INDIAN COUNCIL OF MEDICAL RESEARCH

NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS

ANNUAL REPORT
2023 - 2024

WHO Collaborating Centre for Tuberculosis Research & Training

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PREFACE

I am pleased to present this edition of our Annual Report, showcasing the significant strides made in advancing tuberculosis (TB) research and its translation into impactful public health solutions. This report underscores our unwavering commitment to combating TB and other pressing health challenges through innovative research and collaboration.

Over the past year, our efforts have focused on addressing critical gaps in TB diagnosis and treatment. From pioneering shorter and cost-effective treatment regimens to advancing molecular diagnostics, our work continues to prioritize patient-friendly solutions. We have embraced cutting-edge methodologies such as next-generation sequencing, development of novel biomarkers, and non-sputum-based diagnostic techniques, aiming to enhance accuracy and accessibility of TB detection and care.

Our initiatives extended beyond the laboratory, emphasizing community-focused interventions and operational research. For instance, the socio-behavioral research network has been pivotal in addressing the social dimensions of TB, while training modules for tribal volunteers have demonstrated a tangible impact in improving TB case detection in underserved regions.

Additionally, our studies have expanded to include related health areas such as HIV, COVID-19, and smoking cessation strategies, further diversifying our contributions to public health. The translational value of our research is evident in its direct application to policy-making, such as the adoption of cost-effective diagnostic tests and treatment regimens under the National Tuberculosis Elimination Programme.

This year also marked significant advancements in our international collaborations, with continued support to SEAR member nations and the establishment of infrastructure like the Viral Research and Diagnostic Laboratory at Tiruvallur campus.

As we progress toward the End TB targets with renewed vigor and focus, this report reflects the collective efforts of our dedicated team.

- Director, ICMR-NIRT

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ABBREVIATIONS

ACE2	Angiotensin Converting Enzyme 2
ACF	Active Case Finding
ADAR	Adenosine Deaminase Acting on RNA
ADR	Adverse Drug Reactions
AI	Artificial Intelligence
ARDS	Acute Respiratory Distress Syndrome
ARREST-TB	Accurate, Rapid, Robust & Economical Diagnostic Technologies For Tuberculosis
ART	Anti-Retroviral Treatment
ATT	Anti-TB Treatment
BCG	Bacille Calmette-Guérin
BDQ	Bedaquiline
BEAT	Building Evidence Against TB
BMI	Body Mass Index
BPaL	Bedaquiline, Pretomanid, Linezolid
BSEM	Bayesian Structural Equation Model
Btb	Bovine Tuberculosis
CAD	Computer-Aided Detection
CAPRISA 002	Acute HIV Infection Cohort Study
CAS	Current Awareness Service
CBC	Complete Blood Count
CBL	Clinical Biochemistry Laboratory
CFP	Culture Filtrate Protein
CFU	Colony Forming Unit
COVID-19	Coronavirus Disease – 19
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CTAB	Hexadecyltrimethylammonium Bromide
CVD	Cardiovascular Disease
CXCL	Chemokines
CXR	Chest X-Ray
DC	Dendritic Cells
DHR	Department of Health Research

DLAS	District Level Annual Survey
DLM	Delamanid
DM	Diabetes Mellitus
DNA	Deoxyribo Nucleic Acid
DRMs	Drug Resistance Mutations
DRS	Drug Resistance Survey
DR-TB	Drug Resistant-TB
DST	Drug Susceptibility Test
DTG	Dolutegravir
Dx	Diagnostic
EGFP	Enhanced Green Fluorescent Protein
EID	Early Infant Diagnosis
ELISA	Enzyme Linked Immunosorbent Assay
EMB	Ethambutol
EPTB	Extra Pulmonary TB
EQA	External Quality Assurance
ETH	Ethionamide
FDC	Fixed Dose Combination
FDGs	Focus Group Discussions
FQ	Fluoroquinolone
GIS	Geographical Information System
HATS	Histone Acetyl Transferases
HDACs	Histone Deacetylases
HEPS	HIV-1 Multiply-Exposed Seronegative Cohort Study
HHC	Healthy Household Contacts
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HPLC	High Performance Liquid Chromatography
HRQoL	Health Related Quality of Life
HTA-In	Health Technology Assessment in India
ICT	Immunochromatography
IEF	Iso Electric Focusing
IGRA	Interferon Gamma Release Assay
IMCs	Infectious Molecular Clones

INF	Interferon
INH	Isoniazid
INSTI	Integrase Strand-Transfer Inhibitor
IPT	Isoniazid Preventive Therapy
ISG	Interferon Stimulated Genes
KII	Key Informant Interviews
LATE-PCR	Linear After the Exponential PCR
LDH	Lactate Dehydrogenase
LFT	Liver Function Tests
LIMS	Laboratory Information Management System
LOD	Limit of Detection
LPA	Line Probe Assay
LTBI	Latent TB Infection
LZD	Linezolid
MAM	Moderate Acute Malnutrition
MBPaL	Modified BPaL
MDMs	Monocyte Derived Macrophages
MDDC	Monocyte Derived Dendritic Cells
MDR	Multidrug Resistant
MDR-TB	Multidrug Resistant TB
MDRTI/NR	Multidrug Resistant Treatment Intolerant/Non-Responsive
MGIT	Mycobacterium Growth Indicator Tube
MIC	Minimum Inhibitory Concentration
MIS-C	Multisystem Inflammatory Syndrome in Children
MMP	Matrix Metalloproteinases
MO	Medical Officer
MoHFW	Ministry of Health and Family Welfare
MOX	Moxifloxacin
MOIs	Multiplicities of Infections
MSM	Men Having Sex with Men
MTA	Material Transfer Agreement
MTB	Mycobacterium Tuberculosis
MTBC	Mycobacterium Tuberculosis Complex

NABL	National Accreditation Board for Testing and Calibration Laboratories
NAbs	Neutralizing Antibodies
NACO	National AIDS Control Organization
NDRS	National Anti-TB Drug Resistance Survey
NE	North East
NETS	Neutrophil Extracellular Traps
NK	Natural Killer
NRL	National Reference Laboratory
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NSP	National Strategic Plan
NTEP	National TB Elimination Programme
NTM	Non-Tuberculous Mycobacteria
OSE	Onsite Evaluation
Pa	Pretomanid
PBMC	Peripheral Blood Mononuclear Cells
PCR-RFLP	Polymerase Chain Reaction - Restriction Fragment Length Polymorphism
PD	Positive Deviance
pDCs	Plasmocytoid Dendritic Cells
PFT	Pulmonary Function Test
PK	Pharmacokinetics
PMDT	Programmatic Management of Drug-Resistant TB
PPD	Purified Protein Derivative
PR	Pulmonary Rehabilitation
Pre-XDR	Pre-Extensive Drug Resistant
PRE-EMPT	Predictors Resistance Emergency evaluation multidrug resistant tuberculosis patient and treatment
PTB	Pulmonary Tuberculosis
PZA	Pyrazinamide
QFT	Quantiferon TB Gold Plus
raBCG	Recombinant Bacille Calmette-Guérin
raMTB	Recombinant Mycobacterium Tuberculosis
RePORT	Regional Prospective Observational Research In TB
RFT	Renal Function Tests

RMP/RIF	Rifampicin
RNA	Ribo Nucleic Acid
RRL	Regional Reference Laboratory
RTPCR	Reverse Transcriptase Polymerase Chain Reaction
RUSF	Ready-to-Eat Supplementary Food
SARS-CoV2	Severe Acute Respiratory Syndrome – Coronavirus – 2
SDI	Selective Dissemination of Information
SDS PAGE	Sodium Dodecyl Sulphate Polyacrylamide Gel Electrophoresis
SEARO	South East Asia Regional Office, WHO
SGRQ	St. George's Respiratory Questionnaire
SLI	Second-Line Injectable
SNPs	Single Nucleotide Polymorphisms
SNRL	Supranational Reference Laboratory
SPAD	Single Photon Avalanche Diode
SSI	Semi-Structured Interviews
STREAM	Shortening of Treatment Regimens for MDR-TB Patients
TAT	Turnaround Time
TB	Tuberculosis
TDM	Therapeutic Drug Monitoring
TF	Transmitted Founder
TIMP	Tissue Inhibitors of Matrix Metalloproteinases
TNF	Tumor Necrosis Factor
TNGS	Targeted Next-Generation Sequencing
TST	Tuberculin Skin Test
TTP	Time to Culture Positivity
TU	TB Units
VAP	Vaccine Action Programme
VPM1002	Recombinant BCG Vaccine
VRDL	Viral Research and Diagnostic Laboratory
WGS	Whole Genome Sequencing
WHO	World Health Organization
XDR	Extensively Drug Resistant

REPORT OF RESEARCH ACTIVITIES

DEPARTMENT OF CLINICAL RESEARCH

DEPARTMENT OVERVIEW AND MANDATES

The Department of Clinical Research is the oldest division within ICMR-NIRT and has conducted world renowned studies starting from the Home Sanatorium study. Doctors, Nursing and support staff play a major role in the research studies undertaken by the department. They are well-trained and experienced in the recruitment and retention of participants in clinical trials in TB. The Department of Clinical Research conducts multicentric collaborative studies with Govt. and private Institutions across India. The department offers support to laboratory studies by facilitating sample collection.

The focus of research studies of the Department of Clinical Research is towards elimination of TB. In this context, the mandates of the department include undertaking Clinical trials and observational studies which focus on addressing determinants of TB, shortening TB treatment in drug sensitive and drug-resistant TB, effectiveness of adjunctive therapy in TB, evaluation of TB preventive therapy and vaccines in the prevention of TB. Strategic interventions for TB free Districts are planned to be undertaken. The department supports diagnostic studies which evaluates newer TB diagnostic tools and pharmacokinetic studies in establishment of drug estimation methods and determination of drug levels. The department conducts training as part of capacity building initiative in TB and research.

Studies in Progress

1. **Evaluate the effectiveness, safety and tolerability of various doses of Linezolid in combination with Bedaquiline and Pretomanid in Adults with Pre-Extensively Drug-Resistant (Pre-XDR), Or treatment Intolerant/Non-responsive Multidrug-Resistant (MDRTI/NR) Pulmonary Tuberculosis in India.**

Principal Investigator	:	Dr. C. Padmapriyadarsini
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis Sarvodaya Charitable Trust Hospital, Mumbai Shatabdi Centenary Hospital, Mumbai King's George Medical University (KGMU), Lucknow SN Medical College, Agra Govt. Medical College, Bhavnagar Govt. Medical College, Surat NITRD, New Delhi RBIPMT, Delhi Govt. Rajaji Hospital, Madurai
Source of funding	:	UNION (iDefeat project)
Study period	:	2021 - 2024
Category	:	Development
Pillar	:	Treat

Background

Early diagnosis, prompt treatment initiation, and completion of treatment play a vital role in Drug Resistant -TB management. Currently, longer regimens with injectables and toxic drugs often lead to poor drug adherence and poor treatment outcomes. Modified BPaL (mBPaL) study is proposed with varying doses of Lzd along with Bdq and Pa as planned reduction of Lzd for the treatment of Pre-XDR and MDRTI/NR pulmonary TB patients for 26-39 weeks. Given the poor tolerability and increased frequency of dose interruption in regimens containing Lzd, this trial will help us in deciding the effective dosing of Lzd to be given with Bdq and Pa for a fully oral short-course regimen to treat highly drug-resistant TB in the field setting.

Objectives

To determine the effectiveness of various doses and duration of Linezolid in combination with Bedaquiline and Pretomanid after 26 weeks of treatment in adults with either Pre-Extensively Drug-Resistant (Pre-XDR) OR Treatment Intolerant / Non-responsive multidrug-

resistant ($MDR_{TI/NR}$) Pulmonary Tuberculosis.

Methods

This is a multicentric, randomized pragmatic clinical trial to establish the study objective. The treatment arms will receive Bdq and Pa along with different dosing of Lzd – Arm 1 will receive Lzd 600mg for 9 weeks followed by 300mg for 17 weeks while Arm 2 will receive Lzd 600mg for 13 weeks followed by 300mg for 13 weeks. The control group will receive Bdq, Pa, and Lzd 600mg daily for 26 weeks. The primary endpoint is the proportion of patients with favorable outcomes in terms of cure and treatment completed while the secondary endpoints include unfavorable outcomes comprising of deaths, treatment failure, and loss to follow-up. Safety and tolerability of the various combinations along with TB recurrence will be recorded till 48-weeks post-treatment.

Study progress

A total of 403 persons with pulmonary Pre-Extensively Drug-Resistant (Pre-XDR) OR Treatment Intolerant/ Non-responsive multidrug-resistant ($MDR_{TI/NR}$) Pulmonary Tuberculosis patients were enrolled in New Delhi, Gujarat, Mumbai, Lucknow, Agra and Madurai sites. Participant recruitment was completed and they are on post treatment follow up. Of 403 patients enrolled, 255 (63%) were <30 years old, 273 (68%) had prior tuberculosis episodes, and 238 (59%) were malnourished. At the end of treatment, after excluding those with negative baseline cultures, cure was seen in 120 (93%), 117 (94%), and 115 (93%) in arms 1, 2, and 3 respectively. Myelosuppression seen in 85 patients each in arms 1 and 2 and 77 patients in arm 3, not significantly different. Peripheral neuropathy was noticed in 66 patients (30, 17, and 19 in arms 1, 2, and 3) at 10–26 weeks (P = .02). The linezolid dose was reduced because of toxicity in 13, 2, and 4 patients in arms 1, 2, and 3, respectively.

2. Accelerating efforts to END TB in India (AccEEnd TB)

Principal Investigator	:	Dr. R. Balaji
Participating Institutes	:	All ICMR institutes
Source of funding	:	ICMR ITRC
Study period	:	2022 – 2024
Category	:	Delivery
Pillar	:	Build

Background

Despite the efforts of National Tuberculosis Elimination Program (NTEP) and presence of guidelines for TB and MDR-TB, implementation challenges exist. To achieve the goal of TB elimination by 2025 in India, all partners need to join hands and support the NTEP to intensify the current strategies, adopt promising tools and implement them. Additionally, there is a need for new innovations for intensifying case finding, making available simpler diagnostic methods, shorter treatment regimens, as well as easy & widely available TB screening tools.

Objectives

Primary:

1. To assess the effectiveness of a comprehensive intervention package in reducing the incidence of TB disease in the selected districts
2. To support NTEP in accelerating TB elimination at district level by promoting early case detection, treatment adherence, contact tracing and preventive therapy through the intervention package

Secondary:

1. To screen and initiate ATT for all chest symptomatics / abnormal X ray diagnosed for MTB with molecular test in the community
2. To initiate TPT for all contacts of TB patients and high risk population
3. To assess the feasibility of providing new shorter all-oral regimens in the selected districts

Methods

Proposed Interventions:

ICMR along with CTD, NTEP launched an implementation research project in all districts of India. The project will focus on the intensifying the following 6 interventions as a comprehensive intervention package:

1. Screening and treatment of TB close to home.
2. Identification of all Contacts and Provision of TPT.
3. Use of short course regimes for DSTB and DRTB patient management as soon as approved regimens become available.
4. Providing nutritional supplementation:
5. Psychosocial Support:
   Address / Counselling on
   - Smoking cessation
   - Alcohol cessation
   - Treatment adherence and completion
   - Mental health
6. Intensify IEC activities: Create and Strengthen Awareness on Presentation of TB Early screening (especially in vulnerable groups) Prompt initiation of treatment Prevention of TB and Health seeking

Study progress

- Study is ongoing in 24 districts
- More than 12 lakhs people are screened for TB symptoms
- More than 1200 TB patients diagnosed are initiated on the treatment
- Contacts of TB patients are being line listed and initiated on shorter TPT regimen
- IEC and Psychosocial support is provided simultaneously

3. Prevalence of cardiopulmonary perfusion defects and vascular damage among Post- COVID-19 patients using Q-SPECT/CT hybrid imaging and correlation with biomarkers for prognostication – a longitudinal study (POCOS)

Principal Investigator	:	Dr G. Narendran, Scientist F
Participating Institutes	:	ICMR-National Institute for Research In Tuberculosis(NIRT) Tamil Nadu Government Multi Super Speciality Hospital (TNGMSSH), Chennai Sree Guru Heart Clinic, Chennai Institute of Thoracic Medicine, Chennai Madras Medical College, Chennai Mehta's Hospital
Source of funding	:	ICMR – Call for COVID-19 proposals
Study period	:	2022-2024
Category	:	COVID-19, Description
Pillar wise	:	Detect

Background

Cardiopulmonary sequelae continue to affect the survivors of the acute phase of COVID-19 illness even after recuperation. A visual understanding of the extent and consequence of the disturbed vascular topography of the cardiopulmonary tree could provide vital information that ultimately decides the need for post-COVID-19 surveillance

Objectives

Primary Objective

To estimate the proportion of vascular defects in the cardiopulmonary tree and structural changes in the lung parenchyma by Q-SPECT during the post/ long COVID period among patients with minimal (Mild) and advanced covid disease (Moderate +severe) at the time of initial COVID disease,

Secondary objectives

- To determine if these vascular defects form a prelude to defining clinically overt events of cardio-pulmonary vascular insufficiency in future demanding medical intervention, by following them for one year from COVID-19 onset.
- To ascertain if biomarkers could function as a surrogate, providing early clues towards plausible deterioration subsequently.

To correlate if the severity of initial presentation (acute phase of COVID-19) has a bearing on the presentation and severity of post-COVID-19 sequelae after adjusting for comorbidities

Methods

Post-COVID-19 patients from the first and second wave of COVID would be categorized into minimal (mild), and advanced (moderate + severe) disease based on initial COVID-19 presentation as per guidelines. Using a longitudinal observational cohort of post-COVID-19 patients segregated into minimal and advanced disease, clinical evaluation, cardio-pulmonary vascular defect evaluation using QSPECT/CT hybrid for occult vascular insufficiency in the cardio-pulmonary bed will be done. In addition, ECHO, cardiac markers and immunological markers will be done to validate if these could act as surrogate markers for the QSPECT

Study progress

Of 151 participants enrolled, 27.2% had breathlessness, 21.2% had fatigue, the major symptoms, after a median post covid period of 370 days in the mild, 427 days in the severe variety. Perfusion defects were relatively common irrespective of the severity, and analysis is ongoing to see the progression of these defects

The Echocardiographic features are being compared with the perfusion imaging to arrive final conclusions

4. The Regional Prospective Observational Research for Tuberculosis (Report) India Phase II Common Protocol

Principal Investigator	:	Dr Bhavani P K.
Participating Institutes	:	JIPMER, BMMRC, PGI, CMC, MVDRC, BJMC
Source of funding	:	Department of Biotechnology
Study period	:	2021 – 2026
Category	:	Discovery, Development & Description
Pillar	:	Build and Treat

Background

India ranks number one in global tuberculosis (TB) burden and accounts for 26% of all cases—2.7 million occurring annually. Furthermore, 27% of India's 1.3 billion population is estimated to be latently infected with Mycobacterium tuberculosis (Mtb) and at risk of developing active disease. The World Health Organization (WHO) and the Indian government have an ambitious goal to eliminate TB within 20 years. To accomplish this, new TB research is needed, including development of rapid, sensitive, low-cost diagnostics; identification of biomarkers to assess TB treatment response and risk of developing disease; and deeper understanding of TB immunology and pathogenesis to inform vaccine development.

Recognizing these needs, the Regional Prospective Observational Research in Tuberculosis (RePORT) India was jointly established in 2013 by the Government of

India's Department of Biotechnology (DBT) and the U.S. NIH, under the Indo-US Vaccine Action Program and is now the largest of 6 NIH-supported TB research consortia. RePORT India's mission is to: 1) Advance regional TB science in India; 2) Strengthen TB research capacity and infrastructure; 3) Foster research collaboration within and with India focused on research that can lead to clinically important biomarkers, vaccines, drugs, and diagnostics.

Objectives

AIM 1. DIAGNOSTICS: Evaluate Novel Diagnostics & Biomarkers of Diverse States of Mtb Infection

AIM 2. MARKERS OF TREATMENT RESPONSE:

2.A: Identify TB Treatment Response Biomarkers

2.B: Investigate Host-Related Mechanisms of Treatment Failure

2.C: Investigate Pathogen-related Mechanisms & Predictors of Recurrence

AIM 3. LUNG INJURY & IMPAIRMENT: Identify Markers of Lung Injury Associated with Unfavorable TB Treatment Outcomes.

AIM 4. RESISTANCE TO INFECTION: Mechanisms of Protection against TB in Exposed Persons

4.A: Examine Host Antimicrobial Pathways in Inducing their infection resistant (IR) Phenotype in HHC

4.B: Test if IR & Plasma Differ in Modulating Macrophage-Mediated Restriction of Mtb Growth & Evaluate AB Repertoires of Plasma from the IR and infection susceptible (IS) Cohorts

AIM 5. PROGRESSION TO DISEASE: Identify Immunologic Markers of Persons at Highest Risk of Progress of Latent TB Infection to TB.

5.A: Stored Samples: Validation of PREDICT29 in Progressors & Nonprogressors from RePORT Sites

5.B: Immune & Hormone Studies in Freshly Collected Samples.

Methods

1) Establishment of three prospective, observational cohorts for collection of specimens and associated data; and

2) Analysis of stored specimens and associated data.

Population: Adult and child Participants from India will be enrolled into one of three prospective, observational cohorts:

- Diagnostic (Dx) Cohort: participants with suspected TB (all age groups)
- Cohort A: active TB patients (≥18years)
- Cohort B: household contacts (HHCs) of adult (≥15years) active PTB patients (all age groups)

Study Size: Total

New enrollments include:

- Dx Cohort: 780 TB suspects
- Cohort A: 660 adult (≥18years) pulmonary Tuberculosis (PTB) participants
- Cohort B: 894 household contacts of adult (≥15years) PTB patients

Study Duration:

- Dx Cohort: 2 months
- Cohort A: Approximately 18 months for Drug-susceptible TB cases and approximately 36 months for drug-resistance cohorts (duration of TB treatment and 12 months post-treatment).
- Cohort B: 24 months

Study progress

Study Target – Cohort A – 90; Diagnostic Cohort – 150

Participants screened:

Cohort A – 253 participants;

Diagnostic Cohort: 140

Participants recruited: Cohort A – 88 participants;

Diagnostic Cohort (Adult): 42

Drop out 1 due to emergence of drug resistance.

Study is on-going

5. Multi-centric prospective cohort study of TB recurrence-free cure among microbiologically confirmed new pulmonary tuberculosis patients treated under NTEP with the 4-month moxifloxacin-containing daily regimen.

Principal Investigator	:	Dr. V.V. Banu Rekha, Scientist F
Participating Institutes	:	ICMR, Govt. and Private Institutes across India
Source of funding	:	ICMR-ITRC
Study period	:	2022-2025
Category	:	Development
Pillar	:	Treat

Background

Earlier randomised clinical trial conducted by ICMR-NIRT showed promising results with a TB recurrence rate of 4.1% using the 4-month moxifloxacin-containing daily regimen (2HRZEM $_7$ / 2HRM$_7$). Effective shorter TB treatment regimens are beneficial to both the patients and health system.

Objectives

To determine the TB recurrence-free cure rate among microbiologically confirmed new drug-sensitive PTB patients treated under the TB Program with the 4-month moxifloxacin-containing daily regimen (2 HRZEM $_7$ / 2HREM$_7$).

