigation, precancerous and cancerous lesions were quantified, and screening and prevention strategies were developed. The majority of them consumed smokeless tobacco in varied forms. About 28% of the population had melanosis of the lips. None of the population exhibited facial asymmetry. 16.7% had palpable lymph nodes. But none were fixed. The palpable lymph nodes were attributed to other causes like periodontal and periapical abscesses, deep caries lesions, a grossly decayed tooth, pericoronitis, etc. Results indicated that about 41% of the participants knew about oral pre-cancer and cancer. And 20% of the population knew that chewing tobacco causes oral cancer, and 22.8% thought that the growth of tissue in the mouth could be a sign of oral cancer. A study from Odisha is implementing as an accessible model for oral potentially malignant disorder screening in the tribal settings. A study is being conducted to strengthening the PHCs infrastructure for screening selective cancers has been initiated in a tribal district of Odisha. Monthly cancer screening clinics are being established in selected PHCs. It helps increase the stakeholders' knowledge, like female health workers and ASHAs, about the danger signs of different cancers. A study among North-East tribes of Assam and Mizoram documented various cardio-metabolic related risk factors, including hypertension, elevated fasting blood glucose, obesity, and metabolic syndrome with the help of artificial intelligence (AI) techniques, mainly machine learning tools such as classification, clustering and prediction models, etc. It will further conduct health awareness campaigns on diabetes and cardio-metabolic disease among the tribal population of the North-East region.

In Uttarakhand, the ICAR's National Dairy Research Institute (Karnal) is implementing a dairy-based intervention among tribal communities. With a dairy-based intervention, this study aimed to alter the health-seeking behaviour of the people by enhancing their health and livelihood. Another study from Maharashtra focused on improving access to cancer screening with the existing government health system and identified the challenges for the same. This study is implementedto screen common cancers and NCDs among women in a tribal block involving the state health system and the community. In the first year of the project, the qualitative research component of the study was completed. It was seen that there was limited knowledge regarding NCDs and common cancers among women. The women had heard about cancer and knew few causative factors and symptoms of oral and breast cancers because of advertisements on television and health education provided by health care workers. The women had limited knowledge about lifestyle factors like diet, salt, stress as causative factors for common NCDs like hypertension and diabetes. Traditional healers

like Bhagats were sought for relief of symptoms. Economic burden,including health expenditure, proximity and trust, were the reasons for visiting the *bhagats* (faith healers) when they face discomfort or illness of any kind.

A study is intended to capture the broad transformations witnessed in tribal populations in terms of socio-economic change and issues in accessing health care facilities in the districts of Srinagar, Rajouri and Kargil. This study will also focus on the nature and extent of non-communicable diseases prevalent in the population. This study will specifically engage with barriers to using health care, the social and economic consequences of illness among the tribal population.

Other health systems research and socio-behavioural research studies

Influence of demographic, clinical, genetic, and management patterns in maintaining long term abstinence among patients of alcohol use disorders who received treatment from de-addiction centres in Thrissur district, Kerala, was studied. This study evaluated the management pattern in different de-addiction centres and found the influence of treatment patterns on the outcome. It further studies the status of markers indicative of acute or chronic alcohol consumption (state markers) and markers of genetic disposition for alcohol dependence (trait markers) among the alcohol users.

Perspectives of people, physicians and pharmacists on sociocultural and environmental drivers of antibiotic resistance was studied in Karnataka. This study is developing an innovative provider-based, individual-verified approach to estimate the burden of antimicrobial resistance in rural India. According to the pilot research to enhance the methodology, the first-year findings show that antibiotic awareness, attitude, and practices are sound. Most respondents said it was inappropriate to use antibiotics prescribed by a friend or family member, and it was also inappropriate to repeat a previous prescription.In most cases, healthcare workers were the source of information concerning antibiotic resistance.Structure, staffing and factors affecting infection control nurses were studied in Karnataka. It explored the existing structure and staffing pattern of the infection control department and to identify factors affecting infection control practices. Research from Chandigarh looks at the menstrual hygiene behaviours of adolescent females with intellectual disabilities. Early results suggested the average age of adolescents with intellectual disability at menarche is 13.2 years. Some caregivers informed that their daughters are experiencing irregular periods due to Polycystic Ovarian Disease (PCOD). Personal hygiene was the common, evident check for most of the caregivers of adolescents with intellectual disabilities.IIT-Kharagpur is conducting randomised controlled crossover research on mindfulness training to increase resilience among Indian college students. It developed and compared a mindfulness training intervention for improving attention and emotional regulation.

Obstructive sleep apnea among commercial vehicle drivers and its correlates with road traffic accidents are studied in Delhi. This study determines the prevalence and risk factors for obstructive sleep apnea in commercial vehicle drivers. This study aims to develop strategies to increase awareness of the problem and develop an action plan for managing obstructive sleep apnea.An educational intervention study to bring awareness of head injury while driving among patients with epilepsy is underway in Delhi. This study assessed the awareness in patients with epilepsy and their caregivers about driving prohibitions as per the motor vehicle act, 1938. Patients with epilepsy are to be educated through a multipronged educational intervention, and the intervention is to be evaluated.

The impact of migration on the psychosocial and economic well-being of elderly pandit migrants is being studied from selected north Indian cities. A community-based intervention study is initiated to determine the percentage of adult tobacco users residing in the resettlement colony of Delhi who quit tobacco or attempt to quit tobacco use

after behaviour modification therapy versus those given brief advice. These data on adult tobacco users will be assessed through questionnaires and analyses tests. Behaviour modification will be carried out using the Trans-theoretical Model of Behavior change. This study will help reduce the frequency of tobacco use, reduce the degree of nicotine dependence, and improve motivation to quit smoking as per the contemplation ladder.

A study is initiated to explore the experiences and needs of adolescent children living with a parent with mental illness with the ultimate aim of fostering the inclusion of their needs and concerns into mainstream mental health services. This study would help develop a theoretical understanding of children's experiences of parents with chronic illness and propose an intervention programme based on the needs of the children and test its feasibility. This study will also generate a checklist of the affected adolescent children and access to family functioning, coping and subjective well-being of adolescent children living with a parent with chronic illness. Another study attempts to illustrate the information about vulnerabilities faced by people with disabilities while accessing healthcare. A mixed-method approach will be used for collecting data. This study can be used as a base for formulating strategies to remove barriers and improve integration of persons with disabilities in society and understand healthcare provider's perspectives in the delivery of care for persons with disabilities

A study is being undertaken to examine the association between substance abuse and suicidal behaviour among undergraduate students based on gender differences, behavioural changes, and patterns of substance abuse. It will be conducted in all provincialised colleges of Assam. This study will help the parents and college authorities to understand the youths differently and make them aware of these evil social issues. This study will also assist them to be proactive to initiate appropriate measures to prevent youth suicide and substance use. One study was initiated to help document the screen time in children in Lucknow, and it will help to find out the correlates and health outcomes of children aged 2 to 18 years of age. And this study will also help to analyze screen time along with its correlates in children and would also help in setting guidelines at the national level. Multistage random sampling is used for enrolling students in the study. Counselling to the parents of the children will be provided in this study through a psychologist counsellor about the harms of using screen time and how to change their habit of using screen time.

A study is initiated to estimate the magnitude, burden and determinants of depression among young adults in selected higher educational institutions. This study will help strengthen individuals and communities by providing community-based gatekeeper training programs, inquiring about suicidal ideation, and improving access to services. This study will also help in forming mental health policy and the new mental health care bill. This study will also evaluate the feasibility of Let to Let out Depression Resource Centres among young adults.Another study to assess the self-reported multidimensional and structural relationship of health-related quality of life of TB patients, including multi-drug resistant and extensively drug-resistant TB patient's time points using the BSEM model. This study provides the impairment in HRQoL associated with TB at the initiation, at the end of the intensive phase, at the end of the continuation phase, and after three months of competing for anti-TB treatment. It also focuses on evaluating the impact of TB on quantitative measures of HRQoL of TB patients and demonstrates the association of HRQoL and adherence to TB treatment.

A study to explore the psychological impact of violence, psychosocial and rehabilitation needs, barriers and challenges in accessing services among women affected by gender-based violence (GBV) is going on. The study results will help frame a set of policy-level recommendations in providing comprehensive psychosocial care and protection to women affected by GBV. The

results will also facilitate policymakers, health administration, judiciary and various stakeholders to plan an effective strategy for improving the delivery of services to women affected by violence in the existing delivery system.A study to assess the perceptions of women regarding sexual harassment at the workplace in the health sector. This study will find the prevalence of sexual harassment using the Google forms with strict unanimity and decide how efficient the women are in their work. Thus, the study needs to address these grievances so that institutional efficiency also improves.

A study assesses the cognitive status in the community-dwelling older men and women and assesses the relationship between cognitive status and psychosocial factors among older people. This study tests the efficacy of a psychological intervention to improve the quality of life of older people. Psychological intervention may reduce the overuse of psychoactive medications and improve this vulnerable population's quality of life. A study to assess the lifestyle measures, education, and socio-economic status (SES) and how these traits are correlated with Coronary Heart Disease (CHD) risk factors in adolescent school children of Chitoor District, Andhra Pradesh. This study documents the information about SES, lifestyle, anthropometry, blood pressure, and biochemistry among adolescents. It assesses the CHD risk factors and examines the effect of social, economic, and behavioural factors on anthropometry and biochemistries for confounding factors. This study will also help frame policies for the welfare of adolescents and provide a platform to undertake subsequent genetic studies among adolescents.

To study the socio-cultural and environmental factors involved in Human Animal Interaction (HAI) and to study the stress level of the owners and assess their mental health profile of pet/domestic animal owner's. This shall help us to understand the behavioral change and inspiring social interactions of the pet/domestic animal owners. Whether HAI has enhanced self-esteem and psychological well-being and a pet animal can enable humans to retain health because of caring and exercising with their pets. This will further give scope to understand the complex psycho immunological interactions.