Methods

In this multicentric, single-arm study, eligible adult microbiologically confirmed PTB patients sensitive to isoniazid, rifampicin and quinolone will receive 2 months of HRZEM followed by 2 months of HREM daily (2 HRZEM $_7$ / 2HREM$_7$). Tab. Moxifloxacin 400mg will be given along with the weight-based Fixed dose Combination (FDC) of HRZE. The enrolled patients will be followed up every month during treatment and 2 years post-treatment. Sputum examination will be done during follow-up for response to treatment and for TB recurrence. In addition, drug adverse events will be documented.

Study progress

The recruitment to the study was completed in April 2023 with 557 patients. All the patients have completed treatment. The follow-up is ongoing.

6. A Phase III, Randomized, Double-blind, three arm Placebo controlled study 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

Principal Investigator	:	Dr. V.V. Banu Rekha, Scientist F
Participating Institutes	:	ICMR, Govt. and Private Institutes across India
Source of funding	:	ICMR-ITRC
Study period	:	2019-2024
Category	:	Development
Pillar wise (Discovery, Development, Delivery, Description)	:	Prevent

Background

Research for newer vaccines for tuberculosis (TB) is essential to achieve the End TB targets. Prevention of TB among household contacts of sputum smear-positive pulmonary TB (PTB) patients is crucial since they are at high risk for contracting TB. VPM 1002 is a recombinant BCG vaccine from Serum Institute and Immuvac is a heat killed suspension of Mycobacterium W from Cadila Pharma

Objectives

To evaluate the efficacy and safety of VPM1002 and Immuvac in comparison to placebo among healthy household contacts of newly diagnosed sputum positive PTB patients.

Methods

The Phase III, double-blind, multicentric, randomized clinical trial is being conducted across India and in ICMR-NIRT sites in Chennai, Thiruvallur, Tambaram, Madurai and Vellore. HIV sero-negative household contacts aged $\geq$ 6 years, with no evidence of TB disease are randomized to receive intra-dermal VPM1002, Immuvac or placebo. The first dose (0.1ml) is administered in both upper arms at baseline and the second single dose (0.1ml) is given in the right or left arm at one month. Participants are followed up once fortnightly during initial 2 months and thereafter once in 4 months for development of TB disease over a follow-up period of 3 years. Solicited and unsolicited adverse events are documented.

Study progress

The enrolment to the trial was completed in December 2020. A total of 2214 household contacts were enrolled and vaccinated. The follow-up of enrolled household contacts was completed in March 2024. The data analysis is ongoing.

7. Smoking Cessation among TB patients in Madurai district Corporation centres: aiding TB free Madurai

Principal Investigator	:	Dr. S. Ramesh Kumar, Scientist F (Medical),
Participating Institutes	:	Deputy Director Health Services (DDHS), Madurai district; Cancer Institute, Adyar, Chennai; Department of Respiratory Medicine and Department of Psychiatry, Madurai Medical College
Source of funding	:	Partly funded by ICMR intramural, partly funded (Trainings) from Deputy Director Health Services (DDHS), Madurai district (Implementation Agency for Smoking Cessation activities in Madurai district)
Study period	:	2023 to 2025
Category	:	Delivery
Pillar	:	Prevent

Background

TB burden and tobacco smoking burden high in India. Patients with TB and smoking have more respiratory symptoms, more hospitalizations, more relapse, more death rates; associated with INH resistance; MDR TB. Smoking cessation in TB patients improves TB outcome; importantly reduces the burden of NCD due to smoking. NIRT Operational study on Smoking cessation strategy study among TB patients established the effectiveness of smoking cessation interventions namely Bupropion SR or Enhanced counselling at field level. We propose to deliver these smoking cessation strategies to TB patients attending NTEP centres, Madurai district, aid them in quitting smoking, may have better TB treatment outcomes

Objectives

To estimate the quit rate when the smoking cessation interventions namely Bupropion SR or Enhanced counselling offered to TB patients who are smokers in Madurai district and assess whether that aids in improving TB free indicators in Madurai.

Methods

Study design: Prospective Cohort Study

Study Population:

All adult pulmonary TB patients started on TB treatment at NTEP centres, Madurai district, with H/O of current smoking during the study period. We will exclude Children, too sick and moribund status in providing any of the smoking cessation intervention. Those with Seizure disorder or past history of psychiatric illness, Bupropion S R will not be given.

Study procedure:
The intervention will be delivered by the Medical Officer of the PHC/ Health care worker (MLHP/HI) for Drug and Enhanced counselling respectively
The interventions given to be recorded in existing NTEP records (TB Rx card, mentioning missed dose if any).
Those requiring intensive treatment appropriate referrals to Psychiatric Department, GRH, Madurai
This group of pulmonary TB patients started on TB treatment at NTEP centres for whom the intervention given will be the study intervention cohort where our intervention is not provided ,(but standard of care given) will be the Control group.Quitting smoking will be assessed by Self reporting and Carbon monoxide monitoring tests at 2nd month and at end of ATT, and at 9th month and year one Prior training and sensitization on prescribing Bupropion SR for smoking cessation for the NTEP Medical Officers will be done
Prior Training and sensitization on Enhanced counselling delivery for the health care workers will be done.

Study progress
The study has two phases
1. Training Phase, and 2. Study subjects recruitment phase
Training phase:
Training the Health Care Workers for Smoking Cessation strategies 2 steps:
1. General: General training of all Health Care workers (including MLHPs/HIs) in Smoking Cessation (done in collaboration with Cancer Institute Adyar) completed in August 2023
2. Focused training: The training of the Health Care workers, focused in Smoking Cessation for TB patients (Enhanced Counselling intervention of the study) by NIRT is now being conducted in small groups at the respective sites (Schedule of events coordinated with DDHS) are in progress.

8. Predictors of unfavourable treatment outcomes and emerging drug resistance among patients started on drug regimen for isoniazid (INH) mono-resistant pulmonary TB under NTEP

Principal Investigator	:	Dr Leeberk Raja. I, Scientist E
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis (NIRT) & State TB cell
Source of funding	:	ICMR Intramural
Study period	:	2023 – 2025
Category	:	Delivery
Pillar	:	Treat

Background

Isoniazid mono-resistance is the most common type of drug-resistance in TB. It reduces the treatment success and increases the risk of acquiring additional drug resistance such as rifampicin and fluroquinolones. Isoniazid resistance is 11.06% and 25.09% among new and previously treated TB patients respectively in India. Studies across the globe have reported unfavourable outcome rates of 7-44% among these patients treated with first line drugs. There is a paucity of literature on the exact estimation on the incidence of multi drug or emerging resistance among patients detected to have INH resistance. Similarly, genetic variations when there is a bacteriological reversion after the conversion has not been studied yet.

Objectives

1. To identify predictors for unfavourable treatment outcomes in patients among patients with pulmonary TB who initiated on treatment regimen for INH mono resistance under NTEP in the state of Tamil Nadu and Kerala.
2. To explore emerging drug resistance among patients treated for INH monoresistant pulmonary TB.
3. To describe genetic traits and compare the lineage of *M.Tuberculosis* isolate before and after bacteriological reversion using WGS

Methods

All newly diagnosed pulmonary TB patients initiated on treatment regimen for INH mono resistance under NTEP will be approached. Patients with additional resistance for rifampicin or fluroquinolones will be excluded. Demographic details and sputum sample will be collected at the baseline. Subsequently, sputum samples are collected during month 2, 3 and 6 during the treatment and month 3, 6, 9, 12 post-treatment. During the follow up, details regarding change of regimen, adverse events and TB recurrence are collected. The samples will be sent for smear, first and second line LPA, culture and DST. In case of TB recurrence, whole genome sequencing will be performed and compared with the baseline sample.

Study progress

We screened 1053 individuals with INH mono-resistant pulmonary tuberculosis and enrolled 847 participants across 11 districts in Tamil Nadu and they are currently being followed up.

9. Role of Vitamin C supplement as an adjunct to tuberculosis treatment in new smear sputum positive pulmonary tuberculosis – An exploratory trial

Principal Investigator	:	Dr. D. Bella Devaleenal
Participating Institutes	:	ICMR -NIRT
Source of funding	:	ICMR -intramural
Study period	:	2022 – 2024
Category	:	Development
Pillar	:	Treat

Background

Vitamin C in combination with pyrazinamide was shown to promote bacterial clearance by current first line TB drugs. This effect was demonstrated not only in in-vitro cultures but also in a cell infection model. Cells exposed to vitamin C maintain homeostasis and boost host immune defence functions. Therefore, vitamin C can be seen to modulate two key determinants of TB drug efficacy, namely host factors and antibiotic efficacy in bacteria, offering a unique opportunity to assess its utility in adjunctive therapy for shortening the duration of treatment.

Objectives

1. To understand the Pharmacokinetic profile of Vitamin C and ATT (HRZE) when co administered among new smear positive patients
2. To determine the time to sputum culture conversion when Vitamin C 500mg is given once daily/ twice daily along with the standard first line anti-TB treatment (HRZE) for 8 weeks duration in drug sensitive new sputum positive pulmonary TB patients.

Methods

This is a phase 2b randomized (open-label) parallel arm controlled clinical trial done among new smear positive pulmonary TB patients with drug sensitive TB diagnosed in NTEP centres in Chennai Corporation. The participants were randomized to any one of the following arms

Arm 1: HRZE + Vitamin C 500mg OD for 8 weeks/4 HRE

Arm 2: HRZE + Vitamin C 500mg BD for 8 weeks/4HRE

Arm 3: HRZE (Control arm) for 8 weeks/4HRE

Plasma vitamin C will be analyzed by reverse phase HPLC method and the levels will be measured at baseline (before inducting into the study arm), week 1, at the end of intensive phase (i.e. 8^{th} week) and at the end of treatment. The primary endpoint will be the time from treatment initiation to the first of the two consecutive negative sputum cultures without an intervening positive culture in MGIT culture within the first 8 weeks.

Study progress

The study is ongoing and a total of 45 participants were recruited for the trial.

10. Impact of malnutrition on immune responses to tuberculosis in Indian Children

Principal Investigator	:	Dr Aishwarya Venkataraman
Participating Institutes	:	Institute of Child Health, Madras Medical college Stanley Medical college, Chennai Kanchi Kamakoti Child Trust Hospital, Chennai
Source of funding	:	DBT
Study period	:	2019 – 2024
Category	:	Discovery, Description
Pillar	:	Prevent

Background

Malnourished children have an elevated risk of mortality from infections like TB. It is likely that this increased mortality is due to immunodeficiency caused by undernutrition; however, immune function in malnourished children has not been well characterised to date. Although the WHO states that malnutrition is a contributing factor for childhood TB, there are limited studies to explain the mechanisms underlying this association. There is therefore a strong impetus to better understand the immunology of malnutrition and childhood tuberculosis and more collaborative studies are urgently needed, specifically on how nutritional status affects the risk and progression of tuberculosis and whether nutritional intervention improves clinical outcomes or prevents TB disease.

Objectives

Aim 1: Characterise innate and T-cell immune responses to Mycobacterium tuberculosis (Mtb) in moderately malnourished and well-nourished children with tuberculosis (TB) disease.

Aim 2: Characterise innate and T-cell immune responses to Mtb in moderately malnourished and well-nourished children with latent TB infection (LTBI).

Aim 3: Assess the impact of a nutrition intervention on immune responses to Mtb in children with malnutrition.

Methods

Four groups of BCG-vaccinated, HIV-uninfected children (total 200), age 6-59 months, stratified by age (6-11months, 12-23 months and 24-59 months), were recruited from the TB and nutrition clinics following caregiver informed consent. Differences in innate and adaptive immunological responses to Mtb are analysed and compared between four groups: 1) malnourished children with tuberculosis (TB) disease; 2) well-nourished children with TB disease; 3) malnourished children with TB exposure; and 4) well-nourished children with TB exposure. The longitudinal changes in innate and adaptive immune function, monocyte - lymphocyte ratio, and mycobacterial growth inhibition are evaluated by following children in all

four groups during a six-month period of TB therapy/chemoprophylaxis, with malnourished children receiving a 12-week supply of ready-to-use supplementary food.

Study progress

Currently analysing data and manuscript writing. A total of 119 children with TB exposure (61 – malnourished and 58 – well nourished) and 49 children with TB disease (18 – malnourished and 31 – well-nourished have been included in the study. Immunological and blood cell parameters will be compared between the groups.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1	A longitudinal observational study on the impact of SARS-CoV-2 infection on TB disease and treatment outcome in children	Dr Aishwarya Venkataraman, Scientist E (Medical)	NIH-NIRT-ICER intramural funds	Discovery, Description	A longitudinal observational study investigates how SARS-CoV-2 infection influences the clinical progression and treatment outcomes of tuberculosis in children. It aims to uncover potential interactions between COVID-19 and pediatric TB that could inform future management strategies. Manuscript submitted
2	Serial inflammatory responses in children receiving different treatment regimen for Multisystem Inflammatory Syndrome (MIS-C) - Longitudinal observational study from Southern India	Dr Aishwarya Venkataraman, Scientist E (Medical)	NIRT intramural funds	Discovery, Description	This longitudinal observational study from Southern India examines serial inflammatory responses in children with MIS-C receiving different treatment regimens. It aims to identify patterns that could guide optimized, evidence-based therapeutic strategies. Manuscript submitted
3	Acceptability and feasibility of Mobile app in Adverse Drug Reactions (ADRs) reporting in Revised National Tuberculosis Control Program (RNTCP) centres	Dr. S. Ramesh Kumar, Scientist F (Medical)	ICMR-Intramural	Delivery	Adverse Drug Reactions (ADRs) reporting using 'PvPI ADR reporting App' of Govt of India in the NTEP centres is possible, but feasibility of filling the details in the app by the doctors during the duty hours is not easy

SOCIO - BEHAVIOURAL STUDIES

DEPARTMENT OF SOCIAL AND BEHAVIORAL RESEARCH

DEPARTMENT OVERVIEW AND MANDATES

The Department of Social and Behavioral Research (DSBR) is central to the vision and mission of ICMR-NIRT. DSBR provides crucial support in clinical trials conducted at ICMR-NIRT and other research studies that require effective patient support. The department has conducted numerous social and behavioural studies on TB and HIV at both state and national levels, which have significant policy implications. The department conducts qualitative and quantitative research to evaluate the psychosocial factors influencing TB patients' health-seeking behaviours, treatment adherence, and treatment completion.

DSBR has carried out intervention trials to assess the effectiveness of psychosocial interventions for TB and HIV vulnerable groups. Additionally, the department has implemented operational and implementation research projects for TB at both national and sub-national levels, contributing to various aspects of the NTEP program. DSBR has developed various research tools, intervention materials, and findings, actively shared with policymakers and stakeholders to help translate research outcomes into practical applications. Alongside its research contributions, DSBR is recognized for its active community outreach efforts targeting vulnerable populations affected by TB and HIV. The department regularly organizes Information, Education, and Communication (IEC) interventions for various segments of society to enhance community knowledge, attitudes, and practices related to TB prevention, diagnosis, and treatment. DSBR recently initiated Wings of Support and Nikshay Mitra intervention, which have supported TB patients and family members with nutrition and psycho-social support.

Studies in Progress

1. An integrated psycho-social intervention to improve self-efficacy towards treatment uptake and infection prevention among patients and family caregivers – A multi-centric implementation research study

Principal Investigator	:	Dr. Karikalan, Scientist-C & Head, Department of Social and Behavioral Research, ICMR-NIRT Dr. D. Bella Devaleenal, MBBS, DLO, MPH Scientist E, Dept. of clinical Research ICMR- NIRT
Participating Institutes	:	National Institute for Research in Tuberculosis, Chennai, India
Source of funding	:	ICMR Intramural, Indian Council of Medical Research (ICMR), New Delhi
Study period	:	24 months
Category	:	Delivery
Pillar	:	Treat

Background

The ability of TB patients and caregivers to overcome the multi-dimensional challenges they face is affected by their self-efficacy or their motivation. Interventions to address and improve the self-efficacy of TB patients and their caregivers in the context of TB prevention and treatment uptake are absent in India.

This study aims to adapt and evaluate a self-efficacy-driven intervention to holistically address the multi-dimensional treatment and disease-related challenges experienced and perceived by TB patients and their caregivers. The proposed intervention is based on self-efficacy constructs in which the patients and caregivers are intervened to "enable them to execute their courses of actions, behaviours and self-management skills to effectively deal with challenges and needs of TB disease and treatment". The intervention will incorporate the caregivers of patients as a participant in the intervention in a systematic way and thus would be the first study to use a comprehensive theory-driven intervention that would mutually address the challenges and burden of the patient and their family caregivers.

Objectives

Primary Objectives:

1) To adapt and evaluate the efficacy of a self-efficacy-driven intervention in comparison to the standard of care on primary outcomes: i) improved TB treatment self-efficacy and secondary outcomes ii. improved medication

adherence iii TB stigma & iv improved infection control self-management practices.

2) To evaluate the efficacy of a self-efficacy-driven intervention in comparison to the standard of care on secondary outcomes: improved caregivers' self-efficacy and secondary outcomes i: decreased TB stigma and improved infection control self-management practices

Methods

The study employs a Hybrid 1 effectiveness implementation design to evaluate the preliminary efficacy together with the implementation acceptability of delivering a self- efficacy driven intervention by front line health care staff of NTEP, family care providers and patient champions for improving treatment self-efficacy, decreased stigma improve mental health and infection control self-management practices. The study includes prospective quantitative and qualitative assessment of the proposed intervention. In line with a hybrid effectiveness-implementation design, longitudinal qualitative data will be collected to evaluate intervention effects in triangulation with the quantitative designs. The intervention will be compared to the enhanced standard of care which would involve brief counselling and IEC activities. Participants are enrolled from NTEP facilities in the selected health facilities of TB treatment units of Tamil Nadu in which treatment completion rates (<80%) are low and/or unfavorable treatment outcome (death rate and loss to follow up rate >5%). Chennai, Tiruvallur and Kancheepuram districts are prioritized for Tamil Nadu.

Study progress

The project after obtaining the Institutional Ethics Committee approval began with the preliminary activities such as seeking permission from the state TB cell, the Department of Public Health and other collaborating institutes namely GHTM and ITM. Followed by which study districts namely Chennai, Kancheepuram and Tiruvallur were designated. In consultation with the selected district TB officers study tuberculosis Units were selected. The study team was involved in collecting the patient line list from the selected TU's this was done to ascertain the caseload in each selected TU. The study team was provided with orientation training about the project. Nearly 100 TB patients along with their care givers are enrolled in the study.

2. A peer lead discussant approach to improve TB literacy among transportation workers and to create demand for TB-related information in the community – A quasi-experimental study to study the effectiveness".

Principal Investigator	:	Mrs Chandra Suresh, STO-3, DSBR-ICMR NIRT
Participating Institutes	:	National Institute for Research in Tuberculosis, Chennai, India
Source of funding	:	Departmental funding
Study period	:	2022 to 2024
Category	:	Delivery
Pillar-wise	:	Prevent

Background

Public transportation may serve as a potential pathway for TB transmission due to overcrowding and poor ventilation. There is an unmet need among transportation workers for increased awareness and knowledge about TB who are at increased risk of airway transmission of infection. On the other hand, public transportation is also used by people from different socioeconomic, demographic, and geographical backgrounds and provides an opportunity for engaging with a large volume of the population. This opportunity for public transportation workers to engage with lakhs of passengers every day could be utilised for demand generation for TB related information among the public.

Objectives

1. To assess the outcomes of transport ambassador lead community engagement strategy in improving TB literacy among co-transportation workers in Chennai
2. To assess the outcomes of transport ambassador lead community engagement strategy in increasing the demand for TB literacy among passengers in Chennai

Methods

A quasi-experimental design with pre and post-test to assess the impact of the intervention (TB-IEC tickets). The study population are MTC Bus Drivers and Conductors. The study is carried out in Chennai among drivers and conductors employed under MTC and the bus commuters.

Study progress

In the first preparatory phase of the study, line listing of the bus depots and deciding on sample frame was done. Baseline survey on TB literacy at depot level was collected. TB literacy session was organized at deport level covering basic details about TB and orientation about the ticket distribution was provided. Survey includes details on willingness of conductors to serve as ambassadors and issue tickets to the commuters. Nearly 800 drivers and conductors have been reached in this phase of the study.

3. An innovative approach for engaging student and women organizations in Tuberculosis case finding and Treatment adherence: A step toward Tuberculosis elimination in Senapati District Manipur.

Principal Investigator	:	Dr. A. Stephen, Scientist C
Participating Institutes	:	Rajendra Institute of Medical Sciences (RIMS), Manipur
Source of funding	:	ICMR Extramural
Study period	:	2023-2024
Category	:	Delivery
Pillar	:	Detect

Background

India is heading towards achieving the elimination goal of TB by 2025, however the undiagnosed TB cases still stand a challenge. Further, the tribal in general are highly vulnerable to several health risks including TB. For this, the Government of India has come up with National Strategic Plan (NSP) 2017-25 to address this high-risk group and recommended active case finding (ACF) among high-risk groups as a strategy to detect the "missing" TB patients. However, a North-Eastern (NE) state of Manipur has not conducted separate ACF activity, as it requires a lot of manpower to carry out the activities specially to reach hard-to-reach areas as the settlement of the people are widely scattered, especially where tribal people are inhabited. Therefore, a model/demonstration project will be carried out in a tribal dominated, hilly / hard-to-reach Senapati district of Manipur to identify additional human resources at the community level, to improve TB case finding rates, treatment adherence and completion rates by engaging student and women organizations in comparison to routine program strategies.

Objectives

To determine the incremental increase in TB case finding rates, treatment adherence and completion rates by engaging student and women organizations in comparison to routine program strategies.

Methods

The study is being carried out using quasi experimental pre-post design in the whole district of Senapati, Manipur. The study is done in 2 phases, preparatory phase and intervention phase. Preparatory phase included identification of volunteers, training, door to door enumeration and TB awareness campaign (1-3 months), Intervention phase include 2 rounds of TB symptom screening (4^{th} and 10^{th} month) from door to door. Data is

collected using REDCap hosted at ICMR-NIRT. Quarterly TB case notification data is collected from the baseline period up to the end of the intervention. Trends in PHI/PHCs/CHCs/ DTC specific TB case notifications, adherence and treatment outcome will be analyzed.

Study progress

Since project initiation in February 2023, 594 volunteers have been trained of which 371 active volunteers are carrying out the activities. Of the 189 villages Household Enumeration (HHE) has been completed in 182 villages covering 38140 eligible populations. In the first round of TB symptom screening covering 29977 populations, and 539 (1.8%) were identified as presumptive TB cases. Of the 539 presumptive TB cases 93 TB-positive cases were identified and initiated on treatment.

In the second round of TB screening of the 38140 completed HHE populations of which 16230 completed screening, 72 (0.44%) were presumptive TB cases. A total of 148 cases identified through the study, 143 were initiated on treatment in NTEP.

4. Unmet needs and coping strategies of family caregivers of persons with TB– an exploratory mixed method study – an exploratory mixed method study

Principal Investigator	:	Ms. Priscilla Rebecca M.Phil, Technical Officer
Participating Institutes	:	National Institute for Research in Tuberculosis (ICMR), Chetpet, Chennai-31.
Source of funding	:	Departmental funding
Study period	:	2023-2024
Category	:	Delivery
Pillar	:	Prevent

Background

The involvement of the family is essential in the treatment of pulmonary tuberculosis. Support and attention from the family can help in the fight against TB. Family caregivers are often the primary providers of care for persons with TB, and their involvement can have a significant impact on the person’s treatment outcomes. Family caregivers are a part of the healthcare system; therefore, the assistance they give improves the quality of life for those receiving care while saving costs for the healthcare system. Although research on the aspects of family caregiving has been conducted in chronic disease contexts, still caregiving for TB has not been assessed from a research perspective. There is a need to explore and understand the caregiver's side of psycho-social challenges and needs in the TB context. Also, there is a need to quantitatively measure the economic value of caring for TB.