The effects of intermittent fasting (two meals a day) on weight loss in obese and overweight individuals who are free from other co-morbid conditions are being studied in Gujarat. Study comparing observed changes in the measures of obesity, lipids, inflammation and energy balance across the two arms will establish the impact of intermittent fasting on metabolic mechanism and the components of energy balance in overweight/ obese populations.

One study is designed to quantitatively evaluate associations between CKD and key indicators of socioeconomic status, including income, educational attainment, occupation and a comprehensive index. The cultural impacts like who are the communities that are affected by this CKD and the cultural reasons for their vulnerability starting from the microenvironment of the family, to the village, to the mandal, to the region and to the district level. We will know whether or not social factors like income, education, occupation, health awareness have something to do to control CKD. Finally, what are the direct and indirect economic costs for the family, for the village, region and to the district this CKD is causing.

Study aims to give training for the adolescent girls on identifying, preventing and managing various abuses that they are facing. findings of this primary research will generate insights into implementation of the assertiveness training program towards prevention of abuses among adolescent girls in curriculum at the national level, which can be adopted by the policymakers Multimedia awareness programmes (using pamphlets, articles in the newspaper, videos through billboards,television networks, and social media) to the general public and first responders will decrease the morbidity in potential spinal cord injury victims who have been victims of accidents.

A Study for Crafting Integration Strategies for Health and Community Partnership aims to formulate and test the SDOH model in the rural areas of Jammu, Kashmir, and Ladakh that will provide a complete picture of the interplay between social factors and health outcomes. The study will educate policymakers and healthcare practitioners on the significant impacts of social determinants of health amongst rural communities. In addition, it will make helpful suggestions for improving healthcare and other social needs amongst deprived rural communities. This study aims to look into the scientific, economic, and policy factors that are making it easier for the two fields to work together.

One study at Bengaluru, aims at the role of grievance redressal mechanisms in providing a voice to the community in government funded health insurance schemes in India. In this project we would like to unpack if and through what mechanisms, grievance redressal mechanisms works (or do not work) and to what extent they are useful in providing a voice to the patients. There is very little evidence on whether the beneficiaries of the schemes are able to areable to receive their entitlements in terms of cashless, quality care and if not, how do they cope with it. More importantly we will achieve data on effectiveness on strengthening the schemes after receiving the grievances.

Another research attempting to access whether environment or lifestyle (smoking, excess alcohol, urban living, psychological stress, reduced physical activity, unhealthy diet, excess salt intake, overweight and obesity etc) factors are associated with high blood pressure in urban poor living. We will achieve reduced raised blood pressure through change in lifestyle and with use of technology, awareness of high blood pressure education program on the primary prevention of hypertension and increase in utilization of the Public Health Facility by urban poor in a year. Based on experience of this pilot project, a grant application for scale up project in multi-site will be developed and applied.

A valid and reliable instrument for assessment of Nomophobia severity is being developed at AIIMS, Patna. The novelty from such an exercise would be the development of a validated questionnaire-based instrument that is utilized by number of mental health-care professionals (psychiatrist, psychologist, psychiatric nurses, psychiatric social workers, trained community health care workers) and which reliably assesses the severity of Nomophobia or Smartphone use related problems. At the end of this process, we aspire to have an instrument for assessment of screening and severity of Nomophobia which will be developed and validated through a rigorous process. This instrument will be helpful for youths with problematic use of smart phone/ gadget addiction and associated significant dysfunction. This instrument will pick up symptoms evoked by the unavailability of a smart phone or the thought of not having it, not being able to use it or losing it. This instrument will freely be available on the ICMR website for application to all clinicians and researchers.

Another study aims to generate contextual evidence on the impact of internal migration on the health status of migrants within the existing health systems and to develop policy recommendations to address the issues. The study will specifically analyze the impact of living conditions and socio-demographic characteristics of internal migrants on their health and accessibility to health care services available in the Municipal Corporation of Cochin. It will explore available public health facilities and response of the health system towards migrant labourers in the context of re-emergence of communicable diseases and the existing health-related risk behaviours. The study would help to have an in-depth understanding on the social-epidemiology regarding the health issues of marginalised labours and that would enable to have adequate research and program interventions to defend the problems of the marginalised labours especially in the context of re-emerging infectious diseases.

This project is planned to improve Lab reporting (pre- analytic, analytic phase and post-analytic)

process as it is found to be critical parameter affecting Turnaround time. The reduction in TAT leads to decrease in patient LOS, increased patient satisfaction, quality of care, employee satisfaction and better utilization of resources.

The study aims to test the effectiveness of a community lifestyle modification program on improving healthy lifestyle behaviour including nutrition, physical activity, stress and substance use among adults in selected sites of Puducherry at the end of 6 months and one year, compared to current behavioural counselling (standard of care). Additionally change in anthropomety, blood pressure and select biochemical parameters at the end of 12 months of intervention will be documented. This study also aims at providing cost effectiveness estimates per case of non communicable disease prevented due to the intervention.

An implementation research aiming to identify and strengthen social support networks around patient of terminal illness and their care givers in Western Rajasthan. The long term goal is to build evidence to establish that being part of a caring network for someone at the end of their life has potential to generate social capital, a resource that can be used by the network or community members to address community needs on sustainable basis. One study is to determine the extent and predictors of health care provider switch for overall health-seeking in both acute and chronic illnesses in two districts of Madhya Pradesh. This project would develop, implement and evaluate the effect of behavior change communication strategy to decrease the extent of provider switching for common acute illnesses (eg acute respiratory illness) and chronic diseases (e.g hypertension, diabetes etc) in the study area over a year. Another study is designed to develop a sustainable model for oral cancer self-screening and reporting among long distance heavy vehicle drivers. It is designed for constant, regular monitoring of oral precancerous lesions through self-examination and reporting thereby reducing morbidity and mortality. This will eventually lead to empowerment of the truck drivers for connectivity to professional consultation via Mobile Oral Health assistance and finally an attempt to develop a permanent helpline for oral care.

COMPLETED STUDIES

Studies on healthcare access to the tribal population

A study to educate the tribes through health and nutrition education, group meetings, seminars with the help of tribal, health and women and child departments and NGOs,is initiated in tribal area of Telangana state. The study helps build a national collaborative effort for a multifaceted action plan to combat the growing burden of chronic kidney diseases (CKD) and their complications and focus on the causative factors of CKD burden in the tribal population. Generated data helps the state government of Telangana to develop a strategy for improved nutrition in tribes to reduce the CKD and NCDs burden. An additional Delhi-based study examines the health status of migrating tribal populations in Delhi and the barriers to health care access. As part of a study conducted in Maharashtra, researchers applied the intersectionality theory to identify differences and similarities in indigenous communities. Inequalities in tribal health are examined from a political, social, economic, and cultural standpoint. Health services acceptance and uptake are also highlighted, and the hurdles and facilitators to their acceptance and uptake are identified.

Several tribal communities in Tamil Nadu have reported on the prevalence of primary dysmenorrhea and the impact of a combined fitness training programme on the concomitant menstrual symptoms among girls in school. One hundred and seventy of the 240 individuals had primary dysmenorrhea with pain, with 31% experiencing mild discomfort, 28% moderate pain, 8% severe pain, and 4% excruciating pain. Giving combination exercise training programmes to tribal schoolgirls who have been diagnosed with primary dysmenorrhea has been demonstrated to improve outcomes.

Health systems research on road traffic injuries (RTIs)

Research is carried out to design a novel On-Board Unit (OBU) for the driving environment. Using Dynamic Transportation System (DTS) as a part of vehicles can enhance driving by gathering and analyzing relevant data about the driving environment, giving the driver awareness while driving their car. This research work provides factors that would help in reducing the number of accidents by improving the communication in the VANET framework to enhance the safety of the travellers/people. The framework can identify several types of driving behaviour, such as intoxicated driving, distracted driving, and fatigued driving, among others. OBU architecture was designed with situation awareness in mind. It is divided into three steps, which stand in for the detecting, reasoning, and acting subsystems of DTS. The framework's elements work together to identify unusual driving behaviour, warn the driver, and so prevent accidents. Based on the data provided by vibration sensors, it will notify the closest medical facility when an accident is detected.

A study is conducting on two important National Highways (NH-91 and NH-93) of Aligarh district. It documented the RTIs surveillance in the urban and rural setup of Aligarh. The lacunae in data reporting and usage patterns of post-crash emergency care are addressed and resolved. For better usage of the "golden hour" after the crash, the study is captured the possible barriers and facilitators in providing early rescue. The intervention aims to improve the services at the crash site and a health facility and decrease the time in transportation of the patient from the crash site to the hospital. The study was able to identify the available facilities for post-crash emergency care in Aligarh together with extent of actual utilization of these available facilities. The study documented the status of record keeping related to RTIs at the various health facilities. Also identified the common facilitators and barriers in delivering emergency care who can be specifically targeted to build an improved post-crash program for trauma patients. The study successfully conducted the interventions at the high-risk zones.

Another study conducted a comprehensive study concerning the health systems responsiveness and the timely availability of medical care during the 'Golden Hour' of the road traffic injury. To fulfil this objective, the study included different levels of the hospitals and indoor patients who are victims of RTI. The social impact of RTI on the victim and their families, including their participation and utilization of health and social services, are also studied.

One study intends to examine to what extent road traffic injuries are rendered primary, secondary and tertiary care by the urban health services system. Mapping of the existing mechanisms and services within the health system is carried out. Further, close examination and analysis of these facilities' administrative and medical processes are being done to help delineate the inadequacies in the existing system. Opportunities for strengthening each level of care are also being explored to improve the response to RTIs, which in turn can contribute to the strengthening of the urban health services system. Another study develops a unique online monitoring system with multiple components, aiming to optimise care of victims involved in road traffic accidents using integrated technology and medical delivery systems within the existing government and private health care delivery framework. This project's several components, integrating modern technology with the medial delivery systems, are: good anonymous citizen application, central command centre, central trauma registry and artificial intelligence

Other health systems research and socio-behavioural research studies

Cultural epidemiological research has been undertaken in the Maharashtra districts of Satara and Palghar to provide evidence for enhancing the implementation of the National Collaborative Framework for Tuberculosis-Diabetes Comorbidity.

It assessed the progress made by the Revised National Tuberculosis Control Programme (RNTCP) and the National Programme for the Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases, and Stroke (NPCDCS) in terms of joint TB-Diabetes collaborative activities as envisioned by the National Framework.The study would provide important insights into the ground-zero status of TB, diabetes comorbidity care, control and management issues from patients' and providers' points of view.

In the Alappuzha area, a qualitative study is conducted to determine the factors that influence acceptance and hesitation toward Japanese encephalitis vaccinations. This research covers the community's response, opinions, and perspectives, including their faith in vaccines, as well as the causes for vaccination acceptance and/or hesitation.The study also looks into how peer-to-peer communication affects vaccine reluctance.A prospective cohort study to understand the humanistic and economic burden of rheumatoid arthritis (RA) is studied in Puducherry. It assesses the costs from the societal perspective using a bottom-up approach. The study shows the true burden of the diseases and the constant unease felt by the patients.Among the study population, 74.5% were housewives (home-makers). Most of the patients (64.5%) were not covered by any health insurance. Of those insured, 94.7% were covered by public/ government insurance schemes. Fourteen patients reported the loss of pay out of 65 who had paid work. Also, 47 patient attendees reported the loss of pay for accompanying RA patients to the hospital. The total cost estimated for RA was INR 27,723.12 per person per month. Of the total cost, 5.19% was heath system cost, and 4.9% was an out-of-pocket expenditure. The indirect cost incurred by the patient due to loss of pay and replacement cost was INR 2,022 per patient per month, and it accounted for 18.16% of the total cost for RA. The intangible cost was high and contributed 71.75% of the total cost.

In Aizawl, Mizoram, research on living habits, daytime drowsiness, and chronotypes on sleep disruption and daily and seasonal sleep patternsis conducted among school children. This study looks at the elements that influence sleep length and quality.It also explains how living habits such as watching an electronic display at night, irregular dinner time, frequent caffeine consumption at night, sunlight exposure in the bedroom in the morning, and the room's brightness at night impact sleep and sleep-related variables.First-year results suggested that the morning typehas the best sleep quality while the evening type has the worst. When we compared males andfemales, the effect of gender was not observed. In the different actigraphy parameters duringweekdays and weekends, no significant difference was observed in all parameters.

Cognitive and psychosocial intervention for persons with dementia in Rural India is underway in Chennai. This study identified resources for dementia care, including social support systems in the rural community. The feasibility of delivering a comprehensive intervention model including cognitive stimulation therapy is being studied. Health-risk behaviours among adolescents, particularly the role of difficulties in emotion regulation, parenting style and personality characteristics, are studied fromIIT-Ropar. A case-control study design is being used in which initially assessment of adolescents for their indulgence into health risk behaviours would be done. Then the characteristic attributes of those high and low on specific behaviours would also be identified. Another study from Delhi assessed and identified factors affecting the availability, accessibility, acceptability and quality (AAAQ) of burns care in secondary and tertiary health care facilities. The co-designing approach to developing a care pathway with improved availability, accessibility, acceptability, and quality of burns care and rehabilitation is innovative. It would foster learnings for using a similar approach in other conditions requiring prolonged rehabilitation.

Another study assessed the economic burden of childhood injuries in different sociocultural settings in Tamil Nadu and developed a cost-effective intervention model to prevent childhood injuries.

INNOVATION & TRANSLATION RESEARCH (ITR) & INTELLECTUAL PROPERTY RIGHTS (IPR), DIVISION

Intellectual Property Rights

The IP protection of innovations generated either through intramural or ICMR supported extramural innovation research project had been considered. After carrying out proper due diligence such as identification of IP component, establishment of novelty, non-obviousness and industrial applicability, the protection of IP need to be made through patents, copyright, designs and trademark. Converting the innovative and technical information into techno-legal information involves activities viz. due diligence of new invention reports, patentability examination, patent filing and prosecution (India & abroad), patent grant & monitoring, weeding out unproductive patents. A total of 26 Indian patent applications, 1 design application, 5 copyright applications, 10 PCT applications and 6 foreign patent applications were filed. 5 Indian patent and 3 foreign patents were granted.

Table 1: Indian Patent Application, Design and Copyright applications

S N	Title of invention	Patent Application no	Filing Date	Intramural/ Extramural
1.	An Assay And Method For Detection of SARS-CoV-2 From Human Respiratory Samples	202111015708	01.04.2021	Intramural
2.	Fluorescent Polystyrene Based Nanohybrid ArrayFor Estimation Of Circulating Cell-Free Mirs	202111031427	13.07.2021	Intramural
3.	Screening assay for detection of epidemiologically important SARS-CoV-2 variants	202111032470	19.07.2021	Intramural
4.	A pharmaceutical composition with a recombinant fragment of human surfactant protein-D for pulmonary infection including SARS-COV-2	202111030956	09.07.2021	Intramural
5.	Novel method for concentration of polio viruses and other entero viruses from sewage".	202111037829	20.08.2021	Intramural
6.	Development of microneedle patch for trans-scleral administration of triamcinolone acetonide to enhance choroid, retinal and vitreal concentration	202111042201	17.09.2021	Extramural
7.	A simple user friendly method for extraction of nucleic acids	202111043228	23.09.2021	Intramural
8.	Fever tracker app for the health workers.	202111049722	29.10. 2021	Extramural
9.	Development of HEK293 knock-out cell line of EV-A71 receptors SCARB2 and PSGL1 genes	202111048030	21.10. 2021	Intramural
10.	Human Monoclonal antibodies against SARS-CoV-2 and a method of generation thereof	202111052088	13.11.2021	Intramural
11.	Simple, novel and cost effective Lateral Flow Immunoassay for diagnosis of Glanzmann thrombasthenia	202211003648	21.01.2022	Intramural
12.	Compositions for metabolic reprogramming of cells by modulating the expression of Tumor Suppressor Candidate 1 (TUSC1)	202211003978	24.01.2022	Extramural
13.	Fiber optic nano antenna based excitation of whisper gallery mode resonator and various sensing applications.	202211004683	28.01.2022	Extramural
14.	A nano -dentritic cell construct for selective targeting of tumor cell.	202211005691	02.02.2022	Intramural
15.	Hydroxyapatite-responsive cell-attachable and stable surface-active biocompatible mats.	202211009698	23.02.2022	Extramural
16.	Suture resistant antimicrobial biodegradable and biocompatible fibrous patch constructs	202211008790	19.02.2022	Extramural

17.	Portable Protein gel Electrophoresis Unit	202211008794	19.02.2022	Intramural
18.	Probiotic Bael based nutraceutical for remission of ulcerative colitis.	202211012630	08.03.2022	Extramural
19.	VCRC-ANM Mosquito Feeder-A microcontroller-based device for artificial diet/blood feeding for mosquito rearing in the laboratory.	202211016261	23.03.2022	Intramural
20.	Development of universal method for simultaneously detection of diseases caused by inter and intra species using Hybrid LAMP kit.	202211019752	31.03.2022	Intramural
21.	Vaginal Lactobacilli for urogenital health.	202211019761	31.03.2022	Intramural
22.	Hydroxyapatite-responsive cell-attachable and stable surface-active biocompatible mats	202211009698	21.03.2022	Extramural
23.	Invention of a cost effective mosquito attractant and lethal non-electric ovitrap.	202211015554	21.03.2022	Intramural
24.	Suture resistant antimicrobial biodegradable and biocompatible fibrous patch constructs	202211008790	21.03.2022	Extramural
25.	A probiotic bael based nutraceutical and a process of preparation thereof.	202211012630	8.03. 2022	Extramural
26.	Biomarker panel to diagnose the malaria severity with statistical predictive model method	202211014867	17.03.2022	Intramural
Copyright Filing				
27.	Mobile Application based System for Adherence to prescribed analgesics and adjuvants in Cancer patients receiving palliative care - Part 2.	21105/2021-CO/SW	04.09.2021	Extramural
28.	Mobile Application based System for Adherence to prescribed analgesics and adjuvants in Cancer patients receiving palliative care- Part-1	21107/2021-CO/SW	04.09.2021	Extramural
29.	Health Diary	22461/2021-CO/L	20.09.2021	Intramural
30.	Sehat ki Diary	22462/2021-CO/L	20.09.2021	Intramural
31	Fever Tracker App for the Health Workers	1826392/2021-CO/SW	29/10/2021	Extramural
Design Filing				
32.	A Mechanical Aspirator for the Safe Transfer of Mosquitoes	348640-001	31.08.2021	Intramural

Table 2: PCT International Patent application and Foreign patent application

S .No	Title of invention	PCT Application no	Filing Date	Intramural/ Extramural
1.	A rapid and sensitive method for detecting SARS-CoV-2	PCT/IN2021/050549	05.06.2021	Intramural
2.	Herbal Composition for the treatment of menopausal syndrome	PCT/IN2021/050592	18.06.2021	Intramural
4.	A paper disc based method for determining the drug susceptibility of Mycobacterium tuberculosis	PCT/IN2021/050414	28.04.2021	Extramural
5.	A diagnostic device and method for differentiating Asthma-COPD Overlap Syndrome (ACO) from Asthma and COPD.	PCT/IN2021/050793	17.08.2021	Extramural
6.	A method for developing a rapid immunochromatographic assay for identifying hepatitis E infection.	PCT/IN2021/050758	08.08.2021	intramural
7.	An assay and method for detection of SARS-CoV-2 from human respiratory samples.	PCT/IN2022/050173	01.03.2022	intramural
8	RT-LAMP assay for detection of human β-actin housekeeping gene.	PCT/IN2022/050183	03.03.2022	intramural
9	A pharmaceutical composition with a recombinant fragment of human surfactant protein-D for pulmonary infection including SARS-CoV-2.	PCT/IN2022/050237	15.03.2022	intramural
10	Rapid LAMP assay for detection of *Corynebacterium diphtheria.*	PCT/IN2022/050276	22.03.2022	intramural
	Fluorescent polystyrene based nano-hybrid array for estimation circulating cell-free MiRs.	PCT/IN2022/050239	15.03.2022	Intramural