Objectives

Primary objectives:

1. To understand the experiences, psycho-social challenges, and barriers faced by family caregivers in fulfilling their caregiving responsibilities for persons with TB.
2. To identify the coping mechanisms, strategies, and support systems that family caregivers employ to navigate their caregiving roles for persons with TB.
3. To measure and value the level of family care provided by the caregivers on a day-to-day basis.

Methods

This study employs a mixed methods research design, allowing for an in-depth exploration of the subjective experiences and perspectives of family caregivers and quantitative assessment for measuring, and valuing care.

Qualitative exploration will include serial In-depth interviews (IDIs) with caregivers and patients at two time points aiming to explore and describe the day-to-day experiences of family caregivers, challenges, and barriers faced, coping mechanisms and support systems of caregivers. Patients' perspectives of the family caregivers' attitudes, perceptions, practices, and behaviour which they adopted, to overcome specific challenges faced during the treatment period in providing care.

Quantitative measures will include a diary to document the caregiving activity of the family member. The value of time spent in caregiving would be estimated.

Study progress

We have initiated patient enrolment for the quantitative component of measuring and valuing of caregiving provided. Five patients' caregivers have been enrolled in the study. Care givers were provided with diary to document the caregiving activities to the family member. Qualitative data collection conducted 2 in depth interviews with patients and their caregivers.

5. Reducing pre-treatment loss to follow-up among individuals diagnosed with TB through behavioural nudging intervention - A multi-centric mixed methods implementation study

Principal Investigator	:	Dr. Karikalan, Scientist-C & Head, DSBR
Participating Institutes	:	National Institute for Research in Tuberculosis, Chennai, India ICMR-National Institute for Occupational Health, Gujarat ICMR-RMRC, Bhubaneswar ICMR- NJIL& OMD, Agra
Source of funding	:	ICMR Extramural
Study period	:	2023-2024

Category	:	TB
Pillar-wise (Discovery, Development, Delivery, Description)	:	Delivery

Background

Pre-treatment loss to follow-up (PTLFU) remains a major gap in the TB patient cascade of care in India. PTLFU patients (who are diagnosed but have not initiated TB treatment immediately) remain infectious, experience poor treatment outcomes and suffer high mortality rates. As on 2020 about 6% of the notified patients have not initiated treatment for TB subsequently in India. There is a need for developing behaviour change interventions which could address patient level barriers and gaps which leads to PTLFU.

Objectives

1. To adapt a patient behavioral nudging intervention in NTEP facilities to address Pre-Treatment Loss to Follow up among newly diagnosed TB patients
2. To evaluate the incremental effectiveness of a patient behavioral nudging intervention in reducing PTLFU rates as compared to standard of care
3. Evaluate the implementation process of a behavioral nudging intervention from the perspective of patients, caregivers and health care provider's

Methods

4. This study will employ a hybrid two arm non-randomised cluster intervention design to evaluate the effectiveness and implementation process of delivering a patient behavioural nudging intervention by front line health care staff of NTEP

Study progress

The study has been approved by Institutional Ethics Committee (IEC) and is initiated, with the preliminary activities.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1.	Exploring and understanding the psycho-social factors enabling drug resistant patients to achieve better treatment adherence and completion-A qualitative study in Bengaluru and Hyderabad.	Dr. N Karikalan, Scientist C	USAID through Karnataka Health Promotion Trust (KHPT)	Development	Study was completed and article published in The Lancet Regional Health- Southeast Journal The present study provided opportunity to develop implementable self-driven solutions for PwDR-TB based on their positively deviant peers, which could be tested for their effectiveness using quantitative methods.
2.	Stigma and Disclosure Study – A sub-study on Capacity Building Project in TB Vaccine Trial	Dr. P. Murugesan Senior Technical officer-3	ICMR	Delivery	The study findings sheds light on stigma experiences and perceptions of index TB patients as well as vaccinated household contacts (HHC) who acquired TB during the TB vaccine trial. The study findings help in the understanding of coping strategies and traits made by TB patients, which will help in accelerating the creation of stigma reduction programs for future research and to eliminate TB in India by 2025.

LABORATORY STUDIES

DEPARTMENT OF BACTERIOLOGY

DEPARTMENT OVERVIEW AND MANDATES

The Department of Bacteriology supports clinical trials and operational research studies conducted at ICMR–NIRT, including the establishment of drug susceptibility testing (DST) for newer anti-TB drugs such as Pretomanid, Bedaquiline, and Delamanid. The department also contributes to TB prevalence studies, including the National TB Prevalence Survey and the Tamil Nadu District TB Prevalence Study. The laboratory is certified by the National Accreditation Board for Testing and Calibration Laboratories (NABL).

The department has established methodologies for testing both newer and repurposed anti-TB drugs. Molecular validation studies are being conducted on various in-country diagnostic kits. Additionally, whole genome sequencing (WGS) and targeted next-generation sequencing (tNGS) have been leveraged for the management of drug-resistant TB patients. A targeted next-generation sequencing approach using Nanopore technology is being explored as a comprehensive DST method with potential for point-of-care applications.

Diagnosing pediatric TB remains a challenge. To address this, the department is studying non-sputum-based diagnostic methods, such as stool and urine samples, which show promise for both molecular and culture-based diagnostics. Investigations are also underway to determine the critical concentrations of anti-TB drugs, including newer agents, in *Mycobacterium tuberculosis* isolates—this will aid in understanding pharmacodynamic indices.

A nationwide drug resistance survey (DRS) using next-generation sequencing technology has been initiated by the department. This effort is expected to enhance resistance prediction and support the study of transmission dynamics. The department is also part of the ICMR TB diagnostic network and participates in WHO Prequalification (PQ) evaluations for new TB diagnostic tools.

ICMR–NIRT serves as one of the National Reference Laboratories under the National Tuberculosis Elimination Programme (NTEP), providing technical support for TB laboratory activities across five states and five union territories in India. As a Supranational Reference Laboratory (SNRL), NIRT conducts External Quality Assurance (EQA) for culture and DST under the NTEP. These services are also extended to SEARO member countries, including Myanmar, Bangladesh, and Timor-Leste. Additionally, support was provided for conducting the national TB prevalence survey in Timor-Leste.

Under the Programmatic Management of Drug-Resistant TB (PMDT), the department provides line probe assays for first-line and second-line anti-TB drugs, non-tuberculous mycobacteria (NTM) testing, WGS services, and other diagnostic support for Tamil Nadu.

Studies in Progress

1. **Protocol for the performance evaluation of nucleic acid tests for the detection of drug resistance in *Mycobacterium tuberculosis complex* for WHO prequalification assessment.**

Principal Investigator	:	Dr. S Siva Kumar, Scientist D, Dept. of Bacteriology, NIRT
Participating Institutes	:	ICMR-NIRT
Source of funding	:	WHO PQ
Study period	:	2024
Category	:	Development
Pillar	:	Detect

Background

World Health Organization (WHO) prequalification of in vitro diagnostics (IVDs) is coordinated through the department of Regulation and Prequalification. Focus is placed on IVDs for priority diseases and their suitability for use in resource-limited settings. WHO prequalification of IVDs is a comprehensive quality assessment of individual IVDs through a standardized procedure aimed at determining whether the product meets WHO prequalification requirements

Objectives

To assess sensitivity and specificity for drug resistance detection using clinical specimens by comparing with a designated reference standard;

- To assess analytical performance: Limit of detection; Reproducibility; Inclusivity/exclusivity using a standardized panel of strains; Resistance detection using a standardized panel of strains; Cross-contamination or carry-over;

Methods

The panel for the clinical evaluation will consist of stored sputum specimens, concentrated sputum sediments and clinical MTBC isolates, as applicable according to validated specimen types. The panel will include at least 50 confirmed drug resistant (DR) TB specimens from individual patients for each of the drugs claimed in the instructions for use (IFU) and at least 100 confirmed drug susceptible specimens from individual patients. For at least half of them, the test under evaluation should be performed on the main specimen type, usually sputum. These may consist of archived unprocessed sputum specimens, concentrated sediments (or DNA extracted from sediments if applicable per IFU) for which reference results are

available, from either the same or a paired specimen. The other half of specimens may consist of clinical MTBC isolates if considered a validated specimen type according to the IFU. If other specimen types are claimed, such as BAL or extrapulmonary specimens, they will not be evaluated in this verification exercise. The panel may include left-over specimens submitted for routine testing, if these were collected and stored in agreement with the recommendations provided in the IFU of the assay under evaluation.

Study progress

Regulatory approvals have been obtained for a kit using LAMP technology, which will be evaluated in the first round

2. Development and validation of a Real-Time PCR test for tuberculosis diagnosis and treatment follow up

Principal Investigator	:	Dr. S Siva Kumar, Scientist E,
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR-Intramural
Study period	:	2022-2023
Category	:	Development
Pillar	:	Detect

Background

Early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups is the first pillar of the global TB commitments, strategy and targets according to WHO's global tuberculosis report 2022. Even though TB is one of the oldest diseases known to human, diagnosis and treatment has always been a nightmare. With the TB elimination deadline fast approaching, research has been proliferated worldwide. Easy and timely diagnosis of TB is one the priorities in controlling the disease. While the gold standard for TB diagnosis is still mycobacterial culture which is a long process, quick and precise techniques are being developed. With RTPCR machines available in the farthest regions of the country, we have designed this study in order to develop a kit, which can be used with these machines for rapid diagnosis and prognosis of tuberculosis. This study will help us to determine the possibilities of using MTB DNA, RNA and host plasma to detect the presence of MTB and its drug susceptibility.

Objective

To develop Real-Time PCR assay for M.TB and drug-resistant gene detection and validate as compared to MGIT culture to detect Rifampicin, Isoniazid, fluroquinolone, Bedaquiline, and Linezolid resistance.

Exploratory objective:

a. To develop Real-Time PCR assay for differentiation of nontuberculous mycobacteria and Mtb complex.
b. To develop Real-Time PCR assay to detect live M.tb using RNA from the stored M.tb isolates.

Methods

A proof-of-concept study protocol for developing and evaluating diagnostic/ prognostic performance of tuberculosis drug sensitive and drug resistance genes and M.tb specific cell-free DNA using Real-Time PCR test in comparison with MGIT culture and GeneXpert/TrueNat for detection of Tuberculosis with drug resistance from stored M.tb isolates is written here. The protocol includes evaluation algorithm, required sample size, laboratory procedures and quality control measures. Based on results of this proof-of-concept study, a multicentric clinical diagnostic validation study may be conducted as a next phase.

Study progress

The primers for the primary objective have been designed and tested for the performance.

3. Culture-Free Detection of Drug-Resistance in Clinical Samples for MDR-TB patients treated under the National Tuberculosis Elimination Program.

Principal Investigator	:	Dr. S Siva Kumar, Scientist E, Dept. of Bacteriology, NIRT
Participating Institutes	:	ICMR-NIRT, NRL-RMRC Bhubaneshwar, IRL Ahmadabad
Source of funding	:	ICMR Intra-mural
Study period	:	2023-2025
Category	:	Development
Pillar	:	Detect

Background

Currently, TB diagnostics and resistance detection tests provide only limited data on drug susceptibility. Accurate and timely drug resistance detection is to key to global tuberculosis management. Comprehensive DST is only possible by whole genome sequencing which is difficult to decentralize to point of care test. The proposed targeted next generation approach as a comprehensive DST method with Nanopore sequencing has potential as a point of care technology.

Objectives

- To evaluate the existing TB tNGS assay kit for spoligotyping and drug resistance prediction for 1st line 2nd line and newer drugs.

- Capacity building to perform TB tNGS assay at NRL Bhubaneshwar and IRL Ahmadabad.
- The develop in-house primers to perform TB tNGS assay kit for spoligotyping and drug resistance prediction for 1st line 2nd line and newer drugs.

Methods

Methods: We evaluated targeted next generation sequencing (tNGS) for tuberculosis on uncultured sputum, M.tb isolates, and samples. Resistance profiles from tNGS were compared with profiles from Xpert MTB/RIF, line probe assay (LPA), and phenotypic testing. Concordance, sensitivity, specificity, and overall test agreement were compared across assays.

Study progress

The first objective of the study has been completed and a manuscript is under preparation titled: Programmatic Approach to Rapid Diagnosis of Direct Drug-Resistant Tuberculosis Samples by Targeted Next-Generation Sequencing in a High TB Burden Setting.

- Runs were successful in order first - cTAB DNA method for LJ culture then >Trueprep DNA extraction from MGIT/sputum then >Genolyse DNA.
- LJ or MGIT culture is better for successful DNA preparation and tNGS run. For rapid tNGS testing, direct sputum combined with Trueprep for DNA extraction works the best

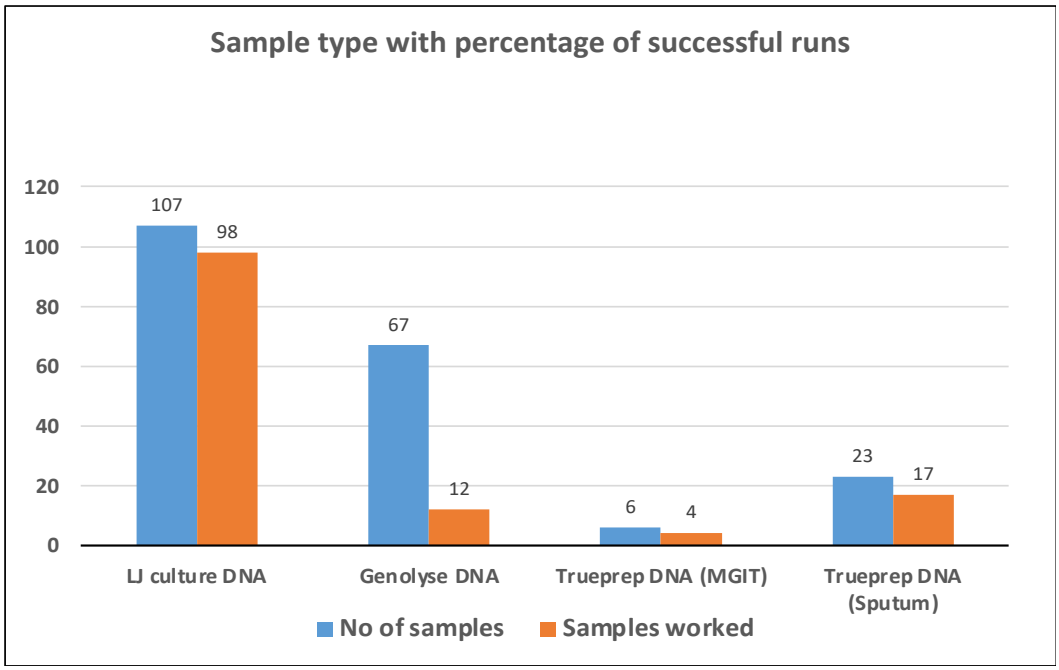


Figure 1: The figure provides information on the different Runs:

4. Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain lineage in India: A structured Nationwide approach (Sentinel surveillance of drug resistant tuberculosis in India)

Principal Investigator	:	Dr. S Siva Kumar, Scientist 'D', Dept. of Bacteriology, NIRT
Participating Institutes	:	ICMR NIRT
Source of funding	:	DBT and ICMR Extra-mural
Study period	:	2023-2025
Category	:	Description
Pillar	:	Detect

Background

The first ever national anti-tuberculosis drug resistance survey (NDRS) was conducted between 2014 and 2016. The implementation of a surveillance system for drug-resistant TB leads to improved access to timely and appropriate treatment and care. Additionally, it could provide information on outbreaks, and real-time monitoring of the effectiveness of the programmatic interventions. The inclusion of sequencing technologies in drug resistance surveillance can provide insights into the phylogenetics of the circulating TB strains. It is currently the only approach with the ability to investigate genome-wide targets for multiple first and second-line anti-TB drugs detecting even the rare mutations that could be missed by rapid molecular assays. Additionally, it provides details on species identification, genotyping, detection of mixed populations and hetero resistance in a given sample.

Objective

Primary objectives

- To monitor the proportion and pattern of drug resistance among new and previously treated microbiologically confirmed TB patients in selected districts of India over a period of three years.
- To monitor the pattern and emergence of drug resistance mutations and phenotypic resistance of microbiologically confirmed TB patients in India over a period of three years.

Exploratory objectives

- To describe the genetic traits of circulating strains of M. tuberculosis and outbreaks
- To establish a biorepository of whole genome sequenced *Mycobacterium tuberculosis* isolates.

To update the Indian Catalogue of *Mycobacterium tuberculosis* mutations and their association with drug resistance.

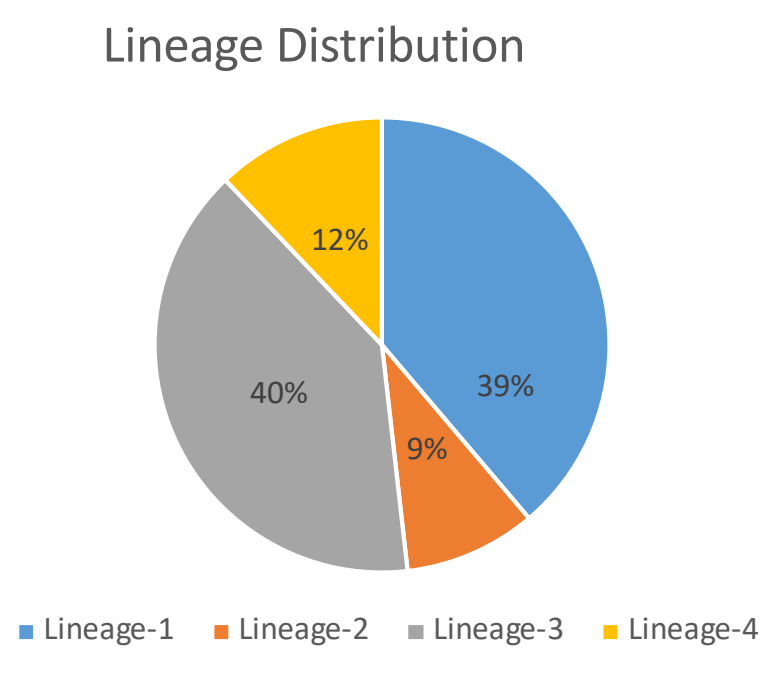
Methods

Total sample size for the high and low burden districts will be 6525 samples from 276 Districts across India. The total period of study will be 4 years. Quarter II of each year will be the sample collection period for the next four years (2022 to 2025). The rest of the quarters will be distributed for training, diagnostic activity, Sequencing, Data Analysis, and reporting each year as appropriate.

Study Progress

The study began in March 2023 with three months of preparatory work. Sample collection and processing started in April 2023. Of the 5200 samples received, 4500 showed culture growth. DNA extraction was completed for 4200 samples, and liquid DST was performed on 1000 isolates. A culture positivity rate of 92.3% was achieved, further improved by backup recovery from LJ media. DST has been completed for 1500 samples and is ongoing. Sequencing has been performed on 1500 MTB isolates.

WGS DST findings (n=700) show 39% resistant and 61% sensitive isolates, with resistance figures likely to change after data curation and classification by treatment history. WGS genotyping indicates predominant presence of lineages 1 and 3.



5. Evaluation of anti-tubercular, safety and immunomodulatory activities of Unani pharmacopeial formulations (UPF) Qurs-e-TabasheerSartani and &Arq-e-Hara Bhara through in-vitro and in-vivo studies

Principal Investigator	:	Dr. V. N. Azger Dusthackeer, Scientist D,
Participating Institutes	:	ICMR-NIRT, RRIUM
Source of funding	:	CCRUM
Study period	:	2 years
Category	:	Development
Pillar	:	Build

Background

Alternative source of medicines are a major viable source which could aid in this concept and among them Unani system of medicine which leads to the betterment of the immune status proves to be an effective strategy. The drugs being used are known to improve the immune status leading to better prognosis among TB patients, and can be considered as adjuvants along with anti TB drugs. In Unani medicine, *QursTabasheerSarthani* (QTS) and *Arq Hara Bhara* (AHB) are commonly prescribed drugs for the treatment of TB-like conditions (*SilwaDique*). A recent study has revealed that the co-administration of QTS & AHB with CAT-I anti-TB drugs at human equivalent dose improved the plasma peak rifampicin (RIF) level without altering the liver and kidney functions in rats. The study indicates a potentiating effect of QTS & AHB on RIF, and a protective effect on the liver and kidney caused as a result of the adverse effect of the anti-TB drugs

Objectives

Phase I:

- To determine the in-vitro efficacy of the two formulations namely Qurs-e-TabasheerSartani (QTS) and Arq-e-Hara Bharaalone(AHB) and in combination with the four first line Anti-TB drugs against *Mycobacterium tuberculosis* (Mtb).
- To determine the immunomodulatory role and Ex-vivo efficacy of Qurs-e-TabasheerSartani and Arq-e-Hara Bhara in Mtb infected and uninfected cell lines.

Phase II:

To determine the In-vivo toxicity of the formulations in infected animal model using guinea pigs alone and in combination with INH and RMP.

To determine the immunomodulatory role played by the formulations In-vivo.

Methods

Inhibition activity of UPF against Mtb-H37RV by Broth Micro Dilution assay against H37RV strain;

Drug-Drug interaction of UPF along with Rifampicine and Isoniazide against H37Rv;
Invivo efficacy studies in Mtb infected guinea pigs

Study progress
The in-vitro efficacy of UPF against MTB was determined by BMD method to evaluate MIC of UPF and combination assay to evaluate synergistic effect of UPF along with 1st line ATT drugs. There was no inhibition against MTB for UPF up to the concentration of 1mg/ml, but AHB alone showed inhibition at the concentration of 5mg/ml when the concentration has been increased up to 10mg/ml against Mtb-H37Rv and the MIC ranged between 5 to 10 mg/ml against the drug-resistant isolates of Mtb. There was no inhibition found while both UPF combined together against MTB. AHB showed synergistic effect with the combination of RIF and INH. Liver function tests, PK estimations, viable counts along with the macroscopic observation of the organs were all recorded and the analysis is ongoing

6. In-vitro and In-vivo studies on newly identified MDR-TB efflux pump inhibitors

Principal Investigator	:	Dr. V. N. Azger Dusthackeer, Scientist D, Dept. of Bacteriology, NIRT
Participating Institutes	:	ICMR-NIRT, ICMR-NARFBR, Hyderabad
Source of funding	:	ICMR
Study period	:	2 years
Category	:	Discovery
Pillar	:	Build

Background
Alarming increase in multidrug resistance including resistance to Bedaquiline and Delamanid necessitates aggressive research intervention to achieve success in tuberculosis treatment outcome. Mycobacterium tuberculosis gains resistance through genetic mutations predominantly besides efflux pump mediated drug resistance. In recent decades attempts are being made to trounce this hurdle by unearthing novel molecules, repurposing existing drugs, or by adjuncting the first-line anti-TB drugs with other drugs / molecules to reduce the related toxicity, to increase the efficacy and/or to reintroduce the drugs known to harbor resistance conferring mutations through novel approaches. The use of efflux pump inhibitors (EPIs) as adjuvant therapy to combat bacterial resistance to several antibiotics can be examined. Antibiotic-expelling efflux pumps, which are found in bacterial cell membranes, play a major role in the development of multidrug resistance. Therefore, EPIs,

which are meant to inhibit these pumps, have the potential to make the current antibiotic arsenal more effective.