	Foreign Patent			
S N	**Title of invention**	**Foreign Application no**	**Filing Date**	**Intramural/ Extramural**
1	Device for Germfree and gnotobiotic mosquitoes.	i) Indonesia App. no. awaiting ii) Singapore App. no. 11202202863Q	31.03.2022 29.03.2022	**Intramural**
2	Apparatus, Method and Kit for Detection of Von Willebrand Factor and Factor VIII	i) USA, US 17/440,677 ii) South Africa 2021/07051	17.09.2021 21.09.2021	**Intramural**
3	Biomarkers for predicting malaria severity and methods thereof.	i) Mozambique App. No. AP/P/2022/013793 ii) Nigeria App. No: F/P/2021/493	26.01.2022 17.12. 2021	**Intramural**

Table 3: Indian and Foreign Patent granted during the period				
S N	**Title of invention**	**Application no**	**Grant Date**	**Intramural/ Extramural**
	Indian Patent			
1	A PCR method for the detection of *Chlamydia Trachomatis*	362608	23.03.2021	Intramural
2.	Rapid detection of drug resistant *Plasmodium falciparum* through a novel approach using loop mediated isothermal amplification.	380417	27.10.2021	Intramural
3.	Method of processing of feeder cells suitable for adult stem cell proliferation.	385296	28.12.2021	Intramural
4.	Water re-circulated garment for auxiliary body cooling for protection against high heat exposure.	384530	24.02.2022	Intramural
5.	A process for the preparation of a fibrinolytic enzyme.	391961	14.03.2022	Intramural
	Foreign Patents			
6	A novel molecular diagnostic technique for detecting the different species of plasmodium.	Congo Democratic Republic 373/2016	27.05.2021	Intramural
7	RNAi agent for inhibition of chikungunya virus.	Australia AU 2014285701	01.04.2021	Intramural
8	Alginate Chitosan Nanoformulation of OmpA - a Shigella Protein Subunit.	US 11,298,415	26.03.2022	Intramural

HUMAN RESOURCE PLANNING AND DEVELOPMENT (HRD), DIVISION

FELLOWSHIPS

ICMR-JRF (Junior Research Fellowship)

The ICMR JRF-2021 exam was conducted successfully through a computer based examination held on 12.09.2021 at 23 Centers across India in collaboration with the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh and Tata Consultancy Services (TCS). A total of 134 candidates were selected and out of which twenty-one (21) as on 31.03.2022 have joined different Institutes/Organizations for pursuing Ph.D. under the program.

ICMR Centenary PDF (Post-Doctoral Fellowship)

A total of 53 PDF proposals were received during the year 2021-22, out of which 29 proposals were shortlisted as per the eligibility criteria for personal discussion, out of which fifteen (15) PDF were selected by the Selection Committee and were approved for funding. Twelve (12) of them have joined for the year 2021-22.

ICMR-MD-MS/Ph.D. Fellowship

Programme is being carried out at three Centres *viz*; King George's Medical University (KGMU), Lucknow, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru and Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai. During 2021-22, out of 15 allotted slots, a total of five (05) candidates were selected (KGMU=None, NIMHANS=01 and SRIHER=04).

ICMR Chairs for Sr. retired medical/ biomedical teachers/scientists

ICMR-Dr. C.G. Pandit National Chair

This is a prestigious Chair of ICMR have a provision of remuneration of Rs 2.00 lakh per month per Chair. The duration of Dr. C.G. Pandit National Chair is for five years (three years extendable by another two years after assessment of the progress and plans). Retired medically qualified persons are eligible for one Chair and retired non-medical/ biomedical/professors/bio-medical teachers are eligible for the other Chair. The persons should preferably be the Fellows of all the National Science Academies. At a given point of time, only two such Chairs will exist. For the year 2021, two (02) Chairs are ongoing.

ICMR-Dr. A. S. Paintal Distinguished Scientist Chair

Distinguished Scientist Chairs are open to retired scientists/ medical teachers who may belong to Medical/Biomedical/Life Sciences with the excellent track record in the field of medical application. All the perks/ remuneration of Distinguish Scientist Chairs of ICMR will be at par with the existing Chairs of ICMR *i.e.* Rs. 1.75 lakh per month per Chair. The duration of Chair will be for five years (three years extendable by another two years after assessment of the progress and plans). Usually, two Chairs will be established at one point of time; their number will not cross five at any given point of time. For the year 2021-22, three (03) Chairs are ongoing.

ICMR-STS (Short Term Studentship)

During the year 2021-22, the call for applications was not opened by the ICMR because due to the COVID-19 pandemic situation, the STS-2020 students were not able to submit the due reports in October, 2020. Hence, a total of 942 STS-2020 students who had qualified for carrying out the STS-2020 research project submitted their final due reports in the month of November, 2021, and 894 reports were finally selected after review done by the Experts from the ICMR Institutes/Centers.

ICMR-Nurturing Clinical Scientists (NCS) Scheme

A total of thirteen (13) Clinical Scientists are already continuing as on 31.03.2022 and five (05) candidates were selected for the year 2021-22.

ICMR-Adjunct Faculty Scheme

The Scheme was implemented from April, 2019 onwards after approval from the GC of ICMR. Four (04) Adjunct Faculties have joined in the year 2021-22.

FINANCIAL SUPPORT

ICMR-MD/MS/DM/MCh/DNB/DrNB/MDS thesis support

This scheme is primarily aimed at promoting good quality research in medical/dental colleges through students pursuing post-graduation courses as well as to improving visibility and accessibility of their research work to a larger research audience, as it is mandatory to publish one paper in an indexed journal. For the year 2021-22, 584 thesis proposals were received and 101 proposals were selected for financial assistance.

MISCELLANEOUS PROGRAMS

ICMR Awards & Prizes

The ICMR Awards/ Prizes 2020 were awarded in the year 2021. A total of 244 applications were received in the year 2021out of which 27 Scientists

and young researchers were awarded in 24 different ICMR Awards/Prizes categories in the field of biomedical research.

INTERNATIONAL HEALTH (IHD), DIVISION

The International Health Division (IHD) in ICMR co-coordinates international collaboration in biomedical research between India and other countries as well as with national & international agencies such as Ministries of Health & Family Welfare and Science & Technology, Indian and foreign missions and WHO etc.

Purpose of International Cooperation

The purpose of these Memorandum of Understanding (MoU) and Joint Statements has been for exchange of scientific information; exchange of scientists/technicians; joint execution of scientific projects and organization of joint scientific, seminars, workshops and symposia in identified areas of cooperation.

Joint Working Group (JWG) and Joint Steering Committee (JSC) Meetings

Regular meetings of Joint Working Group (JWG) or Joint Steering Committee (JSC) with various countries/international institutes/organizations are organized to review, develop and finalize joint collaborative programmes, decide future plans of action and identify priorities for bilateral cooperation.

In addition, the International Health Division has also represented ICMR in various bilateral/ multilateral Joint Committee Meetings coordinated by MEA, MoH&FW and DST Govt. of India for cooperation with various countries.

Following JWG/JSC meetings under various MoUs have been held during the year:

1. First virtual meeting of Joint Working Group (JWG) between India and Iran, organised by MoHFW, New Delhi on 6th April, 2021.
2. 4th virtual meeting of the BRICS Working Group on Biotechnology & Biomedicine, organized by DST on 25th May, 2021.
3. 4th Meeting of Indo-US Health Dialogues organized by MoH&FW at New Delhi on 27th & 28th Sep., 2021.
4. Joint Steering Committee virtual meeting of Indo-US collaboration on Diabetes research at ICMR Hqrs, New Delhi on 29th Oct., 2021.
5. 1st virtual meeting of the Joint Working Group (JWG) on 'Health Cooperation' between Republic of India and Republic of Colombia, organized by Ministry of Health & Family Welfare, GoI on 15th Feb., 2022.

Renewal/Signing of MoUs/LoI

- An MoU between ICMR and the GARDP Foundation on Antimicrobial Resistance Research and Innovation, Switzerland, was signed in March, 2021/April 2021 by ICMR, New Delhi and GARDP, Switzerland respectively.
- Signing of MoU between ICMR/DHR & NIAID/NIH, USA for cooperation on an International Centre of Excellence in Research (ICER) signed in Sept, 2021 at Ministry of Health Family Welfare, Nirman Bhawan, New Delhi.
- Signing of LoI between ICMR/DHR, Ministry of Health & Social Protection, Bogota & Ministry of Science, Technology & Innovation, Bogota, Colombia, at Hyderabad House, New Delhi on 2nd Oct., 2021.
- Signing of MoU between ICMR/DHR, Ministry of Health & Family Welfare, Government of India & the University of Oxford/IDDO, UK at New Delhi/London in Nov., 2021.
- Signing of MoU between ICMR/DHR, Ministry of Health & Family Welfare, Government of India & Deutsche Forschungsgemeinschafte.V. (DFG), Germany at New Delhi/Bonn in Dec., 2021.
- Signing of MoU among the Indian Council of Medical Research (ICMR), India and the

Department of Biotechnology, Govt. of the Republic of India DBT and International AIDS Vaccine Initiative (IAVI), USA at New Delhi/ USA in Feb., 2022.

Health Ministry's Screening Committee (HMSC)

The research projects involving foreign assistance and or collaboration in biomedical/health research are submitted online by the Indian investigators to ICMR for approval of Govt. of India through Health Ministry's Screening Committee (HMSC). The International Health Division of ICMR acts as the Secretariat for HMSC. The projects are peer reviewed by the concerned Scientific Divisions at ICMR and then placed before the HMSC for consideration and decision. During the year 2021-22, six meetings of Health Ministry's Screening Committee were held wherein 313 projects were considered and out of which 204 projects were approved for international collaboration/assistance with agencies from USA, Germany, France, Canada, Australia, Sweden, UK, WHO and several other foundations and foreign universities.

India Africa Health Sciences Platform

Second call under ICMR/AU-STRC Health Practitioners/Research Capacity Building Scheme (Training Courses in India 2020) was launched with the last date of submission of applications on 29th February 2020. Call was for 8 training courses at 4 ICMR Institutes-NICPR, Noida; NIRT, Chennai; NIRRH, Mumbai and NIV, Pune.

Other initiatives

1. Newton Bhabha Fund Programme: Indian Council of Medical Research partnered with British Council UK for the Researcher Links Workshops under the Newton Bhabha Fund Programme for a period of 3 years. Researcher links workshops are designed to provide financial support to bring together a UK/Indian bilateral cohort of early career researchers to take part in workshops to meet the overarching objectives.

For the year 2020-21, the second joint call of the programme was advertised in the areas of Cardiovascular pharmacotherapy in Covid-19 infections, Bio-banking, Public health preparedness and response to emerging diseases outbreak/ pandemic, Capacity building of maternity care providers to improve perinatal outcome. Two applications in the area of COVID-19 and Reproductive Health were selected for Researchers Link Workshop and result was announced. One Joint workshop entitled "India Birth Network Registry" by CMC Vellore & University of Liverpool was held on 21st- 22nd January, 2022.

2. ICMR/NIH/BMGF Clinical Research Fellowships: The Indian Council of Medical Research (ICMR), the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) and the Bill & Melinda Gates Foundation (BMGF), signed a Declaration of Intent on 17th November, 2019, on clinical research fellowship programme. It is a programme for early and mid-career scientists within India and the USA to help in expanding the cohort of physician scientists focused on research that will advance discovery to improve clinical practice and benefit public health in both countries. The implementation plan and guidance document were prepared in consultation with NIH & BMGF and the 1st Call for fellowships announced in March, 2022.

Fig. 10: Meeting between DG, ICMR & H.E. Mrs. Mariana Pacheco, Ambassador of Colombia to India & Mr. Juan Esteban Sanchez, Executive Director, Embassy of Colombia, New Delhi for exploring possibility of joint collaboration, held on 25th Aug., 2021 at ICMR Hqrs., New Delhi.

Fig. 11: Visit by German delegation led by Mrs. Maria Flachsbarth, Parliamentary State Secretary (MoS) in the Federal Ministry of Economic Cooperation and Development (BMZ), Federal Republic of Germany to ICMR Hqrs., New Delhi on 11th Sep., 2021.

Fig. 12: 4th India-US Health Dialogue held on 27-28th September, 2021 at New Delhi.

Fig. 13: Virtual meeting and announcement of winners of 2nd edition of the India-Sweden Healthcare Innovation Challenge held on 31th January, 2022.

Fig. 14: Signing of MoU among the Indian Council of Medical Research (ICMR) and the Department of Biotechnology, Govt. of the Republic of India DBT and International AIDS Vaccine Initiative (IAVI), USA at New Delhi/USA in Feb., 2022

RESEARCH MANAGEMENT, POLICY, PLANNING & COORDINATION (RMPPC), DIVISION

Through coordination with several ICMR Institutes and stakeholder discussions, RMPPC Division is working on projects connected to health communications (including communications during COVID-19), creation of various policy, planning documents, write-ups on successes, impact analysis, etc. The Division also participates in research synthesis through the Evidence to Policy initiative, which aims to assist people in making well-informed decisions about policies, programmes, and projects by placing the best available evidence from research at the heart of policy development and implementation. The Division also creates policy briefs on effective interventions.

Fig. 15: International symposium cum workshop on One Health

- **International symposium cum workshop on One Health**: On April 12, 2021, an international symposium and workshop on one health was organized with great success in order to bring together national and international stakeholders and generate ideas for the future. The Hon HFM's directives on the formation of a high-level group on eco health and the organisation of cross-sector learning and collaboration events were followed by the ICMR International One Health Symposium and Workshop. Global perspectives on One Health, Strategic Initiatives for One Health readiness, and Country Specific Initiatives and Partnerships Enabling One Health were the main topics of the technical presentations.
- **AzadikaAmritMahotsav**:Thedivisiontailored branding for Bharat kaAmrutMahotsav to be adopted by all institutes along with the hashtag #ICMR4New India. Community engagement programs were planned and conducted across institutes and regularly updated on social media. Social media campaigns on key health days and moments under the ongoing theme of Bharat KaAmritMahotsav or India at 75 were conceptualized.
- **Bilingual Monthy Newsletters:** Published monthly e-newsletter "**e-samvaad**" that highlights the activities and accomplishments of the ICMR in accessible language. There were 12 editions (April 2021–March 2022) printed, each featuring an average of 10 stories about the event. Additionally, a special edition of "**e-samvaad**" called AzadikaAmritMahotsav was released to mark the 75th anniversary of India's independence. The special issue highlighted ICMR progress and accomplishments during the last 75 years, structured decade.
- **Regional Communication Hubs**: ICMR seeks to intensify its regional communication initiatives in order to support the public narrative around the organisation and ensure greater visibility and brand memory among significant stakeholders at the regional level. In order to achieve this, three regional communications hubs were proposed and established. These hubs serve as a forum for institutes to meet and discuss strategic regional media outreach in the region and offer vital assistance to the CU in order to broaden the reach of the ICMR communication initiatives.
- **ICMR COVID-19 Timeline**: An ICMR COVID-19 timeline was created and made available on the ICMR website in an effort to showcase and communicate the extensive work completed by ICMR during COVID-19. The events and contributions from December 2019 through March 2021 were collected. The chronology was also made available as a compact brochure.
- **Audio Commentary for ICMR History Timeline:** To enhance the reach of ICMR, based on History Timeline, developed and

released by HFM in September 2020, the audio commentary was developed. The audio commentary was uploaded on ICMR server and is accessed through QR codes printed on the physical installation of ICMR history Timeline.

- **COVID-19 Audio Messages:** Contributed in script writing and development of audio messages in English and Hindi for home-based care guidelines for COVID-19 for Western Railways to be played on railway stations for generating awareness.
- **COVID-19 Research Document**: Developed and released 3 volumes of "Contribution of ICMR to world science literature in the area of COVID-19" containing consolidated research articles on COVID-19 published in peer-reviewed journals by ICMR and its institutes. The first one deals with public health epidemiology, clinical research and therapeutics and the second one contains articles on vaccines research, viral variants and genomics, diagnostics & bioethics. The third volume has compilation of articles on maternal & child health, psycho-social & behavioral issues, traditional medicine and others.
- **Celebrity endorsement for COVID-19Awareness**: The team forged liaison with noted Cricketer Harbhajan Singh to engage him as brand ambassador for COVID-19 awareness and tackling vaccine hesitancy. ICMR developed a short video message and two short films using his famous 'Doosra' to encourage people taking second dose of vaccine. It was posted on ICMR's as well as the celebrity's Social Media handles.
- **Short film on Covaxin Development**: A 2 minute film was developed to showcase the journey of Covaxin development and other achievements of ICMR in tackling COVID. The film was showcased in Geneva during' Going Viral' Book launch and Postal stamp Launch.
- **Going Viral:** Dr Balram Bhargava, DG, ICMR authored a book, Going Viral'. The division coordinated the development, publishing & launch of the book. The book touches upon various aspects of challenges faced by our scientists during the fight against COVID-19. The story starts with the report of mysterious pneumonia cases from Wuhan, China to the first case detection in India and further to the development of each arsenal used in the fight: diagnosis, treatment and vaccines.
- **Press Releases & Communication Plans for various ICMR events:** Coordinated the press release and communications activities various ICMR events like 5th World Congress on Disaster Management, I DRONE, BSL-3 laboratory launch, inauguration of ICMR-RMRC Gorakhpur by Hon'ble PM etc.
- **COVID-19 vaccine (BBV-152) Commemorative postal stamp:** Coordinated the release of COVID-19 vaccine (BBV-152) Commemorative postal stamp by Hon'ble HFM on the occasion of anniversary of COVID-19 Vaccination Drive on 16th January 2022.

Fig.16: Release of COVID-19 vaccine (BBV-152) Commemorative postal stamp by Hon'ble HFM

- **Knowledge Sharing Workshop**: Organised a 6-day Knowledge Sharing Workshop for health journalist on theme, "Journey of Covaxin Development". Over 20 renowned health journalists travelled to ICMR-NIV, Pune and ICMR-NIN & Bharat Biotech, Hyderabad to understand the activities and achievements of ICMR institutes with special focus on the development of Covaxin. The workshop resulted in more than 50 articles and news reports in print and electronic media.
- **Social Media Campaign for World TB Day**: Developed a campaign for World TB Day including social media posts, video clips from ICMR leadership and designed documents and one pager for release by Hon'ble HFM.
- **Vigyan Sarvartre Pujyate**: ICMR Organized the event "VigyanSarvartrePujyate" as partner. The event is organised at 75 locations across India from 22-28 February celebrating Science Week including at two ICMR institutes (ICMR-RMRC, Gorakhpur & ICMR-NIN, Hyderabad). ICMR leveraged the RCH platform to support regional institutes in brainstorming and activating campaigns. The team helped develop campaign agendas, incorporating a variety of activities including lecture series, school and college competitions and book launches to be undertaken by different institutes around various themes of the National Science Week, including 75 Milestones in India Science and Tech, 75 Innovations and Inventions in Indian Science and Techand Annals of History amongst others. As a result of the support from the CU and GHS, ICMR institutes across the country gained significant media traction in both national and regional media outlets and effectively amplified their research and contributions to the country's health systems. ICMR also participated in Mega Science Expo at JLN Stadium, Delhi under the aegis of Vigyan Sarvatre Pujyate.

Fig. 17: Mega Science Expo at JLN Stadium, Delhi under the aegis of VigyanSarvatrePujyate

- **India International science Festival 2021**: Showcased ICMR's research activities and achievements at Expo IISF 2021 held at Goa during 10-13 Dec 2021.

Fig. 18: Expo IISF 2021 held at Goa during 10-13 Dec 2021.

- **Evidence to Policy:** The division coordinated the review and finalized the policy brief on "COVID-19 STIGMA: Correlates and Mitigation Strategies. Also, it facilitated external review and publishing of 3 policy briefs on Smoking, Long term survival of treated TB patients and Active Case Finding in Sahariya Tribe.
- Organised a lecture, "Rajyoga for Emotional Stability in the time of COVID-19" on the occasion of International Yoga Day 2021by Sister BK Shivani.
- Organised the Freedom Run 2.0 at Jawahar Lal Nehru Stadium on 25th September 2021. More than 200 participants joined the run.