Objectives

To identify the ADME properties of the selected molecules and to address the results of the DMPK studies

To study the in vitro and in vivo efficacy of the proposed new efflux pump inhibitors in combination with first-line and second-line anti-TB drugs with MDR and XDR clinical isolates.

Methods

ADME properties of the selected molecules will be tested based on the guidelines provided by Chung et al., (2015). For the in-vitro analysis, tests for log D, aqueous solubility, microsome solubility, plasma stability, plasma protein binding property, permeability, cytotoxicity and CYP450 inhibition will be tested.

Determination of Minimum inhibitory concentration by micro broth dilution method

Checkerboard broth dilution assay will be performed in MDR, XDR clinical isolates and the knockouts (Mtb::rv1212and Mtb::rv1819) will be used to determine the synergism between Methyl stearate, Myo inositol, Palmitic acid and Dodecanoic acid molecules with first and second line Tb drugs.

Study progress

In-silico analysis of the efflux pump inhibitors methyl stearate, myoinositol, dodecanoic acid and palmitic acid was done and it was determined that apart from myoinositol, the other three efflux pump inhibitors have to be encapsulated. So, myoinositol has been directly subjected to determine the efficacy in stored cultures of clinical isolates. The other three were given for encapsulation. Encapsulation was successful in methyl stearate and palmitic acid. Encapsulation with dodecanoic acid is still in progress. Myoinositol when tested with Rifampicin in combination with checker board assay, it was able to reduce the MIC value of Rifampicin.

7. Assessing the utility of different biological samples (Urine, stool and respiratory specimens) for pediatric pulmonary TB detection – a cross-sectional study

Principal Investigator	:	Dr. R. Priya
Participating Institutes	:	ICH, Egmore, Stanley Hospital
Source of funding	:	Intramural
Study period	:	2022 -2025
Category	:	Description
Pillar wise	:	Detect

Background

Pediatric tuberculosis (TB) is a major global public health problem with high mortality and morbidity. Prompt diagnosis of pulmonary tuberculosis (PTB) remains challenging in children because it is highly difficult to obtain the expectorated samples from them. The poor reliability of current pediatric diagnostics has made clinicians to rely entirely on medical history, clinical symptoms, and chest radiography for TB treatment. Therefore, there is an urgent need for development of diagnostic methods using non-sputum-based specimens that would be cutting edge for the diagnosis of childhood tuberculosis. In this study, we aim to detect TB in different biological samples (respiratory samples, urine and stool) collected from the children with presumptive TB and to compare the yield of MTB detected.

Objectives

Primary objective

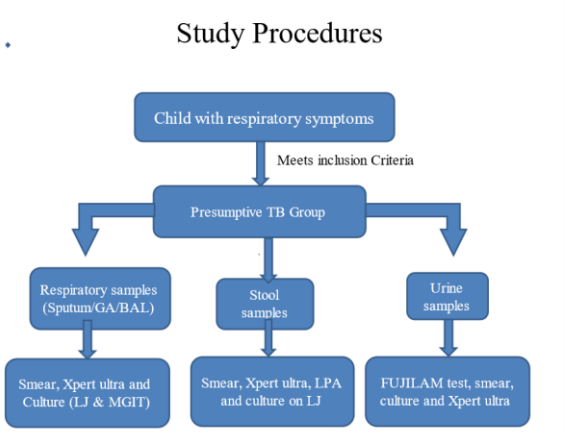
To evaluate the comparative yield of MTB, detected from easily available biological samples such as stool and urine in comparison to respiratory samples.

Secondary objective

To determine the diagnostic accuracy of molecular detection of MTB detection in stool processed by an in-house standardized protocol. 2. To determine the utility of SILVAMP FUJILAM test in urine samples for pediatric TB diagnosis.

Methods

Expectorated or induced sputum specimens, urine and stool will be collected from eligible children. Specimens will be collected in the pediatric clinics in and around Chennai (Mehta hospital, Apollo hospital and Rainbow children hospital and Institute of Child Health), MAMC, New Delhi and RMRC, Bhubaneswar. Further investigations on these specimens will be conducted at NIRT as depicted in the figure below.



Study progress

A total of 373 samples collected so far and the interim findings were presented in APRC conference, held at Taipei, Taiwan.

8. Characterisation of M. abscessus, M. kansasii, M. avium- intracellulare Complex - the most common NTM species isolated from presumptive TB patients

Principal Investigator	:	Dr. R. Priya
Participating Institutes	:	NA
Source of funding	:	Intramural
Study period	:	2022 -2025
Category	:	Description
Pillar	:	Build

Background

Non tuberculosis mycobacteria (NTM) are increasingly recognized as causative agents of opportunistic infection in humans. In general, Mycobacterium tuberculosis (MTB) and NTM infections have identical clinical symptoms leading to misdiagnosis of disease. Patients not responding to treatment, as most of the NTM being resistant to antibiotics and ATT (anti-tuberculosis therapy), instances of them being identified as multi drug resistant TB is common. Appropriate identification methods for differential diagnosis of NTM and MTB are need of the hour. In this study, we aim to identify NTM isolated from presumptive TB patients and further characterize them by genotypic and phenotypic methods.

Objectives

Primary objective:

To identify the pathogenic non-tuberculous mycobacteria causing symptomatic pulmonary disease

Secondary objectives

1. To further characterize the most common species M. abscessus, M. kansasii, MAC isolates using different molecular methods
2. To determine the drug resistance pattern of the isolates using different phenotypic and genotypic methods

Methods

Currently under National Tuberculosis Elimination Programme (NTEP) and as part of patient management, sputum samples of Presumptive TB population from all the NTEP centres of Tamilnadu and other hospitals are sent to NIRT for culture and identification. Details of the sputum growing AFB but not suggestive of MTB complex in culture will be informed to the concerned treating hospital / medical officer/ laboratory for further treatment and these isolates will be used for further characterisation at NIRT for this study.

In brief, the positive MGIT/LJ cultures will be tested with ICT (Immunochromatography) test involving MPT64Ag to differentiate MTB and

NTM. DNA from NTM cultures will be extracted by Genolyse Extraction kit. Speciation of growth from two positive cultures per patient will be done using Genotype Mycobacterium CM/AS kit. In addition, PCR RFLP will be carried out on the species for further subtyping. Genotypic and phenotypic drug resistance testing will be carried out by NTM-DR kit and broth microdilution method respectively.

Study progress

A total of 124 isolates have been subjected to characterisation methods and 79 have been sequenced so far.

9. Diagnostic evaluation of tongue swab-based tests for detection of M. tuberculosis in presumptive pulmonary TB patients

Principal Investigator	:	Dr. R. Priya
Participating Institutes	:	ICMR-NIRT
Source of funding	:	Molbio and Huwell
Study period	:	2022 -2025
Category	:	Development
Pillar	:	Detect

Background

Although the World Health Organization (WHO) recommends molecular diagnostics as the preferred frontline testing option, only 38% of all notified cases in 2021 were tested with a WHO-recommended rapid molecular diagnostic at initial diagnosis. Furthermore only 63% of all notified TB cases were bacteriologically confirmed by any method. Research has shown that people with TB navigate long care-seeking pathways, with multiple visits to health providers before a diagnosis is made. In the absence of simple, point-of-care (POC) testing, primary care providers prefer to empirically manage people with broad-spectrum antibiotics and other non-specific therapies that are more easily available and that help offer immediate relief of symptoms. Decentralized POC tests would enable diagnosis and therefore treatment decisions to be made in the first patient consultation. Efforts are underway to evaluate such POC technologies for TB, especially in combination with non-sputum samples that may be more convenient for patients and providers.

Objectives

Primary Objective

To evaluate the diagnostic characteristics of the tongue swab based NAAT (index test) using MGIT culture as the microbiological reference standard for detection of M. tuberculosis in presumptive pulmonary TB patients”

Secondary Objective(s)

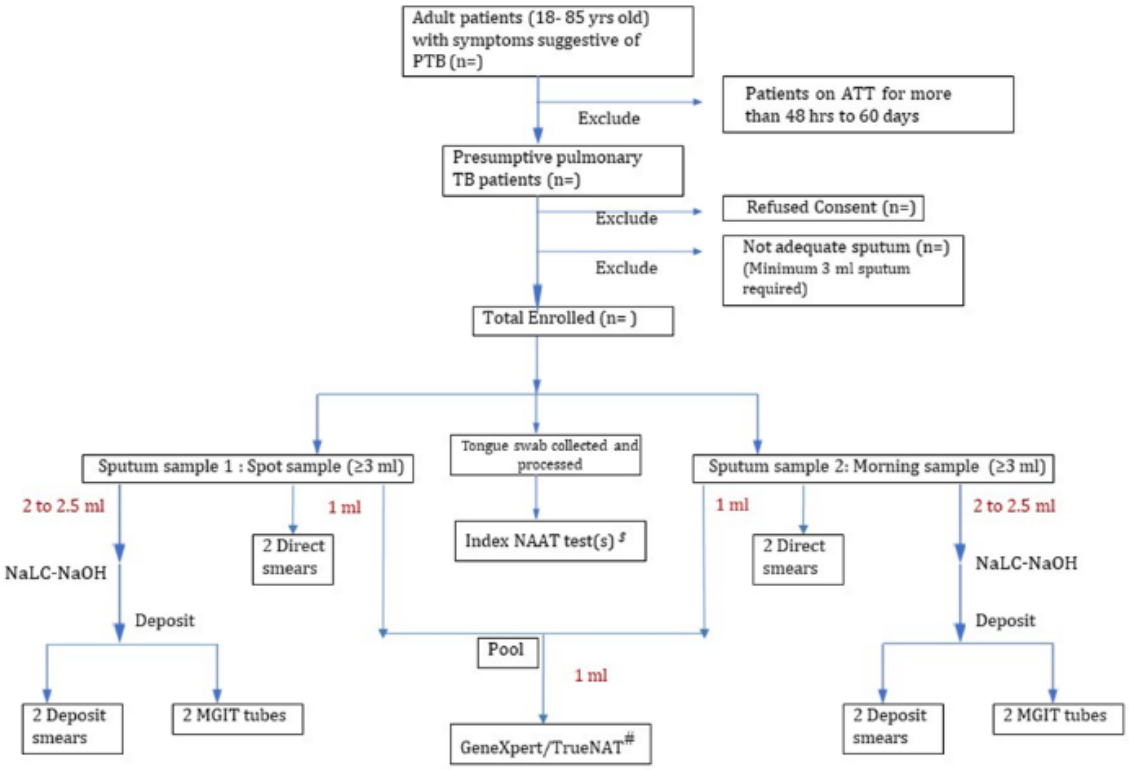
To compare the diagnostic characteristics of the index NAAT versus those of approved NAAT (GeneXpert/Truenat) using MGIT culture as the reference standard for both the molecular tests

Methods

The study will include presumptive adult pulmonary TB patients attending hospital OPDs/Chest clinics/district microscopy centers (DMCs) and Directly Observed Therapy Short Course (DOTS) centers. All such consecutive patients willing to provide consent will be enrolled in the study and subjected to procedures depicted in the figure below

Study progress

Study initiated and recruitment ongoing.



*One positive culture and 2 decontaminated samples per patient will be stored at -80°C for later use, if necessary **
DNA samples will be stored at -20°C for resolution of discrepant results

10. Multicentric validation of phage lysin in comparison with MGIT PANTA to control normal flora in processed sputum specimens for rapid detection of *Mycobacterium tuberculosis* using BACTEC MGIT 960 system

Principal Investigator	:	Dr. Balaji Subramanyam
Participating Institutes	:	1. ICMR-Bhopal Memorial Hospital and Research Centre (BMHRC), Bhopal 2. ICMR- Regional Medical Research Centre (RMRC), Bhubaneswar 3. New Delhi TB Center, New Delhi
Source of funding	:	ICMR
Study period	:	2023-2025
Category	:	Development
Pillar	:	Detect

Background

Cocktail of three bacteriophages namely Chedec 11, Chedec 20 and Chedec 21 were used as an alternative to the traditional use of antibiotics to control the overgrowth of normal flora in sputum specimens. Bacteriophage lysin extracted from these three phages were used to supplement bacteriophages for the effective control of normal flora. Subsequently, bacteriophage lysin alone was used as a substitute for antibiotics to detect *M. tuberculosis* from sputum samples using BACTEC MGIT 960 system. The genome sequencing of these bacteriophages revealed that all the three bacteriophage lysin showed >99% similarity. Hence, it was proposed to clone and express lysin from Chedec 11 and produce the same in bulk leading to the commercialization as a supplement for the growth based rapid methodologies.

Objectives

Multicentric validation of phage lysin in comparison with MGIT PANTA to control normal flora in processed sputum specimens for rapid detection of *Mycobacterium tuberculosis* using BACTEC MGIT 960 system.

Methods

Study design: This is a multi-center, blinded, cross-sectional study to control the rate of contamination in TB patients in comparison to the conventional reference standard. The further course of action will be based on the results of this validation exercise.

Sample size: Considering the Subramanyam et al, (2011) which states that the rate of contamination in BACTEC MGIT 960 system with MGIT-PANTA and MGIT-Lysin were 16.0% and 7.3%, respectively. With an assumption of 95% confidence interval,

80% power, design effect of 2 to adjust the site variability and 10% loss of sample or insufficiency; the minimum required sample size will be 528 per site and overall sample size will be 2112 from four sites.

Large scale production of phage lysin: Cloning, expression and purification of phage lysin from Chedec 11 was successfully completed with support of Translational Research unit of ICMR (Trans. Res./New proj.44/2016). The expression vector bearing phage lysin is stored appropriately and will be used for large scale production of phage lysin. Outsourcing of this activity is being planned with suitable industrial partners as the large scale production is currently not available at NIRT, Chennai. The resultant large scale production of phage lysin will be tested initially at NIRT for its intact and desired effect using the following 4 experiments. Based on the successful completion of these experiments, multicentric validation will be executed.

Methodology: A total of 528 specimens will be processed by NaLC-NaOH method (1.5% NaoH as final concentration) for each site and the deposits thus obtained will be washed with PBS by centrifugation at 3000g for 15 minutes. The pellets will be aliquoted in to two each with 500 µl. One aliquot will be added in to the 7 ml of MGIT tube with PANTA and used as control and the other aliquot will added in to 7 ml MGIT tube with phage lysin at desired concentration. The tubes will be coded and loaded in to the BACTEC MGIT 960 system as per the manufacturer protocol. Further identification tests will be done as per standard protocol. Briefly, the tubes will be subjected to AFB staining to demonstrate the presence or absence of AFB, inoculation on brain heart infusion (BHI) agar to check for growth of contaminating organisms and the commercial MPT64 immunochromatographic test (TBc ID, Becton and Dickinson, USA) to confirm the presence of MTB complex.

Study progress

The large-scale production of phage lysin is currently under progress at Sathyabama Institute of Science and Technology (SIST), Chennai with an existing MoU between ICMR-NIRT and SIST. The first batch of phage lysin was successfully validated at ICMR-NIRT and sent to the participating institutes to complete 200 samples per site as part of multicentric validation. The second batch of lysin production is currently ongoing and the same is expected to completed by first week of October 2024.

11. Comparison of molecular methods Xpert® MTB/RIF Ultra and Genotype MTBDRplus assay for detection of rifampicin resistance from sputum samples

Principal Investigator	:	Ms. K. Silambuchelvi., Senior Technical Officer
Participating Institutes	:	ICMR NIRT
Source of funding	:	Departmental resources
Study period	:	2021-2025
Category	:	Description
Pillar	:	Detect

Background

Drug-resistant TB continues to be a public health crisis and poses grave challenge for the Tuberculosis Control Programme. The Global Tuberculosis Report 2018 states that worldwide in 2017, 558 000 people developed TB that was resistant to rifampicin (RR-TB) and of these 82% had multidrug-resistant TB (MDR-TB). Moreover, globally it was estimated that the MDR/RR-TB as 3.5% of new TB cases and 18% of previously treated cases. Among cases of MDR-TB in 2017, 8.5% were estimated to have extensively drug-resistant TB (XDR-TB). And also the report has added that three countries accounted for almost half of the world's cases of MDR/RR-TB where India contributes about 24% [1]. This alarming situation drives for the early diagnosis and detection of MDR cases without any miss outs.

Recently Xpert MTB/RIF Ultra (Xpert Ultra) has been recommended by World Health Organization (WHO) as the rapid diagnostic tool for rifampicin resistance. Xpert MTB/RIF Ultra showed significantly better performance (increased sensitivity) compared to the current Xpert® MTB/RIF (CBNAAT) cartridge for the detection of *Mycobacterium tuberculosis* in specimens with low numbers of bacilli and also the accuracy was also better in detection of rifampicin resistance. Xpert MTB/RIF Ultra assay target the rifampicin resistance determining region (RRDR) of *rpo*B gene along with the insertion elements such as IS6110 and IS1081. The Genotype MTBDR*plus* (LPA) is also a World Health Organization recommended molecular test targeting the same *rpo*B gene which consists of a 81-bp hot-spot region from codons 507 to 533 in which point mutations at codons 526 or 531 cause high level of rifampicin resistance and mutations in codons 511, 516, 518, 522 and 533 causes low-level resistance to rifampicin. Mutations conferring rifampicin résistance occur rarely in other regions of the *rpo*B gene. These two methods have less turnaround time (TAT) when compared to the conventional drug susceptibility testing

The Genotype MTBDR*plus* (LPA) method is currently used in NTEP while Xpert MTB/RIF Ultra may be implemented in future for the rapid detection for rifampicin resistance for the programmatic samples. Furthermore, discrepancy between Xpert MTB/RIF

(CBNAAT) and Genotype MTBDR*plus* (LPA) methods has been already reported [2.] However, there is no report addressing the discrepancy between Xpert MTB/RIF Ultra and Genotype MTBDR*plus* (LPA). This may be due to the wide variation in circulating MTB strains across the globe and also the presence of unique genetic mutations in the different settings may lead to the missing of rifampicin resistance cases. This study will enlighten with any such discrepancies between these two molecular methods and also there is a need for documenting the same.

Objectives

To compare the two molecular methods - Xpert MTB/RIF Ultra and Genotype MTBDRplus (LPA) assay for detection of rifampicin resistance in the discordant samples of presumptive MDR cases from Tamil Nadu.

Methods

The DR-TB diagnostic algorithm presently followed in the National Tuberculosis Control Program is given below in figure-1 as a flow diagram. Being a prospective study, mucopurulent samples of 3-5 ml will be collected from presumptive TB and from all diagnosed TB patients as per the guidelines and will be subjected to Nucleic acid amplification test (Xpert MTB/RIF (CBNAAT)/ TrueNat MTB) for diagnosis of MDR-TB. Those samples sensitive to rifampicin by Xpert MTB/RIF (CBNAAT)/TrueNat MTB will be subjected again to Genotype MTBDRplus assay (LPA) as per manufacturer's protocol3 to know the sensitivity pattern of both rifampicin and Isoniazid. If the sample shows discrepancy in the diagnosis of rifampicin between these molecular methods, then the samples are known to be discordant samples. Those discordant sputum specimens will be identified from both the adult and children from different NTEP sites

Those discordant samples received will be selected, coded and subjected to decontamination by NALC-NaOH method4. Samples will be decanted following centrifugation at 3000 g for 15 min, and the pellets were re-suspended to make 2.5 ml using phosphate buffer solution. Aliquots of 0.5 ml from each sample will be used for florescent microscopy, MGIT960 culture and for Xpert MTB/RIF Ultra assays. Another 1 ml aliquot of each sample will be stored at − 80 °C as backup.

Culture will be the gold standard. Culture by MGIT will be raised for all samples and DST by MGIT and/or targeted sequencing or sequence for entire rpoB region will be done to resolve any discrepancy between the methods. The samples those turned positive MGIT DST will be performed immediately and simultaneously the DNA will be extracted and stored for performing sequencing. In future, if any troubleshoot arises these samples may be used for addressing and resolving for the same. Whole genome sequencing/Nano pore sequencing will be performed for unique strain if any to explore for the presence of unique genetic mutation in the said settings and thereby aid in preventing the missing of rifampicin resistance cases.

Study progress

A total of 76 discordant samples received from different NTEP sites were collected so far and the study is still ongoing.

Completed studies

Sno.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1.	Intrinsic lineage specific susceptibility of mycobacterium tuberculosis to Pretomanid	Dr. S. Siva Kumar, Scientist E	The UNION	Description	Lineage 1 was associated with higher MIC than other lineages to Pretomanid
2.	Molecular epidemiology of *Mycobacterium tuberculosis* from patients treated under the National TB Elimination Programme (NTEP), India	Dr. S. Siva Kumar, Scientist E	ICMR-Extra-mural	Description	There is a clear demarcation of CAS spoligotype predominant in north and EAI spoligotype predominant in South India. Spoligotyping showed several clusters which was reduced to reduce to 6 when the WGS was done on the clustered samples. Predominant (EAI3, EAI5 and CAS) and low prevalent (Beijing) clusters evaluated for intracellular growth rate, demonstrate reduced proliferation in THP1 macrophages contrast to H37Rv. Among the clinical strains EAI3_IND ST11 showed maximum intracellular growth rate followed by Beijing and CAS, EAI5 ST126 cluster exhibited lowest intracellular growth rate.
3	Genomic investigation for metagenomic profile of SARS-CoV-2, Tuberculosis and in their co-infection.	Dr. S. Siva Kumar, Scientist E	IIT Madras, Chennai	Discovery	Metagenomic profiling of SARS-CoV-2 and TB co-infection

Sno.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
4	Comprehensive assessment of Truenat invalid and indeterminate results at identified sites under NTEP and recommend possible solutions.	Dr. S. Siva Kumar, Scientist E	IDDS-USAID	Description	Root cause analysis identified that strengthening raining, external quality control and supervision could improve inconclusive results. Ensuring hands-on training of technicians for Truenat testing and retesting of samples with inconclusive results are major recommendations while planning for Truenat scale-up. The recommendations from the study were consolidated into technical guidance documents/videos and disseminated to laboratory staff working at the tiered network of TB laboratories in NTEP to improve the Truenat MTB-RIF testing performance
5.	MIC distributions of Bedaquiline, Delamanid, Pretomanid, Linezolid, clofazimine, moxifloxacin and levofloxacin among wild-type, MDR and XDR isolates of *M. tuberculosis* among South Indian population	Dr. V. N. Azger Dusthackeer, Scientist D	ICMR-Intramural	Delivery	Newer cut-off levels for Bedaquiline, clofazimine, delamanid determined.
6.	Multicentre trial to assess the performance of centralized assay solutions for detection of MTB and resistance to Rifampicin and Isoniazid	Dr. R. Priya, Scientist D	FIND	Delivery	The FluoroType MTBDR assays together with an automated DNA extraction and PCR set-up platform seem to improve laboratory operational efficiency for the diagnosis of MTBC and resistance to rifampicin and isoniazid.

DEPARTMENT OF BIOCHEMISTRY

DEPARTMENT OVERVIEW AND MANDATES

The Department of Biochemistry provides uninterrupted clinical chemistry analytical support to various clinical trials and basic research activities at ICMR-NIRT through the Clinical Biochemistry Laboratory (CBL), a sophisticated and dedicated service unit. During 2023–24, the CBL generated approximately 4,000 externally quality-assured, high-quality clinical chemistry reports to meet various in-house requirements.

The Laboratory Information Management System (LIMS), designed to document pre- and post-analysis processes, report generation, and distribution, has significantly improved the turnaround time (TAT) of clinical chemistry reports and enhanced clinical care management for study participants. All necessary procedures and documentation for NABL accreditation of the CBL have been completed, and we are hopeful of receiving the NABL Accreditation Certificate by the end of 2024.