Fig. 19: Freedom Run 2.0 at Jawahar Lal Nehru Stadium on 25th September 2021.

- Coordinated the virtual launch of i-DRONE (First time in South Asia, a "Make in India' drone used to transport COVID-19 vaccines) by Hon'ble HFM on 4th October 2021.
- Coordinated the virtual stone laying ceremony of new building of ICMR's School of Public Health by Hon'ble HFM on 19th October 2021

INDIAN JOURNAL OF MEDICAL RESEARCH (IJMR), UNIT

The Indian Journal of Medical Research (IJMR) is a monthly biomedical journal of national and international repute and is the flagship journal of the Indian Council of Medical Research (ICMR). During the financial year 2021-22, it has completed 108 successful years of uninterrupted publication, with 12 issues brought out in two volumes each year. The IJMR is available as full text, free on the internet with a searchable menu. With a wide circulation within and outside India, IJMR is included in all global indexing and abstracting services. The journal is also available full text free on the web at www.ijmr.org.in. The IJMR App has been made available for the Android version of the tablet as well as iPad since January 2017. Article submissions to the IJMR are now invited via a new platform https://review.jow.medknow.com/ijmr.

Besides publishing original research articles, the IJMR publishes Editorials, Commentaries and Review/Mini review articles on topics of contemporary biomedical interest contributed by eminent global experts. Other than these, Research Correspondences, View Points, Perspectives, Systematic reviews & Meta-analyses, Clinical Images, Student IJMR, Letters to the Editors and Book reviews are also published in addition to Policy Documents and Special/Status Reports occasionally. The impact factor for the year 2020 increased to 2.374 (Clarivate Analytics, 2021) which was an all-time high.

A total of 10 issues (including 3 special issues & 1 special section) were published in the 2021-22 financial year with the total number of submissions amounting to more than 3000. There was an increase in the number of submissions from countries other than India in this financial year amounting to over 33% out of the total submissions. A total of 1124 reviewers were involved in the peer-review process, of whom close to 12per cent were from foreign countries. Among these, 49 per cent were from USA, 8 per cent from UK,11 per cent each from Italy and Turkey, 5 per cent from Singapore, 4 per cent from Canada, Greece, South Africa& Japan,3 per cent from Spain, 2 per cent each from

Australia, Brazil, Denmark, France, Hungary, Indonesia, Mexico, Saudi Arabia & Switzerland and1 per cent each from Belgium, Brunei, Bulgaria, Egypt, Ethiopia, Germany, Ghana, Iran, Ireland, Israel, Jamaica, Nepal, Norway, Nigeria, Serbia, Sri Lanka, Sweden, The Netherlands & Uganda.

Fig 1 depicts the total number of articles published in the IJMR during the financial year of 2021-22 under various categories. The number of original articles published increased to 40percent, followed by 19per cent in the review articlesand8 per cent in the research correspondences categories respectively. Other than these View Points, Perspectives, Special reports, Policy guidelines, Clinical Images, Editorials and Commentaries were also published.

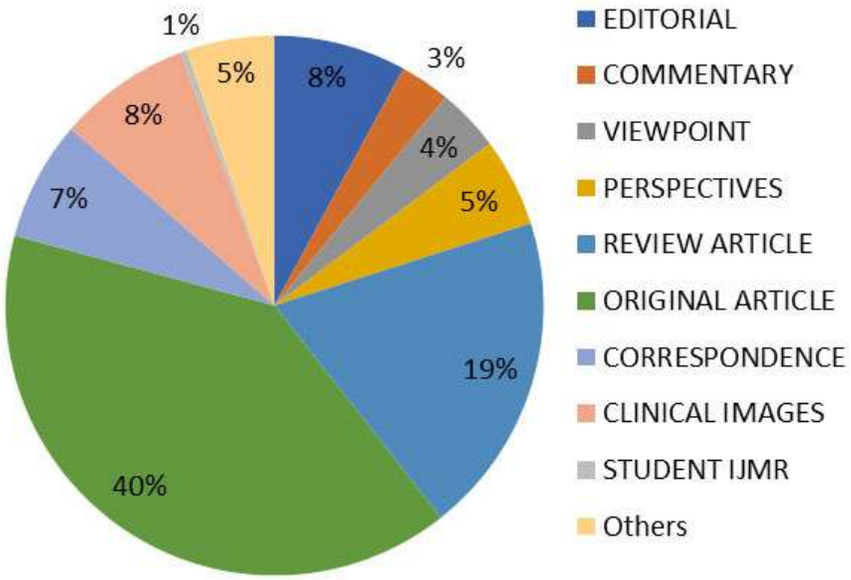


Fig 20: Articles published in the IJMR under various categories during 2021-22 financial year.

A total of 387 articles were published in the said financial year, with around 13per cent articles from foreign countries such as the USA, UK, Thailand, Turkey, Egypt, Germany, Brazil, Australia, Austria, France, Iran, Italy and Jamaica. Fig 2 depicts the percentage of articles submitted, published and reviewers' contribution from India and foreign countries.

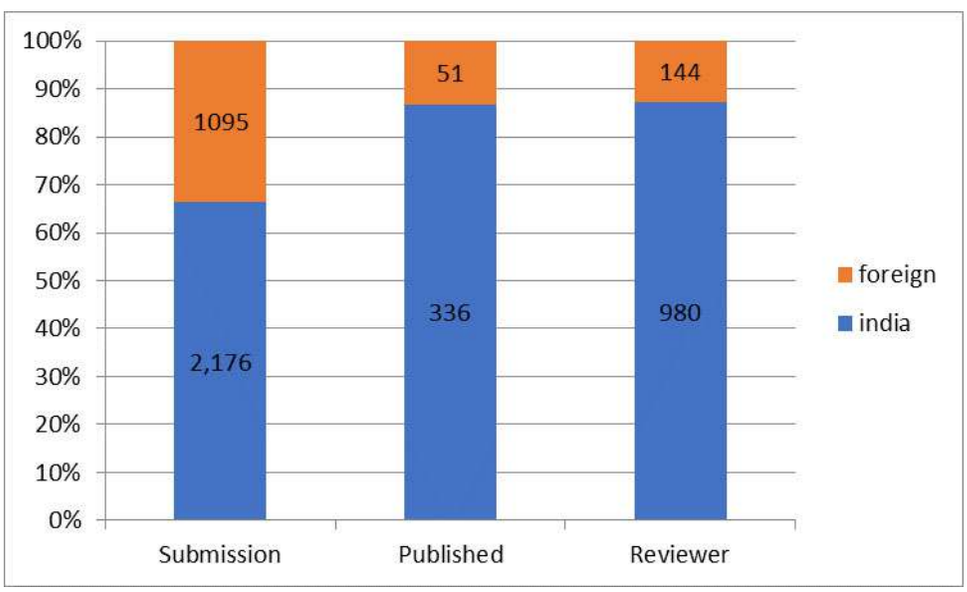


Fig 21: Indian vs. foreign articles submitted, published & reviewers contributed in the IJMR during 2021-22.

In 2021-22, given the second year into the COVID-19 pandemic, efforts were doubled at IJMR to publish articles most relevant to the evolving national healthcare priorities pertaining to COVID-19 on fast track to ensure dissemination of most opportune information which can inform policy decisions. Alongside COVID-19, keeping in view of the other healthcare priority topics were also considered. In this regard, such articles were made available online as Ahead of Print on www.ijmr.org.in on timely basis. Three special issues were published in the requisite financial year including COVID-19, which was the May & June 2021 issue while one special issue was published on 'One Health' in March 2021 (Fig.3).

The special issue on 'One Health' was released by Dr. Harsh Vardhan, Honorable Minister of Health and Family Welfare, Government of India on the April 12, 2021.Dr. M.D. Gupte was the Guest Editor of this issue. 'India &COVID-19 (PartV)' was very well received by authors/readers/media and included important topics pertaining to each of the three waves of COVID-19 with potential policy implications. Drs Rajesh Bhatia &Priya Abraham were the Guest Editors of this special issue. The special issue on 'Women Health and Cancer' (Fig.4) was noted as opportune. Drs Sudeep Gupta, Supriya Chopra & Neeta Nair were the Guest Editors of this issue.

The January 2022 issue included a Special Section on 'India & COVID-19'. This issue covered topics pertaining to diagnosis, vaccination and post-vaccination adverse events in COVID-19, among others.

Fig. 22: Special issues on 'One Health'& 'India & COVID-19 (Part-V)'.

Fig. 23: Special issue on 'Women Health and Cancer'

BIOMEDICAL INFORMATICS (BMI), DIVISION

Data Management and Dissemination

In line with the objectives under the Pillar II of the ICMR Strategic Vision Document 2030, the division developed data collection and analysis portals for several programs of ICMR and other organizations. A few important programs for which the Division developed data collection and analysis portals include:

- **National COVID-19 testing data portal (https://cvstatus.icmr.gov.in) and COVID-19 Analytics Portal (https://cvanalytics.icmr.org.in):** The division has designed and developed nation vide COVID-19 testing data portals. The portals facilitate the COVID-19 testing data entry across the country. Based on the stakeholder requirements, the COVID-19 testing data management system can be subdivided into two main modules i.e., cvstatus (for data collection) and cvanalytics (for data analysis). The data collection tool is mainly used by laboratories (labs) for entering the testing data. The data collection tool has the provision to submit data for samples tested using different techniques including RTPCR, TrueNAT, CBNAAT, and RAT. The data is collected based on a standardized Specimen Referral Form (SRF) developed by a group of experts. The data analytics tool is

intended to use by officials at national, state and district levels for visualizing the data entered from the labs. The data analytics tool (https://cvanalytics.icmr.org.in) presents a detailed analysis of the collected data to the users (based on their role) for monitoring the ongoing scenario and formulating policies.