The department's basic research activities are focused on strengthening the 'Treat' and 'Detect' pillars of the National Tuberculosis Elimination Programme (NTEP). We have initiated research on nano-delivery systems for therapeutic applications and on identifying adjuvant therapeutic leads from natural compounds. Studies have also been initiated on point-of-care triage tests as screening tools for active TB detection in high-risk populations. Further, the department aims to focus on biomarker discovery through omics approaches, using advanced techniques such as LC/MS/MS.

Studies in Progress

1. **Point of care estimation of Vitamin D and C-Reactive Protein for tuberculosis screening in household contacts of active pulmonary tuberculosis patients in Tamil Nadu, India.**

Principal Investigator	:	N SARAVANAN
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR
Study period	:	2023-2026; 3 Years
Category	:	Delivery
Pillar	:	Detect

Background

The problems associated with missed or delayed diagnosis of active TB with poor access to high quality care led to a higher risk of death, suffering, longer duration of infectiousness, increased transmission. In order to achieve maximum possible elimination of TB. The WHO stressed the importance of 'active screening' of high-risk populations such as household contacts of index cases to detect TB early and thereby accomplish decreased risk of (a) transmission (b) adverse social and economic consequences, and (c) adverse treatment outcomes. It is essential to have active screening strategies among household contacts that could be better than the 'symptom-based screening' and could be effective in decreasing the costs of implementing intensified case finding.

C Reactive Protein (CRP) an acute-phase reactant, the levels increase during infections. There are several reports on the point of care CRP testing as a tool for active TB screening suggesting an increase of CRP (≥8 mg/L) could be considered as a predictive marker for active TB. Vitamin D, classically known as nutrient essential for bone mineral homeostasis, suggested to be an effective immunomodulator and has proven role in inducing antimycobacterial activity. It is established that a serum vitamin D concentration ≤25 nmol/L is significantly associated with increased risk of active TB.

Objectives

Primary objective

To compare the diagnostic accuracy (sensitivity and specificity) and the predictive value (negative and positive predictive value) of point-of-care (POC) estimation of C-reactive protein and Vitamin D with WHO symptom-based screening for active TB in household contacts of PTB patients.

Secondary objectives

To compare the diagnostic accuracy (sensitivity and specificity) and the

predictive value (negative and positive predictive value) of point-of-care (POC) estimation of C-reactive protein & Vitamin D and Chest X Ray (CXR) with WHO symptom-based screening for active TB in household contacts of PTB patients.

To compare the diagnostic accuracy (sensitivity and specificity) and the predictive value (negative and positive predictive value) of point-of-care (POC) estimation of C-reactive protein & Vitamin D with laboratory-based estimation of C-reactive protein & Vitamin D using bio analyser for active TB in household contacts of PTB patients.

Methods

Design: Prospective cross-sectional cohort

Study site: National Institute for Research in TB, Chennai

Study Population: Household contacts of newly diagnosed Pulmonary TB patients recruited for clinical studies at National Institute for Research in Tuberculosis, Chennai and any contacts of new PTB patients in Chennai and parts of Tamil Nadu

Inclusion criteria

Household contacts of smear/culture positive pulmonary of culture positive pulmonary TB patients (children > 12 years of age and adults), with no IPT and ATT at the time of enrollment and willing for study procedures and ready to provide written informed consent / parent or guardian consent for children

Exclusion criteria: People under treatment for active TB, with moribund state

Upon proper enrolment of participant, 2-3 drops of whole blood will be collected via finger prick and the POC test for Vitamin D and CRP will be conducted. A 5 mL of blood will be collected from the participant and plasm glucose, HbA1C, serum lipid profile, cytokine profile and liver function test will be analysed at the clinical biochemistry division, NIRT and rest will be bio-banked at NIRT. Simultaneously the levels of Vitamin D and CRP will be estimated using Bioanalyzer (Beckman coulter). The data on CXR recording of household contacts will be accessed by the study coordinator from the respective principal investigators of the trials, if the principal investigators HHC does not have the CXR recordings of HHC the study coordinator will acquire the CXR recordings. The diagnostic accuracy and the predictive value POC estimation of CRP & Vitamin D with or without CXR will be compared with symptom-based screening for active TB in household contacts of PTB patients with reference to culture results and Xpert MTB/RIF data independently.

Study progress

66 participants are recruited. Various bacteriological, biochemical & haematological tests pertaining the above study have been completed. Participant recruitment is in progress.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category/pillar (Discovery, Development, Delivery, Description)	Outcome
1	Development and characterization of a novel nanopeptide system for therapeutic application in residual lung injury caused by pulmonary tuberculosis	Dr N Saravanan Dr N Usharani,	ICMR	Development	A Nanodelivery system using carnosine and anti TB drugs is developed. A patent on the development process is filed through ICMR-IPR unit. So far four papers were published in peer reviewed journals and Five posters were presented in the scientific meetings

DEPARTMENT OF CLINCIAL PHARMACOLOGY

DEPARTMENT OVERVIEW AND MANDATES

The primary mandate of the department is to undertake pharmacokinetic (PK) profiling of anti-tuberculosis (anti-TB) drugs in various clinical trials conducted by ICMR-NIRT, as well as studies from other organizations across the country. Another key mandate is the development of new, simple, and novel HPLC methods to measure anti-TB drugs in plasma and other biological fluids. The department also offers services and support for therapeutic drug monitoring (TDM) of anti-TB drugs for patients undergoing treatment at various government hospitals, research institutes, and organizations at both state and national levels.

The department conducts core research in the area of “factors associated with pharmacokinetic variability and TB treatment outcomes.”

It is also a member of the External Quality Assessment Scheme (EQAS) for proficiency testing of plasma anti-TB drugs, organized by the Dutch Foundation for Quality Assessment in Medical Laboratories (SKML), Netherlands.

Studies in Progress

1. Bioavailability of fixed dose combination of first line anti-TB drugs in patients with pulmonary tuberculosis

Principal Investigator	:	S.M.Jeyakumar
Participating Institutes	:	GHTM and ICH, Chennai
Source of funding	:	Intramural grant
Study period	:	2021-2024
Category	:	Description
Pillar	:	Build

Background

Fixed dose combination (FDC) of drugs is one of the methods to improve compliance and reduce errors. The rationale of FDC is that the presence of all these drugs combined in one tablet can facilitate dosage calculation, prevent prescribing errors, increases patient's acceptance and decreases pill burden. In India, FDC's are recommended for TB patients under the National Tuberculosis Elimination Programme (NTEP) during daily treatment both in intensive and continuation phase. There are four weight bands for adult TB patients receiving INH, RMP, PZA and EMB (75/150/400/275mg) and 6 weight bands for children receiving dispersible FDC's (50/75/150/100) in addition to streptomycin for 2 months in the intensive phase. No study to date has assessed the combined use of the three drugs (FDC's) for TB treatment in different weight bands, both in adults and children, which is of great clinical relevance.

Objectives

To assess the bioavailability of RMP, INH and PZA when administered as FDC in adults and children with pulmonary TB treated in the NTEP in India

Methods

This study is an observational and bioavailability study, carried out at the Institute for Child Health, Egmore for children and at Government Hospital for Thoracic Medicine, Tambaram for adults. As per the sample size, 12 patients each receiving treatment under 5 different weight bands in adults and while 6 different weight bands in pediatric population, receiving anti-TB treatment will be included according to the inclusion criteria, i) newly diagnosed pulmonary TB patients (both adult and children) as per the NTEP guidelines, ii) willing for blood draws and iii) adult patients or parent/guardian of pediatric patients willing to give written informed consent.

On the day for PK evaluation, eligible patients will be requested to report at the

hospital in the morning under fasting condition. A sample of blood (2.5ml) will be collected in a heparinised vacutainer tube, followed by administration of anti-TB medications. The time of drug administration will be noted in the lab reception form. Blood samples (2.5 ml equivalent to half teaspoon) will be collected at 2, 4, 6, 8 and 12 hours in heparinised vacutainer tubes after drug administration. Plasma RMP, INH and PZA levels will be measured by validated HPLC methods.

Study progress

Patient recruitment is in progress in the adult weight band >75.0kg.

Due to low intake in pediatric pulmonary TB across different weight bands, the protocol was submitted to IEC for amendment for approval to include children with extra-pulmonary TB cases, who are on FDC.

2. Pharmacokinetics of linezolid when administered with other second line anti-TB drugs in MDR-TB/Pre-XDR-TB Patients

Principal Investigator	:	S.M.Jeyakumar
Participating Institutes	:	GHTM and SMCH, Chennai
Source of funding	:	Intramural grant
Study period	:	2021-2024
Category	:	Development
Pillar	:	Build

Background

Drug-resistant TB (DR-TB) is more difficult to treat than drug-sensitive TB (DS-TB) and the treatment options are very limited. Addition of linezolid (LZD) in the treatment regimen of DR-TB has been associated with improved treatment outcome with reduction of mortality among MDR-TB and Pre-XDR TB patients. However, limited information is available on the pharmacokinetics of second-line drugs used in the treatment regimen of MDR-TB and Pre-XDR TB, particularly in the Indian context. Therefore, here we plan to undertake a pharmacokinetic study of LZD and other second-line anti-TB drugs used in the treatment of MDR-TB and Pre-XDR TB.

Objectives

1. To develop and validate methods for the estimation of linezolid (LZD) in plasma and saliva by HPLC.

To study the pharmacokinetics of LZD and other second-line anti-TB drugs in adult patients with multi-drug resistant (MDR) and pre-extensive drug resistant (pre-XDR) tuberculosis patients

Methods

It is a prospective study, which will be carried out at the Government Hospital for Thoracic Medicine, Tambaram and Government Stanley College Hospital, Chennai. The study population will be of adult MDR-TB and pre-XDR-TB patients (>18y) being treated in these centres, based on the following inclusion and exclusion criteria. Inclusion criteria: i) Bacteriologically confirmed adult MDR-TB & pre-XDR TB, ii) Treatment regimen containing LZD along with other second line drugs for minimum period of 15 days, iii) Willing for hospitalization for the purpose of the study & willing to give informed written consent. Exclusion criteria: Patients with HIV-seropositive, moribund, pregnant & breastfeeding women, chronic diarrhoea, and liver and renal abnormalities.

On the day for PK evaluation, study participants will be requested to report at the hospital in the morning under fasting condition. A sample of blood (5mL) will be collected in a heparinised vacutainer tube, followed by administration of anti-TB medications. The time of drug administration will be noted in the lab reception form. Blood samples (5mL) will be collected at 2, 4, 6, 8 and 12 hours in heparinised vacutainer tubes after drug administration. Similarly, saliva (5 ml) will be collected from these patients at each time point of blood collection.

Study progress

Currently, a new HPLC-UV method is developed to measure LZD in saliva and the validation is yet to be completed. A new HPLC method for plasma LZD along with other second-line drugs (fluoroquinolones and ethionamide) is being developed and validated.

DEPARTMENT OF ELECTRONIC DATA PROCESSING

DEPARTMENT OVERVIEW AND MANDATES

The ICMR-NIRT Electronic Data Processing division is a key supporter of research related to IT and data processing. It plays two major roles within the organization: 1. Maintains IT equipment and network services and provides troubleshooting services2. Facilitates online server-based data collection /verification for the research undertaken in the epidemiological unit, clinical division, laboratory, and other operational research studies. The department also plays a key role in the conduct of epidemiological surveys.

ICMR-National Institute for Research in Tuberculosis pioneers the TB Research system making digital transformation more user-friendly through National Knowledge Network (NKN). NIRT maintains digital technology that meets international standards, with a 200 TB storage capacity and 1 Gbps NKN connectivity. It has both physical and virtual machines (VMs) to support more than 30 projects with real-time server-based data collection using handheld devices such as mobile phones and tablets. The department has provided more than 500 network points to NIRT users across the four campuses in Chennai, Tiruvallur, Madurai, and Vellore. Tiruvallur and Madurai are connected to the main campus through Radio Frequency from the nearest NKN-serviced location, thereby promoting seamless collaboration among all campuses.

As per the Director’s vision, the upcoming state-of-the-art Data Centre at the NIRT-Tiruvallur campus, with proposed 1 Gbps NKN connectivity, is expected to be the hub of TB research, leading the nation in TB management and elimination by 2025.

EDP plays a vital role in capturing real-time server-based data collection in various projects in NIRT. REDCap is a secure web application for building and managing online surveys and databases. While Redcap can be used to collect virtually any type of data, it is specifically geared to support online or offline data capture for research studies and operations. NIRT has obtained a license under the Redcap consortium and has become functional since August 2018. Currently, there are 82 studies in the REDCap database, out of which 31 are ongoing.

Studies in Progress

1. Application of multiple imputation approaches to the prevalence estimation in large-scale tuberculosis prevalence surveys

Principal Investigator	:	Mrs. Basilea Watson, Scientist D
Participating Institutes	:	Nil
Source of funding	:	Not applicable
Study period	:	2021-2023
Category	:	Development
Pillar	:	Build

Background

The analysis of the TB prevalence surveys using analytical methods adjusted for clustering and correcting for missing data will provide a robust estimate which uses the collected data to the maximum without any compromise on data wastage due to incomplete data records.

Objectives

1. To obtain overall point estimates of TB prevalence using robust standard error and random effects logistic regression methods with and without correction for missing data using multiple imputation.
2. To determine the method that yields the most unbiased estimate of TB prevalence among the methods mentioned in objective 1.

Methods

This is a secondary analysis of existing data. Multiple imputed data sets of the studies mentioned below are being used:

1. Surveys of PTB undertaken on representative population samples aged ⩾15 years before (1999 – 2001) and three repeat surveys (2001-2003, 2004-2006, 2006-2008) after the implementation of the DOTS strategy.
2. An independent survey conducted to estimate the prevalence of TB in 2008–2009 using a different set of villages and employing repeat survey methodology.

Study progress

The project has been initiated and the analysis is on-going

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category/pillar (Discovery, Development, Delivery, Description)	Outcome
1	Development of a quantitative tool to assess barriers and facilitators in the completion of TB treatment	Mrs. Basilea Watson, Scientist D	Intramural	TB Treat	Manuscript in preparation.

DEPARTMENT OF EPIDEMIOLOGY

DEPARTMENT OVERVIEW AND MANDATES

The Department of Epidemiology plays a pivotal role in understanding the transmission dynamics of Tuberculosis and addressing them through community level intervention studies. The department is actively engaged in estimating the burden of tuberculosis (TB) in India by conducting comprehensive field studies that integrate meticulous surveys with advanced modelling techniques. These initiatives aim to identify epidemiological trends and risk factors associated with TB transmission within diverse populations. By leveraging quantitative data and qualitative insights, the research enhances the understanding of the disease's impact on public health. Furthermore, the utilization of sophisticated modelling allows for the simulation of various intervention strategies, ultimately guiding policymakers in the development of targeted programs designed to reduce the prevalence of tuberculosis across the country. By conducting rigorous monitoring and evaluation at national, state, and district levels, the department ensures that TB control strategies are effective and aligned with the evolving needs of the population. Additionally, the department engages in implementation research that focuses on aligning its findings with the priorities of the National TB Programme. To enhance the capacity of future epidemiologists, it offers a variety of seminars and internship programs aimed at educating students about the complexities of TB epidemiology. Furthermore, the department is instrumental in providing essential technical support to both State and National TB programs, reinforcing its commitment to combating this significant public health challenge.

Studies in Progress

1. **DLSS-Sentinel Surveillance for tuberculosis burden in India 2023-2024. To develop national TB curve fitting mathematical model for incidence estimation on annual basis using community-based sentinel survey in India.**

Principal Investigator	:	Dr.Mukesh Kumar Sathya Narayanan,Scientist B,/ Dr.Sriram Selvaraju,Scientist E, Department of Epidemiology,National Institute for Research in Tuberculosis, Chennai
Participating Institutes	:	1.ICMR- National Institute for research in Tuberculosis(NIRT) ,Chennai.(Co-ordinating Institute) 2. .ICMR National JALMA Institute for Leprosy& other Mycobacterial Diseases(NJILOMD),Agra 3.ICMR National Institute for Implementation Research on Non-Communicable Diseases (NIIRNCD),Jodhpur 4.ICMR National AIDS Research Institute(NARI)Pune 5.ICMR National Institute of Cholera and Enteric Diseases (NICED),Kolkata 6.ICMR Regional Medical Research Centre(RMRC),Bhubaneshwar 7.ICMR National Institute for Research in Tribal Health(NIRTH),Jabalpur 8.ICMR-National Institute of Nutrition (NIN),Hyderabad 9.ICMR Regional Medical Research Centre(RMRC),Dibrugarh 10.ICMR Rajendra Memorial Research Institute of Medical Sciences (RMRIMS),Patna 11.ICMR National Institute of Cancer Prevention and Research (NICPR) 12.NTI National Tuberculosis Institute, Bengaluru 13. ICMR Regional Medical Research Centre(RMRC), Gorakhpur
Source of funding	:	Global Fund
Study period	:	2021-2025
Category	:	Description
Pillar	:	Prevent

Background

National Strategic Plan 2017-2025, India has set the goal to achieve the sustainable development goals related to TB to be achieved by the year 2025. This requires measurement of TB incidence and mortality at least for baseline and 2015. Since the country has diverse epidemiology as well as implementation coverage in terms of proportion of patients provided care under the programme. It is important to monitor the changing trend of the TB prevalence by implementing further rounds of national TB prevalence surveys in general population and sentinel surveillance in high-risk groups to provide insights into impact of interventions and to inform public health action.

Objectives

Primary Objective:

To develop national curve TB fitting mathematical model for incidence, estimation on annual basis using community-based sentinel survey.

Secondary Objectives:

1. To monitor national trends of TB prevalence, TB infection, health seeking behavior, Prevalence to Notification ratio at national level
2. To estimate the prevalence of TB infection in India
3. To monitor the tuberculosis mortality rate at the National Level in India among the surveyed population using verbal autopsy.
4. To explore the feasibility of using artificial intelligence tools for improvement of existing AI tools in sentinel survey.

Methods

1.Curve fitting mathematical model for TB incidence estimate:

Curve fitting mathematical models for disease incidence estimation involve analyzing historical data on the occurrence of a specific disease to determine the best-fitting mathematical function that describes the trend. This function can then be used to predict and estimate future disease incidence. By adjusting the parameters of the chosen model, such as exponential, logistic, or polynomial functions, the model can capture the pattern of disease spread and provide valuable insights for public health planning and intervention strategies. We will develop mathematical model for incidence estimation from the prevalence estimates from the TB survey and calibration will be done with baseline of 2015, using the WHO estimates as a starting point and curve fitting will be done using the latest national TB prevalence Survey based incidence estimation till 2021 and for subsequently from 2023 onwards the survey findings will be used to update the model every year. Design of this survey is described below.

2. Survey Study design:

Population-based cross-sectional survey. Sampling Strategy: Multi Stage Cluster sampling design will be used to estimate the sample size for the survey. Cluster selection: Cluster is defined as a population in a given village or a ward listed in the state group as per census 2011. Probability Proportionate to the Size (PPS) of the population method will

be used to select the number of clusters. 3.Sample Size: Assuming that the average of TB prevalence in India would reduce to 150 per lakh in India during the period 2023-24,for prevalence estimation at the National level, we need a total sample size of 1,50,000

Study progress

The Survey has been initiated in Tamil Nadu and so far, 16 cluster have been completed and 8000 participants have been enrolled.

Training has been completed in the states of Uttar Pradesh, West Bengal, Bihar, Maharashtra and would be initiated in the coming months.

2. Scaling up short course TB preventive regimen containing Isoniazid and Rifapentine given once-weekly for three months (3HP) among and household contacts of sputum positive pulmonary TB patients in India: - A demonstration study

Principal Investigator	:	Dr. G. Prathiksha, Dr. S. Ramesh Kumar
Participating Institutes	:	ICMR – Regional Medical Research Institute, Bhubaneswar ICMR-National Institute of Tuberculosis and Respiratory Diseases, New Delhi ICMR-National Institute for Research in TB, Chennai TB Elimination Programme of Tamil Nadu,Karnataka, Gujarat, Pondicherry and Andaman
Source of funding	:	Indian Council of Medical Research, New Delhi
Study period	:	4 years
Category	:	Description
Pillar	:	Prevent

Background

Household contacts of TB patients are at a high risk of TB infection and disease due to prolonged and proximal exposure to source TB case. The National Tuberculosis Elimination Programme (NTEP) of India recommends TPT for Household contacts of bacteriologically positive pulmonary TB patients. The TB preventive therapy guidelines of India, 2021 also recommends 3HP as an alternative to 6 months of isoniazid Monotherapy

Objectives

Primary objectives

1. To determine the feasibility of providing the 3HP preventive therapy to household contacts of bacteriologically positive pulmonary TB patients under program settings.

2. To describe the pattern of adverse drug reactions to 3HP preventive therapy and its management under program settings.
3. To determine the proportion of household contacts developing TB over a 2 year follow up period.
4. To understand the barriers and facilitators for providing 3HP preventive therapy under program settings.

Secondary objectives

1. To determine the proportion of ineligible household contacts (TBI test negative, not on TPT) developing TB over a 2 year follow up period.
2. To look for the transmission of TB from index case to household contacts through whole genome sequencing

Methods

STUDY DESIGN: Multi-centric prospective demonstration study.

Study population:

Household contacts of sputum positive pulmonary TB patients

Sample size: A total of 6250 study participants

This is a multi-centric prospective demonstration study where Household contacts of sputum positive pulmonary TB patients above 2 years of age are administered short course TB preventive regimen containing Isoniazid and Rifapentine given once-weekly for three months (3HP) after ruling out active TB under programmatic conditions. Focus Group Discussions (FGD) will be conducted among participants and health Care workers to understand the barriers and facilitators for 3HP implementation and ADRs will be captured using a treatment card for 3 HP.

Study progress

Training part completed, in Tamilnadu sites (Madurai, Chennai, Thoothukudi, Kancheepuram) Pondichery.Karnataka, Gujarat, Orissa and New Delhi sites. Enrolment of 3HP recipients done

3. Implementing Community based Case Finding Interventions (CCCFI) for improving TB notifications in Maldives

Principal Investigator	:	Dr.Sriram Selvaraju,Scientist E, Department of Epidemiology,National Institute for Research in Tuberculosis, Chennai
Participating Institutes	:	Health Protection Agency, Maldives
Source of funding	:	SEAR RRP
Study period	:	2.5 YEARS
Category	:	Delivery
Pillar	:	Build

Background

The Republic of Maldives is an archipelago located in the Indian Ocean, with 1190 coral islands that form a chain spanning 648 km north to south and 130 km east to west. The total land area is 298 sq. km, of which only 10% is suitable for agriculture. The islands are small and low-lying, with an average elevation of 2 meters above sea level. The geographical area is divided into 20 atolls, apart from the capital city Male. Outcomes from the National Tuberculosis Programme (NTP) indicate that some TB cases are still being missed, particularly among high-risk groups, due to a lack of adherence to the updated national diagnostic guidelines. There is a continuous need for training of the staff and contact tracing teams. Also, there is an urgent need to strengthen early diagnosis systems and treatment of TB.