- **COVID-19 Testing Kit Validation (https://cvtestkit.icmr.org.in)**: The portal is being used for the validation of the new COVID-19 testing kits available in the market and to facilitate this validation process, cvtestkit portal was developed. The portal enables vendors to register their kits for the necessary validation and approvals. BMI Division enabled for electronic process of kit validation and testing.
- **COVID-19 Testing Lab Quality Control (covidqcqa):** To monitor the quality of testing for COVID-19 test done by the approved laboratories, ICMR has followed inter-laboratory comparison i.e. random rechecking of the samples tested by these labs (ILQC). To ensure transparency and facilitate standardized data collection, covidqcqa portal was developed as is a web-based tool. The testing lab, regional QC lab and National QC lab entered their data on the web portal, which is collated by a team at ICMR headquarters.
- **COVID-19 Data APIs**: ICMR has provided APIs to several state authorities and labs for timely reporting of COVID-19 testing data. During the second wave, the COVID-19 testing database grew rapidly in size, impeding the fetching of data. The COVID-19 Data APIs were developed to handle the challenge of the huge testing database and were provided to different organisations (NDMA, NHA, AarogyaSetu App etc.), states and city administration for real-time monitoring of the situation.
- **National Covid-19 test report portal (https://report.icmr.org.in):** BMI division has developed a public service window for accessing COVID-19 test reports. The individuals may access through https://report.icmr.org.in. The individuals may access through https://report.icmr.org.in using mobile number provided at the time of testing.
- **ICMR Vaccine Portal (https://vaccine.icmr.org.in):** This portal gives information about COVID-19 available vaccines in India, development phase of vaccine, approval type of the vaccine, details about the vaccine make/technology, India's initiatives for COVID-19 vaccine, Symposiums regarding COVID-19 vaccine, FAQs about vaccine, latest news about COVID-19 vaccines etc. The vaccination details of each day also display on the home page of the website.
- **INTENT Portal (https://intent.icmr.org.in)**:Indian Clinical Trial and Education Network (INTENT) is an initiative to build a network of Research Institutes which has been launched with an overarching goal of providing evidence based, robust and culturally sensitive solutions to urgent health problems, in a reasonable time frame, by conducting large multi-centric clinical trials.
- **ICMR-NIV Pune websites Portal (https://niv.icmr.org.in)**: Website designed and developed for the institute ICMR-NIV Pune.
- **Myconet Portal (https://myconet.icmr.org.in)**:ICMR Advanced Mycology Diagnostic Research Center Network (MycoNet) is an ICMR initiative for capacity building of mycology laboratories throughout the country with an ambit to provide complete advanced diagnostic services for fungal diseases and research with a long term goal of fungal mapping in the country.
- **STW Portal (https://stw.icmr.org.in):**With the vision to make Universal Health Coverage a reality in the country, Government of India has started many initiatives, development of Standard Treatment Workflows is a catalytic step in this direction. Department of Health Research and Indian Council of Medical Research are working together to develop these workflows for common and serious

diseases to help the healthcare providers across the country.

- **National Clinical Registry of COVID-19 (https://www.icmr.gov.in/tab1ar1.html):**Coronavirus disease 2019 (COVID-19) is a novel disease caused by a newly identified virus, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The novel disease which begun in Wuhan, China in Dec 2019 was declareda pandemic by World Health Organization on 11 March 2020.We are currently facing a unique situation where new knowledge regarding the virus and the illness are being made available by the scientific community regularly. Documentation and description of the cases infected by SARS-CoV-2 and their course of illness is imperative for obtaining useful information regarding the illness, its behavior in various groups of patients and the natural history of COVID-19. Context specific information in patients with tuberculosis or malnutrition as comorbidity is pertinent to document as it may particularly influence clinical decision making and policy updates in the Indian setting.
- **i-Drone Page under ICMR website (https://www.icmr.gov.in/idrone/index.html):** The project 'i-DRONE' (ICMR's Drone Response and Outreach for North East) assessed the feasibility of using drone to deliver vaccines and medical supply. This was carried out in difficult geographical terrains including land, island, foothills and across the hills. Collaborations with the State Health Mission of Manipur and Nagaland were key to such assessment. All necessary regulatory approvals from the Ministry of Civil Aviation (MoCA), Directorate General of Civil Aviation (DGCA), Airport Authority of India (AAI) and the State Health Authorities of Nagaland and Manipur were obtained prior to implementation of this initiative. Eighty drone sorties were undertaken in three districts of Manipur namely Imphal West, Bishnupur and Churachandpur and two districts of Nagaland-Mokokchung and Tuensang. The aforementioned operations connected the district hospitals to the community and primary health care centres in the study districts.
- **Antimicrobial Resistance Surveillance Network (AMRSN) (https://iamrsn. icmr.org.in)**: It is a web based tool for collection, management and analysis of data generated by the ICMR AMRSN. The tool has recently been used for contributing AMR data to Global Antimicrobial Resistance Surveillance System (GLASS). The division signed a LoI with Department of Informatics, University of Oslo, Norway on developing an integrated system for surveillance of antimicrobial resistance.
- **Leprosy Data Management System (Nikusht) available at (https://leprosy.gov.in)**: It is a Web and Mobile based solution for systematic collection, management and real-time monitoring of Leprosy suspects and patients. The solution has been handed over to National Leprosy Eradication Program (NLEP).
- **JalJeevan Mission portal hosted at (https://neer.icmr.org.in):** It is being implemented in partnership with States, to enable every household in villages to have functional household tap connection by 2024. The web-base and mobile app solution has been developed and made available to people/ functionaries so as they are able to either test their water on their own using water testing kits or get it tested at the nearest lab. The portal is used to generate nationwide reports for decision support system at the appropriate levels. The system is helping in ensuring safe drinking water to every household, thus improving the quality of life of the people.
- **Mental health data portal hosted at (https://mentalhealth.icmr.org.in): Data** collection portal for projects under the implementation research in mental health wherein the Division digitized mental health related scales.

- **Indicleft tool available at (https://indicleft.icmr.org.in):** It is a comprehensive web based tool developed for an ongoing study at AIIMS that collects data on various aspects of cleftlip and also provides information to the parents of cleftlip patients.
- **DHR ePMS Portal (https://dhrschemes.icmr.org.in):**Portal is developed to receive and process proposals under various DHR schemes viz. Grant-in-Aid (GIA), Human Resource Development for Health Research (HRD), Establishment of Multi-Disciplinary Research Units (MRUs) in Government Medical colleges /Research Institutions, Establishment of Model Rural Health Research Units (MRHRUs) in the States, Establishment of VRDLs (Viral Research & Diagnostic Laboratories) throughout the country.
- **HMSC Portal (https://hmsc.dhr.gov.in):** Portal is developed to receive and process the Health Ministry's Screening Committee (HMSC) proposals
- **Recruitment Portal (https://recruit.icmr.org.in):** Portal is developed to receive online application for permanent positions. After receiving the applications admin management system is developed for scrutiny of applications.
- **Project Recruitment Portal (https://projectjobs.icmr.org.in):** Portal is developed to receive online application for project staff positions.

Task force – AIIMS-ICMR system for identification of unidentified dead bodies (https://umid-aiims.icmr.org.in**):** This database stores phenotypic (physical appearance) and genotypic (genetic) information of unidentified dead bodies autopsied at the Department of Forensic, AIIMS New Delhi. It caters to both South and South East districts of Delhi. We aim to provide all concerned authorities and families of missing persons the required information with just a few clicks.

Centralised Source Code Management System (https://git.icmr.org.in): It is a centralised repository for the source code management system of all the artefacts of the Software development activities of the Council.

In addition, the division is developing analytic dashboards and hosting services to various programs of ICMR and non-ICMR institutions such as Integrated Disease Surveillance Program (IDSP), Indian Rare Disease Registry available at https://irdr.icmr.org.in/irdr. The division developed websites for Health Technology Assessment (https://htain.icmr.org.in).

ICMR-AIIMS Computational Genomics Centre

Genomics tools and techniques are revolutionizing medical research through better diagnostics and prognostic markers and personalized risk models for non-communicable disease such as cancer. ICMR established a Computational Genomics Centre in collaboration with AIIMS. The Centre is fully operational and is assisting medical professionals from AIIMS and other medical research institutions in analyzing genomics data. The Centre has developed customized pipelines for making pangenomes, trios data analysis, association studies and rare variant identification. The centre has also developed the customised pipeline for the analysis of the COVID-19 genome sequence for ICMR institutes. Information about the activities of the Centre is available at https://genomics.icmr.org.in

ICMR Electronic Project Management System (ePMS)

Extramural research is promoted by ICMR through Open-ended research on the basis of applications for grants-in-aid received from researchers/scientists in regular employment in the Universities, Medical Colleges, Postgraduate Institutions, recognized Research and Development Laboratories and NGOs from all over in India. In order to improve efficiency of processing of its Extramural Research Program and to save efforts of the Investigators, ICMR has shifted from manual

receipt and processing of extramural projects to web-based interactive system. ePMS is a cloud service for Project proposal submission, evaluation and monitoring system. The main vision of ePMS system is to provide Transparent & Centrally Controlled electronic Proposal Evaluation and Grant Disbursement to support R&D Institutions.

Table 4. Adhoc Scheme and Fellowship (SRF/RA) open call during the period 2021-22.

Scheme Name	Total Proposals received
Adhoc full proposals	3690
SRF/RA Fellowship full proposals	3220

Table 5. Concept proposals received during the year 2021-22.

Advertisement	Total Proposals received
Call for Concept Proposals on COVID-19	2878
India Cancer Research Consortium	1237
Call for proposal on Air Pollution viz-a-viz Infectious Disease including Covid-19, Air Quality and Microenvironment	235

Table 6. Call for detailed proposals received during the year 2021-22.