Objectives

To measure the change in TB notification rates after introduction of community-based case finding interventions in 100 islands of Maldives

Methods

a. Study Design: Quasi-Experimental Design with pre-post comparison
b. Study Settings:100 Selected islands 20 Atolls of Maldives
c. Study Population: Population in 100 Selected islands in 20 Atolls of Maldives.
   Eligibility Criteria: All willing participants in the 100 selected islands including the migrants
d. Sample Size:200000 population in the 100 Selected islands in 20 Atolls of Maldives.
e. Intervention:
   The intervention package will be rolled put in the 100 Selected islands in 20 Atolls of Maldives
   i. Community outreach for community Engagement and Mobilization
   ii. Implementation of newer TB Active Case Finding Guidelines with strengthened sample transportation
   iii. Rollout of newer diagnostic algorithm with portable x-rays and molecular tests for TB Disease
   iv. Rollout of newer diagnostic algorithm with portable x-rays and Cy-TB Skin test for TB Infection
f. Control: The time period of 2 years in the 100 Selected islands in 20 Atolls of Maldives before implementation of these intervention packages in-terms of TB notification, treatment outcomes will serve as controls

Study progress

MOU under process

4. A study to determine the effectiveness of Adult BCG Vaccination/ revaccination in Prevention of TB among High-risk Groups in Identified States of India

Principal Investigator	:	Dr.Sriram Selvaraju,Scientist E, Department of Epidemiology,National Institute for Research in Tuberculosis, Chennai
Participating Institutes	:	Bhopal Memorial Hospital and Research Centre,Bhopal Central TB Division, New Delhi
Source of funding	:	ICMR
Study period	:	5 YEARS
Category	:	Development
Pillar	:	Prevent

Background

In spite of the controversy around the efficacy of the BCG vaccine, BCG has complex and diverse immunomodulatory influences and revaccination with BCG is safe and carries very minimal risk. So far, there is no other vaccine available for TB prevention apart from live attenuated BCG. BCG is effective against the severe forms of TB and has off-target effects, which prevent a large number of deaths every year. In addition, recent studies have shown promising effects of BCG revaccination. Therefore, revaccination with BCG probably (a) improves protection against all forms of TB and (b) enhances the off-target (nonspecific) effects of BCG against infections other than TB (mainly pneumonia and sepsis), and (c) prevents recurrence or progression to active TB following LTBI treatment.

Objectives

Primary Objective

To evaluate the effectiveness of adult BCG vaccination/revaccination under programmatic settings in the prevention of TB disease among High-risk Groups in Identified States of India

Secondary objective

To determine the safety of adult BCG vaccination/revaccination under programmatic settings among High-risk Groups in Identified States of India

Methods

A.Study setting and sites Healthcare centres in the selected NTEP Districts of identified states (Madhya Pradesh and Tamilnadu or other State) of India where the Central TB Division, MoH&FW, GoI, is introducing Adult BCG (re)vaccination.

Study Design :In depth follow-up of participants enrolled in a cluster randomised study

B. Study Eligibility Criteria

I. Any participant with the age 18 to 59 years, who satisfy any one or more of the following criteria for high-risk population, will be enrolled in the study, after obtaining informed consent

1. Patients who have completed TB treatment in the past 2 years
2. Household/close contacts of current TB patients as well as all those contacts of index TB cases enrolled in Nikshay as follows.
3. Individuals with a Body Mass Index of less than 18 kg per sq.mts
4. Smokers: Regular smoker of smoking 1 or more cigarettes per day with at least 100 cigarettes smoked in their life time within 5 years prior to enrolment in this study
5. Adults with a history of Diabetes (Self- reported; however, wherever feasible, prescription/diagnosis by a physician will be recorded)

II. Individuals who are aged 60 years or above Exclusion criteria in Intervention arm

1. Individuals with a known history of immunodeficiency or on immunosuppressive drugs or any procedure interfering with immune status or transplant or malignancy
2. Pregnant or lactating women

The eligibility for the study in both intervention and control arm are similar except that in the intervention arm they are BCG Vaccinated/Revaccinated while in control arm they are not BCG Vaccinated/Revaccinated.

All enrolled participants in the Intervention and Control districts will be followed up for a period of 3-years from the day of study enrolment. In the intervention district, participants who refused BCG vaccination will also be followed, after obtaining their consent.

After enrolment, the participants will be followed up in-person at the health facility at 1, 3, 6, 12, 18-, 24-, 30-, and 36-months post-recruitment both the intervention and control districts

Study progress

Awaiting funding and to be initiated.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1	District-wise prevalence of microbiologically confirmed pulmonary tuberculosis in Tamil Nadu, India.	Dr. Prathiksha.G, Scientist-C,	NHM, Tamil Nadu	Description	Estimates Districts wise estimates of TB prevalence and Prevalence to Notification ratio has been generated for the state of Tamil Nadu which will help the state to plan intervention strategies

DEPARTMENT OF HEALTH ECONOMICS

DEPARTMENT OVERVIEW AND MANDATES

Health Economics is increasingly recognized in public health and health research settings. The health economics is now foundational and integral to healthcare decision-making at every level. In this background, Department of Health Economics was established in ICMR-NIRT, Chennai on 4th July 2018. The mandate of the department is to conduct research on economic aspects of diseases with focus on tuberculosis. In addition, the department is providing technical support to generate health economics evidence to make policy decisions relating to drugs, devices, treatment pathways, and preventative health intervention strategies. One of the key mandates of the Department of Health Economics is to build the capacity for health economic research and practice in the country through various trainings, workshops, and capacity-building programmes. The department also acts as regional resource centre for health technology assessment in India, which analyses health technologies viz. medicines, devices and health programmes for its cost-effectiveness, clinical-effectiveness and equity issues by means of Health Technology Assessment (HTA).

Research focus of the department is to

- Estimate the economic burden of TB and other poverty-related diseases in the country.
- Study the cost-effectiveness of new drugs, devices, treatment pathways, and preventive health intervention strategies.
- HTA is undertaken to prioritize national health spending on various health technologies.

Studies in Progress

1. Health Technology Assessment in India (HTA-In) Project

Principal Investigator	:	Dr. M Muniyandi
Participating Institutes	:	ICMR-NIRT
Source of funding	:	HTA, DHR, New Delhi
Study period	:	2018 – 2026
Category	:	Delivery and Description
Pillar	:	Build

Background

The Ministry of Health and Family Welfare's Department of Health Research established the Health Technology Assessment in India (HTAIn) to evaluate the appropriateness and cost-effectiveness of health technologies. HTAIn follows international best practices, emphasizing transparent, inclusive, fair, and evidence-based decisions. It provides crucial evidence for prioritizing national health spending on various technologies like devices, medicines, vaccines, and procedures, thereby improving healthcare quality. HTAIn's recommendations guide the Indian government in health-related decision-making.

Objectives

1. To undertake HTA studies aiming at maximising health in the population, reducing out of pocket expenditure (OOP) and reducing inequity.
2. To support the process of decision-making in health care at the Central and State policy level by providing reliable information based on scientific evidence.
3. Develop systems and mechanisms to assess new and existing health technologies by a transparent and inclusive process.
4. To collect, analyse and disseminate evidence in a systematic and reproducible way and ensure its accessibility and usefulness to inform health policy.

Methods

Health Technology Assessment and cost-effectiveness analysis (CEA) use several methods, including systematic reviews, meta-analyses, decision-analytic models like Decision Trees and Markov models, and economic evaluations such as cost-effectiveness, cost-utility, and cost-benefit analyses. These methodologies consider clinical effectiveness, cost, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs). Sensitivity analyses, like probabilistic sensitivity analysis, and one-way sensitivity analysis, assess uncertainty.

Study progress

The project staff have been working closely with the Government of Tamil Nadu and the Government of India. Based on their demands and priorities we received different topics for Health Technology Assessment. So far, we have developed 12 proposals and five HTA studies have been completed and approved by the Technical Appraisal Committee of DHR, New Delhi. Based on the findings of the studies, the policy briefs was submitted to DHR for approval. In addition to that for the capacity building, we have conducted health system costing workshop at Pune. Under this project, studies are in progress.

2. Assessing the cost-effectiveness of the new treatment BPaLM/BPaL for Multi-drug resistant, rifampicin resistant, tuberculosis (MDR-RR-TB) as compared to the shorter oral Bedaquiline containing regimen under the National Tuberculosis Elimination Programme (NTEP)

Principal Investigator	:	Dr. M Muniyandi
Participating Institutes	:	ICMR-NIRT
Source of funding	:	HTA, DHR, New Delhi
Study period	:	Six months
Category	:	Delivery
Pillar	:	Build

Background

Current options for treating tuberculosis (TB) that is resistant to rifampicin (RR-TB) are few, also regimens are often long and poorly tolerated. Following recent evidence from the TB PRACTECAL trial, countries are considering programmatic uptake of 6-month, all-oral treatment regimen (BPaLM/BPaL). We conducted an economic evaluation to assess whether the introduction of BPaLM/BPaL regimen under National Tuberculosis Elimination Programme (NTEP) for the treatment of MDR/RR-TB is a cost-effective strategy.

Objectives

1. To estimate the cost and effectiveness of BPaLM/BPaL regimen for drug resistant tuberculosis (MDR/RR-TB).
2. To estimate the incremental cost incurred from BPaLM/BPaL regimen in comparison with the current mix of (Longer regimen 58% and shorter regimen 42%) SoC regimen.
3. To estimate the incremental cost effectiveness ratio and quality adjusted life years (QALYs) gained due to roll out of BPaLM/BPaL regimen.

4. To estimate the budget incurred by the programme if BPaLM/BPaL regimen is implemented.

Methods

The study uses an economic model comprising a Markov chain analysis. The study estimated the incremental costs, life years gained and QALYs gained by the introduction of a BPaLM/BPaL regimen for MDR/RR-TB patients. Scenario analysis for different proportions of shorter and longer regimen for BPaL/BPaLM was done. Cost threshold analysis has been done to assess the ideal cost of which the drug BPaL/BPaLM turns into cost-saving. Budget impact analysis has been conducted to assess the financial implications of adopting BPaL/BPaLM compared to mixed SoC.

Study progress

The analysis of the study has been completed, the study report was submitted to the DHR for approval, and the manuscript has been prepared for publication. As soon as we receive approval from the DHR, we will proceed with the publication. The findings of the study indicate that BPaL-based regimens are likely to be cost-saving and more effective than the current mixed standard of care (SoC) across a range of settings. Countries should consider the programmatic uptake of BPaL-based regimens.

3. Cost-Effectiveness of Upfront CB-NAAT using different Algorithms for diagnosing DS/DR-TB among Presumptive Pulmonary TB Patients in India

Principal Investigator	:	Dr. M Muniyandi
Participating Institutes	:	ICMR-NIRT
Source of funding	:	HTA, DHR, New Delhi
Study period	:	Six months
Category	:	Delivery
Pillar	:	Build

Background

Tuberculosis (TB) remains a significant global health challenge, especially in India, which has the highest TB burden worldwide. Traditional diagnostic tools for TB have limitations in terms of accuracy and speed, particularly in detecting drug-resistant TB (DR-TB). To address these gaps, the molecular diagnostic tool CB-NAAT (GeneXpert) was developed, enabling rapid detection of TB and rifampicin resistance. This study assesses the cost-effectiveness of using CB-NAAT with different diagnostic algorithms to improve TB diagnosis and management in India.

Objectives

To estimate the cost effectiveness of upfront CB-NAAT using different diagnostic algorithms as compared to current diagnostic strategy for diagnosing DS/DR-TB in India.

Methods

This economic modelling study was conducted from a health system perspective. We used decision tree analysis to estimate the incremental costs, number of QALYs gained for presumptive TB patients by using the Upfront CB-NAAT Using Different Diagnostic Algorithms along with DS/DR treatment. Secondary data were collected from the published literature. The uncertainty in the model is evaluated using one-way sensitivity analysis and probability sensitivity analysis. The analysis is done using Microsoft excel and TreeAge pro software.

Study progress

The data collection was done and analysis is under process. This study highlights the significance of DS/DR-TB screening and treatment in TB control efforts. The four strategies are NAAT only, smear followed NAAT and smear followed X-Ray followed by NAAT and LPA, focussing on Upfront NAAT. Findings help in decision making, reducing time delays and improving diagnostic accuracy.

4. Comparing Cost-effectiveness of Shorter Course Regimens for Multi Drug Resistant-Tuberculosis (MDR-TB) Treatment

Principal Investigator	:	Dr. M Muniyandi
Participating Institutes	:	ICMR-NIRT, Chennai and International Union Against TB and Lung Diseases, New Delhi
Source of funding	:	Union
Study period	:	Six months
Category	:	Delivery
Pillar	:	Build

Background

TB remains a leading global health challenge, especially with the rise of drug-resistant strains like multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). India, with 27% of global TB cases, faces a significant public health challenge due to MDR-TB. The standard treatment regimens for MDR-TB are lengthy, costly, and often associated with severe side effects, impacting adherence and overall effectiveness. To address this, several shorter regimens, such as BEAT, BPaL, and mBPaL, are being evaluated for their cost-effectiveness compared to the current standard of care.

Objectives

1. To find the most cost-effective shorter regimen to treat MDR-TB when compared to the current standard of care (SoC) 9-11 months regimen.
2. To estimate the incremental cost incurred from shorter regimens to treat MDR-TB in comparison with the current standard of care (SoC) 9-11 months regimen.
3. To estimate the incremental cost effectiveness ratio and quality adjusted life years (QALYs) gained by the shorter regimens.

Methods

Study settings and population the study will be conducted taking into consideration of adults who are above 18 years and those who are having DR-TB undergoing treatment in the public health facilities of a high TB burden country. Study population represents a hypothetical cohort of 100000. Study design and perspective A hybrid economic model involving a decision tree and Markov model will be conducted to analyse the cost effectiveness of the shorter regimen for DR-TB in compared to the mix SoC regimen. The economic evaluation model will be conducted primarily from the provider perspective, which includes cost incurred by the health system.

Study progress

This study will provide information on the cost-effectiveness of a shorter regimen for DR-TB patients. No such previous studies have been conducted by comparing all the shorter v/s longer regimen, so this study findings will be useful for policymakers to implement shorter regimen over longer regimen in the Indian health system. The data collection and analysis was done. The manuscript is under preparation.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1	Assessing the cost-effectiveness of Latent TB Infection Tests (LTBI) in India	Dr. Muniyandi M, Scientist-E	DHR	Delivery	The Cy-Tb test for diagnosing LTBI is cost-effective at the current price, and price negotiations could further change it into a cost-saving strategy.
2	Health Technology Assessment for Vagal Nerve Stimulation intervention (VNS)	Dr. Muniyandi M, Scientist-E	DHR	Description	Our meta-analysis showed that 47% of DRE patients have experienced ≥50% seizure reduction with VNS treatment. It should be considered in patients in whom ASM has failed or who continue to experience seizures after medication.

DEPARTMENT OF IMMUNOLOGY

DEPARTMENT OVERVIEW AND MANDATES

The Department of Immunology focuses on the biological, immunological and molecular aspects of mycobacterial infections. The department is involved in studies on basic pathogenic mechanisms that may lead to better tuberculosis (TB) diagnostic tools, development of vaccines and other immune interventions for the prevention and control of infection and disease. The department has adopted a multidisciplinary approach which includes clinical immunology, molecular biology, genomics and proteomics together with molecular epidemiology to explore immunology of TB.

Immunologic studies focus on genetic regulation of the immune response, the role of both HLA and non-HLA polymorphisms, and cellular immune responses in TB. The researches in the department aims to understand the molecular mechanisms of infection and diseases, by extensive transcriptomic studies, along with the specific roles of mycobacterial antigens and their interactions with monocytes and other soluble immune components. More recently, the department has added facility for Next Generation Sequencing of mycobacterial clinical isolates and performing research activities towards understanding the drug resistance, transmission dynamics and identification of novel mutations driving resistance to the anti TB drugs. Apart from these, the department is also focused on understanding the Zoonotic and reverse zoonotic transmission of tuberculosis between human and cattle.

Studies in Progress

1. CRISPR Mediated platform for diagnosis and rapid detection of drug resistance pattern in Mycobacterium Tuberculosis

Principal Investigator	:	Dr. K. R. Uma Devi, Scientist F Mr. P. Venkatesan, Technical Assistant
Participating Institutes	:	ICMR- National Institute for Research in Tuberculosis (NIRT), Government Hospital of Thoracic Medicine (GHTM), Tambaram
Source of funding	:	ICMR Intramural
Study period	:	2018-2024
Category	:	Development
Pillar	:	Detect

Background

The available gold standard culture techniques for TB diagnosis have several drawbacks, and therefore there is an urgent requirement for a more precise and reliable diagnosis method for TB. Currently, several nucleic acid-based amplification techniques, such as the Xpert MTB/RIF assay and Line Probe Assay, are also available to diagnose and detect the drug resistant pattern of pulmonary clinical specimens. These techniques, however, are limited in identifying drug resistance patterns for a few drugs. In this context, it is important to develop tools using newer technologies like CRISPR based tools for diagnosis and detection of drug resistance in Mycobacterium tuberculosis with less turnaround time and high sensitivity and specificity.

Objectives

1. To develop CRISPR mediated programming platform for detection and identification of drug resistance in Mycobacterium tuberculosis.
2. To evaluate the performance of developed CRISPR Cas13a detection tool in clinical isolates of Mycobacterium tuberculosis.
3. To evaluate the performance of developed CRISPR Cas13a detection tool in biological specimens of Mycobacterium tuberculosis.

Methods

Step 1: Expression and Purification of Cas13a: The Cas13a bacterial expression system was purchased from Addgene.

This Cas13a bacterial expression vector was transformed in to Rosetta competent cells for expression of protein. All subsequent steps of protein purification were performed according to Gootenberg et al., 2017 with slight modifications.

Step 2: CRISPR RNA PREPARATION [crRNA Preparation]: The CRISPR RNA for MTB detection and drug resistance

was designed and the construct was ordered as DNA (integrated with appended T7 promoter sequence). Using Hiscribe T7 quick high yield RNA synthesis Kit(NEB), crRNA was synthesized from the template then purified using Monarch RNA purification kit(NEB).

Step 3: DNA and RNA extraction: The DNA and RNA extraction from the respective samples was carried out as per optimised protocol and the samples were subjected to Cas13a assay.

Step 4: Collateral detection assay: Detection assay was performed for both detection in target nucleic acid with the purified Cas13a, crRNA, quenched fluorescent RNA reporter [RNAse alert V2 Thermo scientific]. The reaction was read on a fluorescent plate reader.

Study progress

CRISPR-Cas13a-based molecular diagnostic tool for detecting Mycobacterium tuberculosis (M.tb), involves fluorescence-based quantitative detection of M.tb nucleic acids in real time. Based on the findings and performances a provisional patent application has been filed on 20th Oct. 2023 and application number assigned is 202311071943.

2. Molecular Analysis of Monocyte Subsets from Humans Infected with Mycobacterium tuberculosis

Principal Investigator	:	Dr. Ramalingam B, Scientist E
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis (NIRT), Greater Chennai Corporation (GCC)
Source of funding	:	DBT Ramalingaswami Fellowship
Study period	:	2022-2023
Category	:	Description
Pillar	:	Detect

Background

Transcriptomic studies of peripheral blood mononuclear cells (PBMC) revealed the immune protective and defective functional behaviour of monocytes against TB. In addition, monocyte abundance with differential gene expression was observed between latent and active TB and those genes are found to be associated with inflammatory responses. However, PBMCs often confound the transcriptome data due to the mixed expression of heterogenous cell population. Hence, studying the single cells particularly monocytes is essential as they are the precursor of macrophages and the prominent innate cell in PBMCs with marked immune function during mycobacterium tuberculosis infection.

Objectives

1. To study the transcriptome profiles from sorted monocytes and to identify the differentially expressed genes across the TB spectrum.
2. To identify the most promising candidate biomarker genes, together with its pathway networks by comparing active TB patients and healthy subjects.

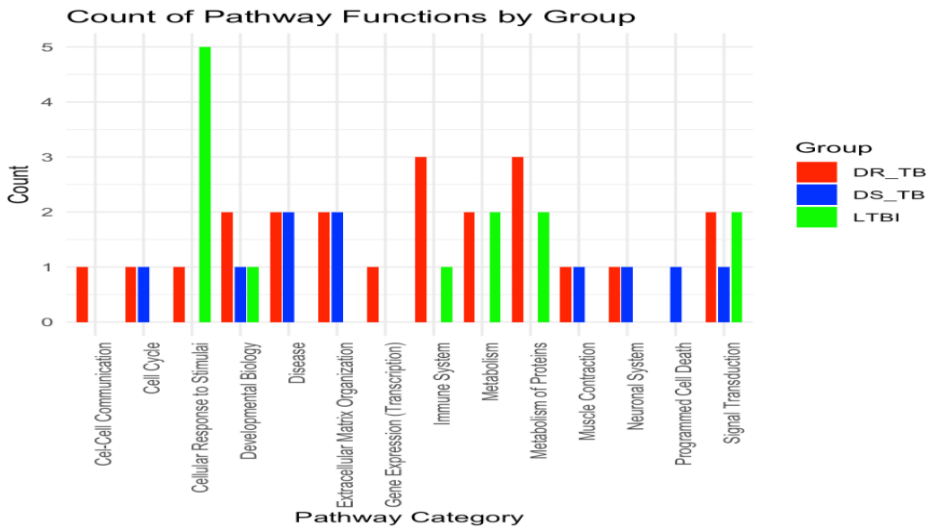
Methods

FACS sorted monocytes (HLA-DR+CD14+ CD16+), (N-32) were subjected to Illumina RNA sequencing, representing four groups [healthy individuals (HC), latently infected (LTB), drug sensitive TB (DS-TB) and single or multi-drug-resistant TB (DR-TB)] with 8 samples each. Differentially regulated mRNAs and their targeted pathways were identified using DESeq2 and GSEA signature.

Study progress

- The monocyte transcriptome data was subjected to bioinformatic pipeline to identify monocyte related genes and their role in TB.
- Large learning model analysis revealed distinct molecular signatures for each group, while also highlighting some shared mechanisms in TB pathogenesis based on artificial intelligence scoring system.
- In addition, reactome pathway analysis revealed the biological processes associated with each TB condition.
- Both analyses revealed characteristic function of each condition such as DR-TB with strong immune response and systemic damage, DS-TB with disease related mechanisms and tissue remodelling and LTB with metabolic activity and immune readiness.
- This comprehensive view provides valuable insights into the complex interplay between the host immune response and MTB in different disease states.

Figure: Functional enrichment of monocyte related genes from reactome database



3. CYP27b1 gene promoter polymorphisms in pulmonary tuberculosis

Principal Investigator	:	Dr. Ramalingam B, Scientist E Mr. Harishanker M, Technical Officer C
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis, (NIRT)
Source of funding	:	ICMR Intramural
Study period	:	2022-2024
Category	:	Description
Pillar	:	Detect

Background

Vitamin D deficiency has been reported in the association of tuberculosis in different ethnic populations. It has been reported that inadequate levels may suppress the human cathelicidin antimicrobial peptide (hCAP18) and associated with increased susceptibility to infections. Several evidence have highlighted the importance of mutations in vitamin D-regulating genes for vitamin D status. Cyp27b1 gene encodes 1α-hydroxylase enzyme which synthesize active form of vitamin D3. Polymorphisms in this gene associated with vitamin D deficiency and TB outcome.

Objectives

1. To find out allele and genotype frequencies of Cyp27b1 -1077, -1260 and -1918 promoter polymorphisms in 100 healthy controls (HCs) and 100 pulmonary tuberculosis (PTB) patients.
2. To find out the association of gene variants with vitamin D deficiency by correlating with vitamin D levels.

Methods

Genomic DNA was isolated from portion of whole blood by a simple salting out procedure. Genotyping was performed by polymerase chain reaction followed by restriction fragment length polymorphism (PCR-RFLP) method from isolated genomic DNA of HCs and PTB patients. Vitamin D levels were estimated by ELISA method.

Study progress

- In -1918 polymorphism, genotype “CC” found higher frequency in HCs and PTB patients.
- In recessive model (TT vs CC+CT), a trend towards TB protection was found in “TT” genotype.
- In Overdominant model (CT vs CC+TT), a trend towards TB susceptibility was found in heterozygous genotype.
- 45 samples needs to be studied and correlate with vitamin D levels in both the study groups.

Table shows number of subjects studied and genotype details using PCR-RFLP method

Cyp27b1 Promoter SNP	So far studied		PCR size in base pair (bp)	Restriction enzyme	Genotypes	Restricted fragment length in base pair(bp)
	HCs	PTB				
-1918(C/T)	80	80	164	Tsp509I	CC CT TT	164bp 164+145+19bp 145+19bp

4. Immunomodulation of Serum Vitamin D levels combined with circulatory proteins towards a prognostic biomarker for pulmonary tuberculosis

Principal Investigator	:	Dr. Ramalingam B, Scientist E Dr Subash Babu, Scientific Director ICER
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis (NIRT)
Source of funding	:	Department of Biotechnology DBT)/ International Centre for Excellence in Research (ICER).
Study period	:	2020-2024
Category	:	Description
Pillar	:	Detect

Background

The molecular mechanism for control of inflammation towards infection is dependent on a set of micronutrients, particularly the trace elements, with that of the inflammatory cytokines are being regulated each other through feed-forward loops. These Trace elements, particularly, iron, Zinc, copper and selenium have an immunomodulatory effect towards controlling the infection and inflammation process. Deficiency of these metals in any form any form, i.e., malnutrition, can lead to nutritionally acquired immunodeficiency syndrome, by all means, it can increase an individual's susceptibility to progression of infection and to disease. Here, in this study, the circulatory levels of the trace elements and micronutrients in the TB patients and the correlation between them and the other inflammatory molecules, vitamin D has been carried out, which

has not been accurately estimated by any study yet.

Objectives

To estimate the levels of circulating trace elements and to correlate with the other soluble inflammatory proteins and vitamin D towards immunomodulation among pulmonary TB patients, during and after the treatment.

Methods

Plasma samples were collected from (1) Pulmonary Tuberculosis (PTB) patients at two time points: baseline and after 6 months of anti-TB treatment (ATT), (2) latently Mtb infected (IFN-γ+) participants, and (3) healthy controls. The PTB patients (n=32) were microscopically sputum smear-positive for Mtb at the time of diagnosis and X-ray positive for TB disease. The LTB group (n=32) was positive for interferon-gamma (IFN-γ) test when diagnosed by 3rd generation QuantiFERON-TB Gold assay. The non-LTB group (n=32) was negative for the IFN-γ test and not symptomatic for TB. Plasma trace element levels and vitamin D were estimated and were correlated with other soluble key inflammatory proteins, together with other demographic data and soluble key inflammatory mediators in TB disease.

Study progress

- Found Vitamin D metabolism has a significant role in PTB, by showing the plasma Vitamin D levels significantly decreased than LTB and non-LTB individuals.
- After ATT in PTB patients, the plasma Vitamin D levels increased significantly than before ATT.
- BMI has a positive correlation in the Plasma Vitamin D levels in PTB.
- Vitamin D is associated with all other immunological parameters that distinguishes inflammation in the host.

IFNγ, TNFα, IL17A, IL-4, Resistin and G-CSF has an impact in Vitamin D metabolism.

5. Identification of Bovine tuberculosis specific proteins by the Immunoproteomic approach

Principal Investigator	:	Dr. P. Kannan, Scientist E
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis (NIRT)
Source of funding	:	ICMR Intramural
Study period	:	2022-2024
Category	:	Description
Pillar	:	Detect

Background

Bovine tuberculosis (bTB) is a major health and economic issue. Mycobacterium tuberculosis and M. bovis cause most human and animal TB. The major diagnostic test for bovine tuberculosis is the TST. In this test, animals receive intradermal M. bovis pure protein derivative (PPD). Bovine PPD is a poorly characterised protein, lipid, and carbohydrate combination. Environmental Mycobacterial species share certain Bovine PPD components. It sometimes causes false positives. In order to uncover bovine tuberculosis-specific antigens, we propose to analyse the immune response of the culture filtrate proteome of Mycobacterium tuberculosis of bovine origin isolated from prior NIRT studies. These methods will detect new bovine TB antigens. This helps produce a more sensitive bovine TB blood test.

Objectives

1. Separation of culture filtrate proteins of the Mycobacterium tuberculosis by Iso Electrofocussing (IEF) and Second dimensional separation of IEF separated fractions by SDS-PAGE followed by whole gel elution
2. Immunologic characterization of the separated culture filtrate proteins in the bovine blood sample and Proteomic characterization of the Immuno dominant proteins by Mass spectrometry analysis

Methods

Mycobacterium tuberculosis strain from infected cattle recovered from glycerol stocks was sub-cultured on Lowenstein-Jensen media at 37℃. Independent colonies formed after 21 days was transferred and incubated in 10ml Sautons minimum media at 37℃ for three weeks. After incubation, 10ml culture was transferred to 100ml Sautons media. BHI agar was tested for contamination and incubated at 37℃ for three weeks. Culture filtrate Protein (CFP) was collected by aseptically transferring the culture to 1 litre new Sautons media and incubating at 37℃ for 45 days. After incubation, the liquid culture was centrifuged at 4000g and 4℃ for 10 min to collect the CFP in a sterile vial. Pellets were stored at -80℃.The CFP was filtered through a 0.22µm sterile cup and concentrated using a semi-automated protein concentrator. As per manufacturer directions, the protein concentration was measured using Pierce™ BCA Protein Assay Kit (Sigma). Standardised culture pellet lysis to extract whole-cell protein after not getting the expected protein concentration. The proteins samples were subjected to isoelectric focusing (IEF)

Study progress

The proteins were subjected to IEF in eight batches and made into 15-20 fractions according to pH ranging from 1-13. Pooled Protein fractions separated by isoelectric focusing (IEF) on pH gradient.

6. Screening for the presence of Mycobacterium tuberculosis complex (MTBC) organisms in wild ungulates (spotted deer and blackbuck) and their environment in Chennai -an explorative study

Principal Investigator	:	Dr. P. Kannan, Scientist E
Participating Institutes	:	ICMR-National Institute for Research in Tuberculosis (NIRT), Madras Veterinary College.
Source of funding	:	ICMR Intramural
Study period	:	2022-2025
Category	:	Description
Pillar	:	Prevent

Background

Wildlife tuberculosis (wTB) is an understudied area in India, a country with a high TB burden and significant zoonotic risk. To achieve the End TB goal with a One Health approach, it's crucial to investigate wTB incidence and the Mycobacterium tuberculosis complex (MTBC) in wildlife. Guindy National Park in Chennai, India, home to spotted deer, sambar deer, and endangered blackbuck, provides a unique setting. We plan to collect and test fecal pellets and post-mortem samples from these animals, along with soil and water samples from their environment, to detect MTBC presence, shedding light on wTB dynamics.

Objectives

To explore the presence of MTBC organisms in the faecal, and post mortem samples from free ranging blackbuck and spotted deer as well as soil water samples in their natural environment at the Guindy national park and adjoining areas in Chennai.

Methods

An exploratory study was conducted at Chennai's Guindy National Park, collecting faecal samples from black bucks and spotted deer, along with post-mortem lung and lymph node samples from wild ungulates whenever available. For faecal, soil, and water samples, MTBC isolation is performed following positive PCR detection of the MPT64 gene, characteristic of MTBC. Post-mortem lung and lymph node samples are decontaminated and inoculated into both liquid and solid media for MTBC isolation. Drug susceptibility testing (DST) is conducted and whole genome sequencing (WGS) is employed to determine MTBC genetic relatedness. Additionally, histopathological analysis is carried out on tissue sections.

Study progress

From Guindy National Park, 70 faecal pellets were collected. GeneXpertUltra and Line Probe Assay (LPA) on 14 samples confirmed MTBC presence in 7 of which one isolate was isoniazid-

resistant, and another was resistant to both rifampicin and isoniazid, (collected from cohabiting black bucks). Eleven tissue samples were collected (4 black bucks, 6 spotted deer, 1 sambar deer). Culture methods detected MTBC in 3 black bucks, 4 spotted deer, and 1 sambar deer. Except for one sambar deer and one black buck and two spotted deer (WGS pending) , all cultured isolates were identified as M. orygis through PCR, spoligotyping (ST587), WGS, and RD analysis (RD7 to RD10, RDOryx_1, RDOryx_4, RD12Oryx, RD301, RD315 deletions). These isolates clustered with global M. orygis isolates in phylogenetic analysis, with SNP differences of 20-153 SNPs, indicating no in-herd transmission. All cultured isolates were drug-sensitive; histopathology revealed Stage III granuloma formation in positive tissue samples.

7. Study on Mutations Associated with Pyrazinamide Resistance in *Mycobacterium tuberculosis*

Principal Investigator	:	Dr. P. Kannan, Scientist E Ms. R. Ananthi (ICMR-SRF)
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR Extramural
Study period	:	2019-2022
Category	:	Description
Pillar	:	Detect

Background

Pyrazinamide (PZA) plays a crucial role in treating TB in active, latent infections and varied drug susceptibility profiles. However, PZA resistance contributes to adverse outcomes, complicating management. This study addresses the evolving challenges of PZA resistance in Mycobacterium tuberculosis, focusing on standardizing the MGIT960 PZA drug susceptibility testing method and identifying novel mutations associated with PZA resistance.

Objectives

The objective of this study is to understand the Pyrazinamide resistance in Mycobacterium tuberculosis strain isolated from presumptive drug-resistant patients from Chennai.

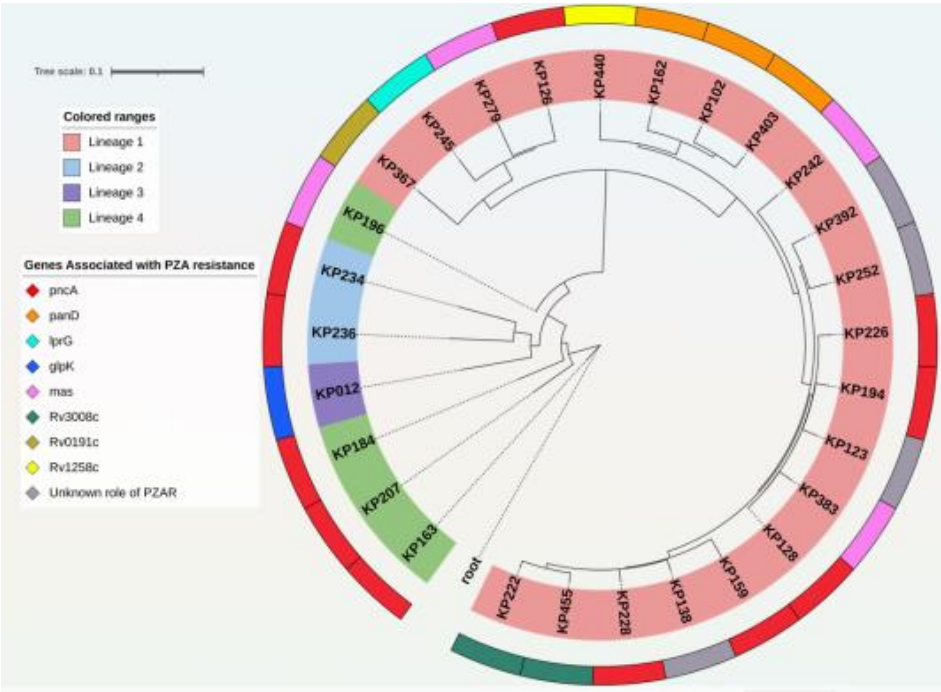
Methods

The study included 401 clinical strains from presumptive drug-resistant patients from Chennai, South India collected during 2017-2018, which were used for this study. The study explored the diagnostic performance of phenotypic and genotypic methods for detecting PZA

resistance. Modifications were implemented to the MGIT960 PZA DST method aim to minimize false-resistant results. Spoligotyping and phylogenetic analysis was done based on PZA resistance to illustrate mutations in genes associated with PZA resistance.

Study progress

1. The study data showed that PZA resistance significantly reduced from 27% to 7.7%, aligning phenotypic results with genotypic findings
2. The genotypic analysis identified mutations in genes such as *pncA* (45%), *panD* (9.6%), *mas* (12.9%), *glpK* (3.2%), and *lprG* (3.2%), along with additional efflux mechanisms. Novel mutations were identified in the *glpK* and *mas* genes with wild-type *pncA* in clinical isolates.
3. The study underscores the importance of minimizing false-resistant results in the MGIT PZA DST by diluting bacterial load and employing minimal inoculum, which could enhance tuberculosis diagnosis.
4. The phylogenetic analysis determined that *M. tuberculosis* lineage-1 was most prevalent among the resistant population. Mutations in *pncA* were found to be dispersed across all four lineages (L1 - L4), while alternative mechanisms, including mutations in the *mas*, *panD*, and *lprG* genes, were observed in Lineage-1, *glpK* gene in Lineage-3, and *mas* gene in Lineage-4.



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

Principal Investigator	:	Dr. N. Pavan Kumar, Scientist D
Participating Institutes	:	ICMR Institutes all over India
Source of funding	:	ICMR Ad Hoc Extramural
Study period	:	2022-2024
Category	:	Description
Pillar	:	Prevent

Background

COVID-19 cases was rising rapidly in countries where Omicron VOC has been reported, indicating its high transmissibility. India's COVID-19 vaccination programme had proposed to initiate additional third dose for healthcare and frontline workers and individuals aged above 60 years with comorbidities. Limited studies from India have documented dynamics of immune response of additional third dose of COVISHIELD/COVAXIN vaccine using homologous regimen.

Objectives

1. To characterise SARS-CoV-2 specific humoral and cellular immune response after homologous precautionary third dose of COVISHIELD / COVAXIN vaccine at different time points.
2. To estimate the incidence of SARS - CoV- 2 symptomatic infection post third dose of COVID-19 vaccine.

Methods

This prospective cohort study will be conducted among fully vaccinated (i. e. who have received two doses) individuals working in different ICMR institutes in India. From the enrolled study participants, SARS-CoV-2 specific IgG (S) and neutralizing antibodies for wild type were estimated. From the Collected samples Invitro cell cultures are undergoing stimulation with the peptide pools of PepTivator SARS-CoV-2 Prot_S1, PepTivator SARS-CoV-2 Prot_M, omicron variant and delta variants. A panel of multifunction T cells, memory T cells and immune activation markers were estimated.

Study progress

44 samples have been enrolled and blood samples were collected from COVID-19 Vaccinated individuals. Additionally, n=32 samples from ICMR-NIE were collected for Cell Mediated Immune Responses analysis.

Laboratory investigations

- From the collected samples PBMC cells, serum and plasma were cryopreserved
- From the enrolled study participants SARS-CoV-2 specific IgG (S) and neutralizing antibodies for wild type

were estimated during pre and post vaccination time points

- From the Collected samples Invitro cell cultures were currently undergoing upon stimulating with the peptide pools of PepTivator SARS-CoV-2 Prot_S1, PepTivator SARS-CoV-2 Prot_M, omicron variant and delta variants. A panel of multifunction T cells, memory T cells and immune activation markers are estimated.

9. Characterization of immune responses against SARS-CoV-2 and variants of concern in SARS-CoV-2 naturally infected and COVID-19 vaccinated individuals

Principal Investigator	:	Dr. N. Pavan Kumar, Scientist D
Participating Institutes	:	Greater Chennai Corporation(GCC)
Source of funding	:	ICMR Ad Hoc Extramural
Study period	:	2022-2024
Category	:	Description
Pillar	:	Build

Background

The emergence of SARS-CoV-2 variants harbouring mutations in the spike (S) protein has raised concern about potential immune escape. Immunological memory is established by an initial priming of the immune system, either by natural infection or vaccination. SARS-CoV-2 infections may induce lasting immunological memory, although the different components of the adaptive immune system exhibit distinct kinetics.

Objectives

1. Characterization of humoral immune response in naturally infected and vaccinated individuals
2. Characterization of immune protection in naturally infected and vaccinated individuals

Methods

This is a prospective Cohort study. Study population included the following:

COVID-19 vaccinated individuals (Covaxin or Covishield) after completion of two doses of vaccine, COVID-19 naturally infected individuals with 15-30 days post PCR confirmation, who had either asymptomatic, mild or severe disease. From the collected samples PBMC cells, serum and plasma were cryopreserved. SARS-CoV-2 specific IgG (S) and neutralizing antibodies for wild type and for other emerging variants were estimated during pre and post vaccination time points. Flowcytometry ex-vivo immunophenotypying (memory T cells, monocytes and B cells) and Invitro whole blood cell cultures were performed upon stimulating with the peptide pools of PepTivator SARS-CoV-2 Prot_S1 and PepTivator SARS-CoV-2 Prot_S.

Study progress

Study Groups		Baseline	Follow-up 1 (Month 2)	Follow-up 2 (Month 6)
COVID-19 vaccinated individuals	Covaxin	66	52	30
	Covishield	36	28	19
COVID-19 naturally infected individuals	COVID-19	44	31	20
	Total	**146**	**111**	**69**

Laboratory investigations

- From the collected samples PBMC cells, serum and plasma were cryopreserved
- From the enrolled study participants SARS-CoV-2 specific IgG (S) and neutralizing antibodies for wild type and for other emerging variants were estimated during pre and post vaccination time points.
- From the Collected samples flowcytometry ex-vivo immunophenotypying (memory T cells, monocytes and B cells)and Invitro whole blood cell cultures were performed upon stimulating with the peptide pools of PepTivator SARS-CoV-2 Prot_S1 and PepTivator SARS-CoV-2 Prot_S.
- Using the stored plasma samples we performed a multiplex assays using Human Magnetic Luminex Assay for a 45-analyte panel. This panel will include the following parameters, IL-1α, IL-1ra, IL-3, IL-4, IL-5, IL-1β, IL-6, IL-2, IL-7, IL-10, TNFα, INFγ, IL-12p70, IL-13, IL-15, IL-17A, IL-17E, IL-33, IFNα, IFNβ, TGFα, PDL-1, CCL2, CCL3, CCL4, CCL-5 CCL11, CCL19, CCL20 CXCL1, CXCL2, CXCL8, CXCL10, CX3CL1, CD40 Ligand, EGF, FGF-2, Flt-3 Ligand, G-CSF, GM-CSF, PDGF-AA, PDGF-BB, TRAIL, VEGF, GranzymeB.

Interim Findings

- COVID-19 vaccination induces enhanced SARS-CoV-2 binding antibodies of IgG spike and NAb levels against the ancestral strain and also against the varient lineages of B.1.617.2 (Delta, India), B.1.1.529 (Omicron, India), B.1.351 (Beta, SA) and B.1.1.7 (Alpha, UK).
- All the proinflammatory cytokines levels are dimnished in vaccinated group in comparison to the COVID-19 naturally infected individuals
- Measurement of frequencies of multifunctional T cells, activation markers, T follicular helper cells and total B cells following stimulation with either SARS-CoV-2-specific antigens or variant of concern in the follow-up samples at various time points.

Translational Potential

- Together, this study provided a novel and previously uncharacterized information about the ability of humoral and cellular immunology in naturally infected and vaccinated individuals.
- Study findings reveals that both the vaccines (Covishield and Covaxin), are more effective toward the wild-type virus and variants of concern
- Findings imply that immunisation may protect against inflammation even in the presence of breakthrough symptoms of infection

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1.	Accurate, Rapid, Robust & Economical Diagnostic Technologies for Tuberculosis (ARREST-TB)	Dr.K.R.Uma Devi, Scientist F	Department of Biotechnology (DBT)	Development and Description	ARREST-TB project aims to develop low-cost, reliable point-of-care TB diagnostics with built-in telemetry, eliminating the need for central labs. The goal is to deliver affordable solutions, costing less than one-tenth of current methods, suitable for resource-limited settings.
2	Cyp27b1 promoter -1077 (C/G) and -1260 (C/A) polymorphisms in pulmonary tuberculosis	Dr. B.RAMALINGAM, Scientist-'E', Dr. M.HARISHANKAR, Technical Officer-'C'	ICMR-Intramural	Description	• In dominant model (GG vs CG+CC), a significant protection was found with TB in -1077 CG+CC genotypes. • In -1077 GG genotype, a significant association was found with TB susceptibility and vitamin D deficiency [median level: 8.1ng/ml]. • Those risk group individuals may be recommended for vitamin D supplementation to overcome the disease.

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
3	Insights into the genomic adaptation of *Mycobacterium tuberculosis* (MTBC) species in Cattle	Dr. P. Kannan Scientist E	ICMR	Discovery	The genomic impact of IS*6110* insertions and their effect on various metabolic processes and pathways suggestive of its pertinence was elucidated
3	Identification of *Mycobacterium tuberculosis* complex (MTBC) organisms in the lymph node samples of slaughtered cattle in Chennai	Dr. P. Kannan, Scientist E	ICMR Extramural	Description	In a study of 500 cattle at a Chennai slaughterhouse, 16 animals (32 per 1000, 95% CI: 16, 47) tested positive for *Mycobacterium tuberculosis* complex (MTBC). Thirteen isolates were *M. orygis*, one was a mixture of *M. orygis* + *M. tuberculosis* and two were pre-XDR *M. tuberculosis* Lineage 2. *M. bovis* was absent, highlighting a zoonotic TB threat.

DEPARTMENT OF STATISTICS

DEPARTMENT OVERVIEW AND MANDATES

The Department of Statistics plays a vital role in study planning, sample selection, data management, interpretation, and reporting, and continues to expand its support across a wide range of medical research studies. Department staff serve as collaborative scientists, offering expertise in diverse statistical methodologies. They are actively involved in both curriculum development and independent research projects. The department’s research strengths include linear, nonlinear, and longitudinal modeling; clinical trial and experimental design; survival and categorical data analysis; causal inference; disease modeling for TB, HIV, and cancer; computational biology and bioinformatics; as well as artificial intelligence and machine learning algorithms for TB diagnostics and data mining. Additionally, GIS-based spatial and temporal modeling and Bayesian methodologies are key areas of focus.

The department's mission is to promote the discipline of statistics by mentoring students in methodological research and its applications, conducting collaborative and multidisciplinary research in medicine and public health, enhancing facilities for PhD scholars, and supporting various professional, academic, and research initiatives.

Studies in Progress

1. Development and validation of artificial intelligence tool for screening/Detection of pulmonary TB and other lung diseases using chest X-RAY

Principal Investigator	:	Dr.C.Ponnuraja
Participating Institutes	:	ICMR-NIRT (& 18 other Institutes)
Source of funding	:	ICMR
Study period	:	2022-2024
Category	:	Development
Pillar	:	Build

Background

India is the leading contributor to the global tuberculosis burden as per the WHO report 2019. Effective and timely tuberculosis screening at the peripheral health sector level and in remote India remains a constant issue for the health sector. AI tools that can mimic human-like thought processing, reasoning, and self-correction abilities. Artificial intelligence technologies include training of tools and deep learning. Deep learning is a particular kind of machine learning that achieves great power and flexibility by learning to represent the world as a nested hierarchy of concepts, with each concept defined as simpler concepts, and more abstract representations computed in terms of less abstract ones. Hence, the development of an AI Tool is needed to bridge this diagnostic gap and facilitate affected individuals to reach the management centers at earnest therefore contributing to the national interest of combating tuberculosis by 2025. It aims to develop a computer-aided detection (CAD) system for using chest X-rays for peripheral settings and under a national Program for screening and diagnosing TB and other lung diseases.