S.no	Advertisement	Proposal Received
1	Call for Ad-hoc Research Proposals "Reproducible AI in Medicine and Health"	463
2	ITRC-Invitation for Full Proposals in area of Implementation/Operational research in Tuberculosis	208
3	Call for proposals on management and analysis of COVID-19 testing data	125
4	Call For Research Proposals on Impact of Climate Change on Vector-Borne Diseases (Vbds),	94
5	Call For Research Proposals Under Malaria Elimination Research Alliance–India (MERA- India)-2022	80
6	India Cancer Research Consortium	57
7	Call for proposals for Indo-Swedish research on ageing and health	42
8	Call For Proposals For Young Malaria Researchers Under Malaria Elimination Research Alliance – India (MERA-India)-2022	24
9	Call for LoIs in VTE for Individual Research laboratories (Single site studies)	6
10	Others	27

ICMR Website

The division launched the improvised, completely GIGW compliant ICMR website, based on CMS frame, to enhance user friendliness, enriched content dissemination, latest technique based pages and user compatible design along with enhanced Security. The division is maintaining the ICMR website at https://main.icmr.nic.in. The site hosts various ICMR programs, activities, notifications, guidelines, reports, career opportunities in research as well as GOI initiatives followed by the organization.

Management of Direct Benefit Transfer (DBT) Schemes

There are currently 5 Direct Benefit Transfer schemes from ICMR. Division collects transaction data pertaining to direct benefit transfer schemes from e-PMS portal, technical divisions and Account section; then updates this information on the DBT portal every month.

MoUs/Agreements

wwMoUs has been signed with the reputed research institutes with Indian Institute of Sciences (IISC), Bangalore, Jawaharlal Nehru University (JNU), New Delhi, All India Institute of Medical Sciences (AIIMS), New Delhi and The Dutch Research Council.

ICMR INSTITUTES/CENTRES

ICMR INSTITUTIONAL NETWORK

1. **ICMR- National JALMA Institute for Leprosy & Other Mycobacterial Diseases (NJIL&OMD)**
   Dr. M. Miyazaki Marg, PO Box 101,
   Tajganj, **Agra -** 282001
   Uttar Pradesh
   http://www.jalma-icmr.org.in

2. **ICMR- National Institute of Occupational Health (NIOH)**
   Meghani Nagar, **Ahmedabad** - 380 016
   Gujarat
   http://www.nioh.org

3. **ICMR- National Institute of Traditional Medicine (NITM)**
   Belagavi, National Highway No.4,
   Belagavi - 590010
   Karnataka
   http://www.icmrnitm.res.in

4. **ICMR- National Centre for Diseases Informatics and Research (NCDIR)**
   Nirmal Bhawan - ICMR Complex (II Floor), Poojanahalli Road,
   Off NH-7, Adjacent to Trumpet Flyover of BIAL Kannamangala Post,
   Bengaluru - 562 110
   Karnataka
   http://www.ncdirindia.org

5. **ICMR- National Institute for Research in Environmental Health (NIREH)**
   Kamla Nehru Hospital Building, Gandhi Medical College Campus,
   Bhopal - 462 001
   Madhya Pradesh
   https://nireh.icmr.org.in

6. **ICMR- Bhopal Memorial Hospital & Research Center (BMHRC)**
   Bhopal Memorial Hospital & Research Center Raisen Bypass Road,
   Near Karond Chouraha, **Bhopal** - 462038
   Madhya Pradesh
   http://bmhrc.ac.in

7. **ICMR- Regional Medical Research Centre (RMRCBB)**
   Chandrasekharpur, **Bhubaneswar** - 751023
   Odisha
   http://www.rmrcbbsr.gov.in

8. **ICMR- National Institute for Research in Tuberculosis (NIRT)**
   No.1 Sathiyamoorthy Road Chetput, **Chennai** - 600031
   Tamil Nadu
   http://www.nirt.res.in

9. **ICMR- National Institute of Epidemiology (NIE)**
   Second Main Road, Tamil Nadu Housing Board, Ayapakkam,
   Near Ambattur, **Chennai -** 600 077
   Tamil Nadu
   http://www.nie.gov.in

10. **ICMR- Regional Medical Research Centre, NE Region (RMRCNE)**
    Post Box No. 105, **Dibrugarh** - 786001
    Assam
    http://rmrcne.org.in

11. **ICMR- Regional Medical Research Centre, Gorakhpur (RMRCGKP)**
    Baba Raghav Das (BRD) Medical College Campus,
    Gorakhpur - 273013
    Uttar Pradesh
    http://rmrcgkp.icmr.org.in

12. **ICMR- National Animal Resource Facility for Biomedical Research (NARFBR)**
    National Centre for Laboratory Animal Sciences, NIN Campus,
    Jamai Osmania P.O. **Hyderabad** - 500 007
    Andhra Pradesh
    http://www.narfbr.org

13. **ICMR- National Institute of Nutrition (NIN)**
    Jamai - Osmania (P.O.), Tarnaka,
    Hyderabad - 500 007
    Andhra Pradesh
    http://www.nin.res.in

14. **ICMR- National Institute for Research in Tribal Health (NIRTH)**
    Nagpur Road, Garha, **Jabalpur** - 482 003
    Madhya Pradesh
    http://www.nirth.res.in

15. **ICMR- National Institute for Implementation Research on Non-Communicable Diseases (NIIRNCD)**
    New Pali Road, **Jodhpur** - 342 005
    Rajasthan
    https://niirncd.icmr.org.in

16. **ICMR- National Institute of Cholera and Enteric Diseases (NICED)**
    P-33, C.I.T. Road, Scheme XM Beleghata
    Kolkata - 700 010
    West Bengal
    http://www.niced.org.in

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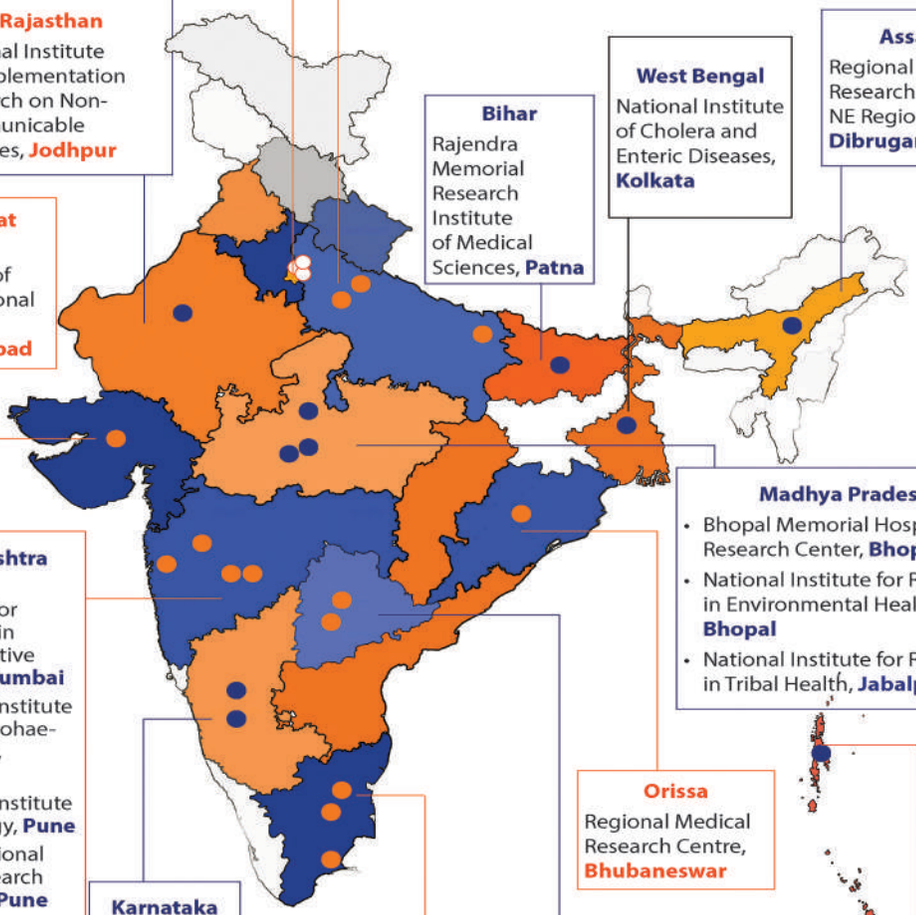

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- Bhopal Memorial Hospital & Research Center, **Bhopal**
- National Institute for Research in Environmental Health, **Bhopal**
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- National Institute for Research in Reproductive Health, **Mumbai**
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17. **ICMR- National Institute of Immunohaematology (NIIH)**
13th Floor, New Multi-storied Building, KEM Hospital Campus,
Mumbai - 400012
Maharashtra
http://www.niih.org.in

18. **ICMR- National Institute for Research in Reproductive Health (NIRRH)**
Jehangir Merwanji Street, Parel,
Mumbai - 400 012
Maharashtra
http://www.nirrh.res.in

19. **ICMR- National Institute of Pathology (NIP)**
Safdarjang Hospital Campus P.O. Box No. 4909, **New Delhi** - 110029
Delhi
http://instpath.gov.in

20. **ICMR- National Institute of Medical Statistics (NIMS)**
Post Box No. 4911, Ansari Nagar, **New Delhi** -110029
Delhi
http://nims-icmr.nic.in

21. **ICMR- National Institute of Malaria Research (NIMR)**
Sector-8, Dwarka, **New Delhi** - 110077
Delhi
http://www.nimr.org.in

22. **ICMR- National Institute of Cancer Prevention and Research (NICPR)**
I-7, Sector - 39, **Noida** - 201301
Uttar Pradesh
http://www.nicpr.res.in

23. **ICMR- Rajendra Memorial Research Institute of Medical Sciences (RMRIMS)**
Agam Kuan, **Patna** - 800007
Bihar
http://www.rmrims.org.in

24. **ICMR- Regional Medical Research Centre (RMRCPB)**
Post Bag No. 13, **Port Blair** - 744 101,
Andaman and Nicobar Islands
http://www.rmrc.res.in

25. **ICMR- Vector Control Research Centre (VCRC)**
Indira Nagar, **Puducherry** - 605006
Puducherry
https://vcrc.icmr.org.in

26. **ICMR- National AIDS Research Institute (NARI)**
G-73, MICD Complex, Bhosari, **Pune -** 411026
Maharashtra
http://www.nari-icmr.res.in

27. **ICMR- National Institute of Virology (NIV)**
20 A Dr Ambedkar Road, **Pune** - 411 001
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