Objectives

- To develop a computer-assisted screening system to differentiate clinically normal chest x-ray from clinically abnormal types.
- To develop a computer-aided detection system that enables auto differentiation of TB from other chest diseases/ other lung diseases using X-rays
- To further develop the computer-aided detection system for auto identification of various presentations of pulmonary tuberculosis.

Methods

Phase 1: Development of tool: (learning and training)

Milestone 1: The initial proposal would consist of the use of retrospective validated data by IPR, provided by participating Institutes for the development of the tool to differentiate

between normal from abnormal chest x-ray and then segregate the X-rays with suspected TB lesions. The data would consist of X-ray images: The participating Institutes would collect the images along with the clinical diagnosis and results of diagnostic tests (gold standard). The images would be annotated by the experts for the demarcation of the lesion clearly indicating the diseased area(s) on the X-ray image. The data would be uploaded to the ICMR portal IPR would access the data through the ICMR Portal and use the images for training of AI tool. There would be a central annotation team that would reconfirm the annotation done by the site before the images are shared with IPR.

Milestone 2 (Objectives 2 and 3): This milestone would be undertaken wherein an algorithm would be built that would detect tuberculosis and differentiate it from other non-tuberculous diseases and other lung diseases.

The AI tool would also detect TB with great accuracy including differentiation of all possible presentations of tuberculosis. The annotated images would be obtained, along with clinical information and diagnosis confirmed via the gold standard method, and uploaded on the ICMR portal via software. The assessment of the performance would be done on a test data set in terms of the sensitivity and specificity of the artificial intelligence tool. Impact Assessment Progress: Evaluation of the progress (technical progress) for the use of AI Tools for automated detection of TB in India. The feasibility study would be conducted in peripheral areas for Implementation, accuracy, and use of AI tools in peripheral settings. The AI Tool for the automated detection of TB projects will be provided to the collaborating partners in the future.

Study progress

The project is currently ongoing and this AI tool with its high sensitivity and specificity for the detection/screening of TB using chest X-rays and other lung diseases. The final version of the tool will greatly facilitate bridging the gap between diagnosis and treatment more so in economically or geographically difficult populations and hence significantly cater to the National Goal of Eliminating Tuberculosis By 2025 as well as the END TB Strategy of the Sustainable Development Goals.

2. Gold Standard Datasets on Tuberculosis with Radiological Images

Principal Investigator	:	Dr. C. Ponnuraja.
Participating Institutes	:	ICMR-NIRT, ICMR-HQ, IISc
Source of funding	:	ICMR
Study period	:	2024-2027
Category	:	Delivery
Pillar	:	Build

Background

Every day, healthcare professionals generate tremendous amounts of clinical data. Electronic Health Records, which are created clinical data maintained digitally as a central repository of information for hospitals (EHR). EHR data is also used for a range of secondary uses, such as clinical research, disease surveillance, and clinical audits for quality improvement. This can be accessed using wired or wireless networks. Recent research indicates that reviewing electronic health records (EHRs) takes more time per patient for the clinician. The ICMR-NIRT has produced a vast amount of data, clinical and sociodemographic profiles, laboratory results, and information on treatments and diagnoses with digital images of X-rays. This aggregated data source could be used effectively and even though a wealth of information is available, very little of it is extracted.

Objectives

- To create a clinical and radiological data repository that combines data such as demographics, lab results, radiology images, referrals, diagnoses, and treatment regimens from several clinical trials and studies.
    - To electronically capture clinical, laboratory, and other relevant data of patients being enrolled at NIRT – both at the base institute and at the other satellite and collaborative sites;
    - To digitize all readily available X-rays into DICOM image and DICOM viewer embedded in EHR
    - To enable a ready analysis of digitized data for day-to-day patient care, follow-up, and treatment compliance and undertake clinical research;
- To integrate artificial intelligence tools for effective and easy integration of the patient characteristics with the radiological image of the individual over the period of treatment and follow-up.
- Create an institutional framework for managing the platform for medical image data, including technical oversight for potential users and other dataset stakeholders

Methods

Electronic Data Capture (EDC) system is software that stores patient data collected in clinical trials. Data is usually recorded on paper and is then transcribed into the system and saved in various types of electronic case report forms (eCRF). System integration that is seamless hospital information systems, document management systems, Integration with diagnostic labs, pharmacies, and other facilities of a similar nature, administration of electronic documents

Study progress

Procurement of equipment and recruitment of staff is in progress.

3. A study on role of Panchayati Raj Institutions in health care system in the state of Tamil Nadu with a special reference to tuberculosis

Principal Investigator	:	Dr.E.Thiruvalluvan
Participating Institutes	:	ICMR-NIRT
Source of funding	:	DHR
Study period	:	Two Years
Category	:	Delivery
Pillar	:	Build

Background

Utilizing the locally available voluminous human resources from PRI institution for TB control is sensible and the first of its kind if initiated, towards control of communicable diseases was initiated under the aegis of the Department of Health Research (DHR). This project was build on the lines of social mobilization theory and its attempts are congruence with *community-based rehabilitation - CBR Guidelines* to equip the study participants (Panchayat Raj Institutions (PRIs)) participation in the National TB Elimination Program (NTEP) in four blocks in Dindigul district, Tamilnadu with knowledge and skills to organize and participate in collective action through training to rise levels of education and literacy. The social mobilization theory is a framework for understanding how social movements and collective action emerge and spread.

Objectives

The core idea is that as people become more socially connected, educated, and engaged with political and social issues, they become more likely to participate in collective action and social movements.

The theory posits that several key factors that contribute to social mobilization:

Increased access to communication and information channels, which allows for the rapid spread of grievances, ideologies, and calls to action.

Rising levels of education and literacy, which equip people with the knowledge and skills to organize and participate in collective action.

Weakening of traditional social ties and institutions, which frees people to explore new forms of social and political engagement.

A growing sense of relative deprivation or perceived injustice, which motivates people to seek change through collective means.

Methods

In consultation with the State TB Officer and, District TB Officers, Dindigul district was chosen. Due approval was obtained from district level authorities like the District Rural Development Authority (DRDA), Deputy Director of Health services (DDHS), District TB Officer, Block Development Officers (BDO), Block Medical officers in block hospitals and Medical Officers in the

additional PHCs functioning under the Block PHCs. Data on tuberculosis patients' registration for TB treatment was obtained from the National TB elimination program to enlist study sites. Simultaneously data on distribution of panchayat Raj institutions was obtained from district Rural development authorities. Detail situational assessment was done in the following eight blocks/block PHCs that were enlisted for the study.

Intervention centers	Control centers
Guziliamparai block PHC	Kosavapatty block PHC
Reddiyarchatram block PHC	Vada Madurai block PHC
Uluppagudi block PHC	Chinnalapatty block PHC
Pappampatti block PHC	Perumal Malai block PHC

On finalizing the control and intervention centres, the study team set out to devise an action plan to involve people's representative in TB control activities at the community level. Methods adopted to arrive at the action plan was Focus Group Discussions and In-depth interviews. Focus Group Discussions were held in four intervention centres. A total of 52 members took part in FGDs. In addition 120 In-depth interviews (TB patients 40 and community members 80) were held. Based on the input derived from FGDs & IDIs the study participants begun.

The presence of political opportunities, such as openings in the political system or the emergence of influential allies, that enable mobilization.

Study progress

During the formative phase, the study team met 490 PRI members who have initially expressed their willingness to participate in the project. However, participation in either a training programme or intensive personal discussion were used to filter out the committed and interested 366 PRI members-the required sample size for the study was finalized.

PRI members' distribution in TB notified village panchayats

Study participants details	PRI members enrolled	Number of village panchayats	Natham Block	Palani	Guijiliam-parai	Reddiyar-chathram
PRI members in Village panchayats where no TB patients are reported	137	31	8	8	0	15
PRI members in Village panchayats where TB patients rare reported	212	41	12	10	13	6
Total	349	72	20	18	13	21

During the follow-up the study team facilitated the study participants to carry out the following programs.

- 132 PRI members have conducted awareness program such groups as SHG, Mastoor workers, School students, ICDS members, office workers and MGNREGA workers. By these awareness program totally 8905 people got awareness about TB
- Flex banner with TB messages installed in 6 VPS Sathampadi, Nilamalakottai, Paraliputhur, T.Pannapatti, Karisalpatti, Neikarapatti and Kanakanpatti VP has done 3wall painting on village panchayat compound wall.
- 185 symptomatics referred by PRI members to PHCs in 4 blocks for TB screening. Gujiliamparai 15 members, Reddiyarchathram 134 members, Natham 16 members, Palani 20 members were referred.
- Motivation assessment was administered on 221 PRI members and Motivation assessment is yet to be done128 PRI members.

Activities to be completed:

Activity	Quantity	Time required
1 Refresher Training to be completed in 20 VPs	Twenty trainings to be completed	One month
2 Follow-up support/linking with NTEP-72 VPs in 4 TUs	At least three rounds of follow-up to be completed and linking not yet complete	Three months
3 End line survey	To be completed	Two months
4 Felicitating best performing PRIs Data analysis & Report preparation	To be completed	One month

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1.	Latent class analysis of health-related quality of life of TB patients during and post treatment in a longitudinal design	Dr. M. Vasantha	ICMR-Extramural	Description	The study found out that the HRQol OF patients improved with treatment
2.	Cost-effectiveness analysis for implementation of smoking cessation strategies at primary health care settings in Tamil Nadu	Dr. M. Vasantha	Nil	Description	Enhanced counselling can be a Cost effective method for increasing the quit rates among smokers compared to standard counselling

DEPARTMENT OF VIROLOGY AND BIOTECHNOLOGY

DEPARTMENT OVERVIEW AND MANDATES

The Department of Virology and Biotechnology plays a key role in providing high quality diagnostic services for ICMR-NIRT's clinical trials and research studies, besides serving as a Regional Reference Laboratory for the National AIDS Control Organization and undertaking its own research. The laboratory is accredited by International Agencies like the NIH and WHO, and has a long-standing record of successful participation in some of the best External Quality Assurance programs implemented globally.

The Diagnostic Serology division of the department provides routine clinical safety parameter testing services required for clinical trials and other studies. The Molecular Diagnostics division supports molecular diagnosis of HIV infection and HIV-1 viral load testing. The Cellular Immunology division supports vaccine immunogenicity testing and other immunological studies. The Sanger Sequencing facility is accredited by WHO for HIV drug resistance testing. The BSL-II laboratory supports virus culture and anti-viral compound screening. The other facilities in the department include a Flow Cytometry facility, Cell Culture Laboratory, a large TB Biorepository and a Viral Research and Diagnostic Laboratory.

The scientific programs of the department are organized into research on TB, HIV and other viruses. The department shares its facilities and expertise with other researchers for screening of compounds for HIV-1 drug resistance testing, pharmacogenomic studies, flow cytometric analysis and anti-viral compound screening. The department holds the status of a National Reference Laboratory for HIV-1 drug resistance genotyping and Regional Reference Laboratory for molecular diagnosis of HIV infection and HIV-1 viral load testing for NACO. The department has been implementing a Proficiency Testing program for isolation and cryopreservation of peripheral blood mononuclear cells for immunological studies (the first and only such program in the country), since 2017.

Research Focus of the Department: The Department's research encompasses several key areas aimed at advancing the understanding, detection and management of TB and HIV. The TB research of the Department focuses on the identification of biomarkers for predicting risk of progression from TB infection to active disease, exploration of novel diagnostic tools for early case detection, identification of factors contributing to increased risk of TB reactivation among HIV-infected individuals and investigating the effects of TB-induced inflamm-aging and immunosenescence on increased risk of mortality among cured TB patients.

In the realm of HIV research, the Department undertakes investigations aimed at understanding the unique features and cellular interactions of HIV-1 transmitted/founder (T/F) viruses, isolation of novel monoclonal broadly neutralizing antibodies and short peptide mimetics effective against HIV-1 subtype C strains circulating in India, understanding the basic principles of HIV latency and the development of cost-effective strategies for early detection of HIV drug resistance.

More recently, the department has been engaging itself in the surveillance of emerging zoonotic respiratory viral diseases and the antigenic characterization of dengue viral strains circulating in the population. This diverse research portfolio aims to provide critical insights into the mechanisms of infection and the host immune response, thereby contributing to the development of innovative diagnostics and treatment strategies for various infectious diseases of clinical significance.

Studies in Progress

1. Identification of Biomarkers that can predict progression from *Mycobacterium tuberculosis* infection to Active Tuberculosis Disease

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Co-investigator	:	Ms. Evangeline Ann Daniel (SRF)
Participating Institutes	:	ICMR-NIRT, BJGMC - Pune, Johns Hopkins University, USA
Source of funding	:	ICMR-Extramural
Study period	:	2021-2024
Category	:	Discovery
Pillar	:	Detect

Background

Identification of TB-exposed individuals at high risk of progression to TB disease continues to be a diagnostic challenge. The currently available diagnostics for latent TB (IGRA and TST) have low positive predictive value and compromised sensitivity and specificity in accurately identifying individuals at high risk of progression to TB disease, resulting in high numbers-needed-to-treat (NNT). Hence, there is a dire need to identify more robust biomarkers/biosignatures with improved diagnostic performance for identifying this subset of high-risk individuals so that they can be easily targeted for prophylactic intervention.

Objectives

To identify soluble cytokine/chemokine, miRNA and small metabolite biomarkers/ biosignatures that are predictive of high risk for progression to active TB from QuantiFERON supernatants of TB Progressors.

Methods

Cytokine/chemokine analysis of QuantiFERON supernatants was performed using the multiplex Luminex assay. MicroRNA profiling of QuantiFERON supernatants was carried out using the Nanostring platform. High throughput metabolomic profiling of was performed with QuantiFERON supernatants using LC MS/MS.

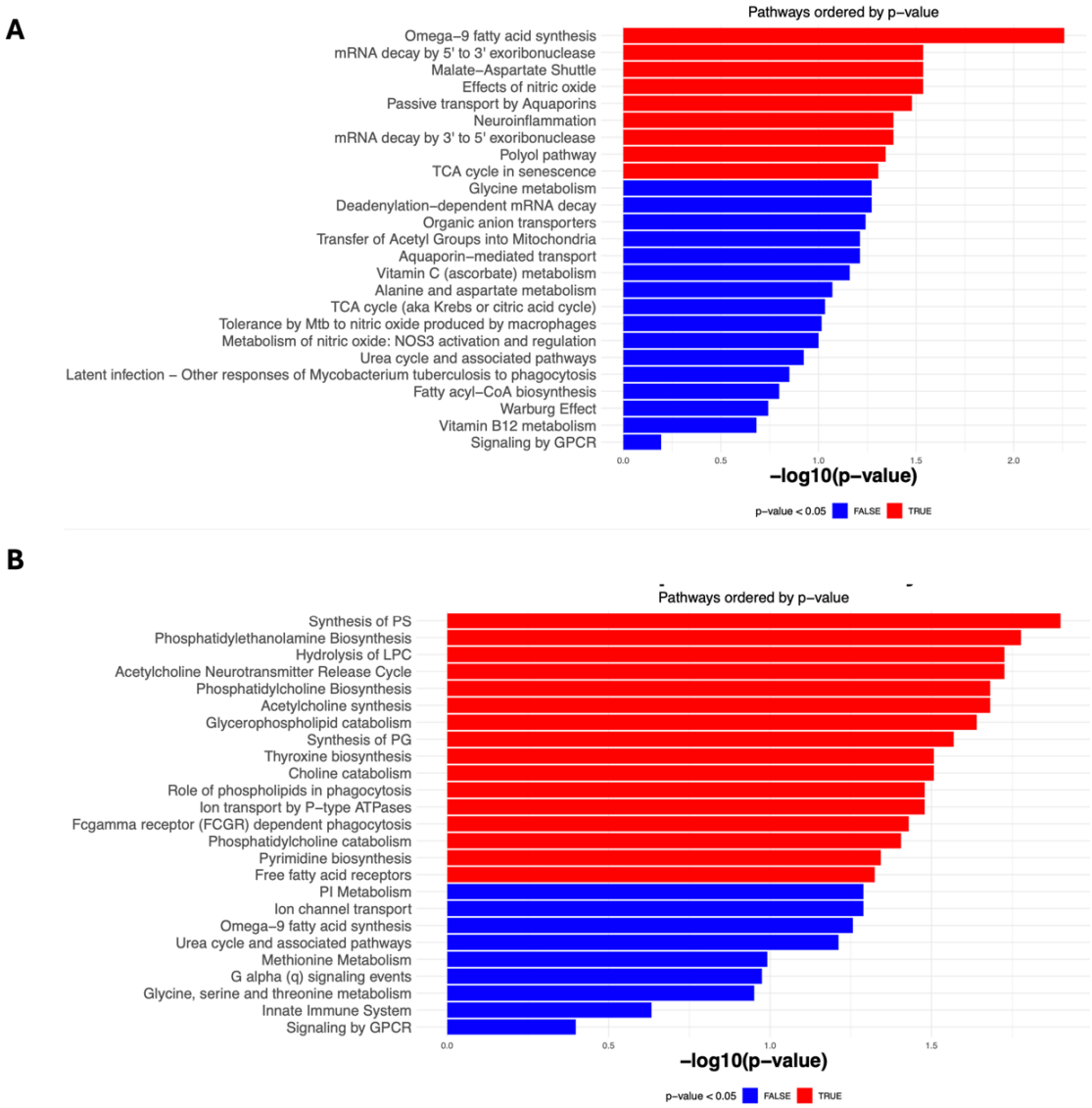
Study progress

Our previous findings on the identified cytokine/chemokine biomarkers (CID, 2023) and miRNA biomarkers/ biosignature (manuscript under review with Front Immunol). Here we report the identification of 21 significantly dysregulated metabolites between TB antigen stimulated QuantiFERON supernatants of Progressors and Non-progressors. Of the identified

metabolites, the combination of Malic acid and N-Arachidonoylglycine gave a maximum predictive accuracy of 94.4% (Figure 1).

We also identified 18 significantly dysregulated metabolites in unstimulated QuantiFERON supernatants of Progressors compared to Non-progressors. Of these, the combination of orotic acid and the phosphatidylcholines PC(O-34:1); PC(O-18:1(9Z)/16:0); PC(O-18:1(11Z)/16:0) gave the maximum predictive accuracy of 87.2%. Most of the dysregulated metabolites were found to belong to the pathways of fatty acid, lipid and nitric oxide metabolism (Manuscript under peer review).

Figure 1: Significantly Dysregulated Metabolites in (A) TB antigen stimulated QuantiFERON supernatants and (B) Unstimulated QuantiFEROn supernatants of Progressors



2. Advancing TB diagnosis through digital PCR-based detection of circulating cell-free *Mycobacterium tuberculosis* in individuals at high risk of developing active TB disease

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Co-investigators	:	Mr. Manohar Nesakumar (Technical Officer B), Ms. Evangeline Ann Daniel (SRF)
Participating Institutes	:	ICMR-NIRT, BJGMC, Johns Hopkins University
Source of funding	:	ICMR Intramural
Study period	:	2022-2024
Category	:	Discovery
Pillar	:	Detect

Background

The traditional diagnostic tests for TB are limited in their ability to detect *Mycobacterium tuberculosis* (Mtb) during the early stages of infection. Recent advances in molecular diagnostics, such as digital droplet PCR (ddPCR) technology, offer enhanced sensitivity for detecting low copy numbers of Mtb cell-free DNA (cfDNA) in plasma. This study aimed to evaluate a dual *Mtb* target (IS6110 and IS1081) based detection of circulating cell-free DNA employing the highly sensitive third generation ddPCR in identifying individuals at high risk of progressing to active TB disease.

Objectives

To determine the sensitivity of circulating cell-free Mtb DNA detection in plasma of TB Progressors using PCR ddPCR.

Methods

Retrospectively analysis of stored plasma samples of 46 healthy household contacts (HHCs) of TB patients who developed active TB during a two-year follow-up (Progressors) was done. An equal number of non-progressors who did not progress to active TB and remained healthy during the entire follow-up period were included as controls. Stored plasma of these individuals collected at baseline (at the time of recruitment), 6, 12 and 18 months before the development of active TB disease were used for the analysis. Circulating cell free (cfDNA) was extracted from 1mL of plasma and analyzed using ddPCR, with primers and probes targeting the Mtb-specific multicopy insertion sequences IS6110 and IS1081. Sensitivity, specificity, and Receiver Operating Characteristic (ROC) curves were determined to assess the predictive value of this method.

Study progress

Mtb ccfDNA was detected in 79·0% of Progressors, as early as 6 months prior to TB breakdown, highlighting the great promise held by this method as a predictive test for early identification of individuals with a high risk of developing infectious TB disease. *Mtb* ccfDNA was also detected in about 50·0% of at-risk individuals even as early as 18 months prior to actual TB breakdown (Figure 2, Table 1).

Figure 2: Mean copies of IS6110 and IS1081 detected/20µL of plasma in Progressors at various time points prior to TB breakdown

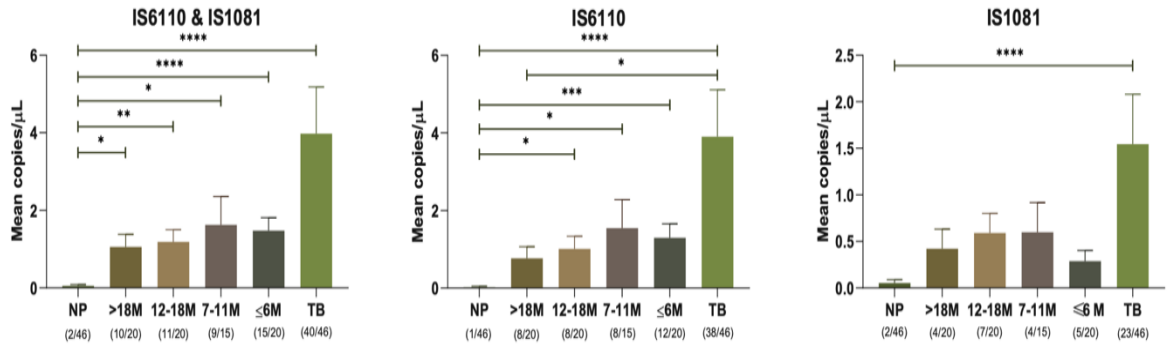


Table 1: Sensitivity of ddPCR assay in detecting Progressors at various time points prior to TB breakdown

Time point of sample collection	No of samples	IS6110&IS1081			IS6110			IS1081		
		Positives detected (N)	Sensitivity (%)	Specificity (%)	Positives detected (N)	Sensitivity (%)	Specificity (%)	Positives detected (N)	Sensitivity (%)	Specificity (%)
At the time of TB breakdown	46/46	40/46	87·0 (74·3-93·9)	95·7 (85·5-99·2)	38/46	82·61 (69·3-90·9)	100·0 (92·3-100·0)	23/46	50·0 (36·1-63·9)	95·7 (85·5-99·2)
≤6 months prior to TB breakdown	20/46	15/19	79·0 (56·7-91·5)	95·7 (85·5-99·2)	12/19	63·2 (41·0-80·9)	100·0 (92·3-100·0)	5/19	26·3 (11·8-48·8)	95·7 (85·5-99·2)
7-11 months prior to TB breakdown	15/46	9/15	60·0 (35·8-80·2)	95·7 (85·5-99·2)	8/15	53·3 (30·1-75·2)	100·0 (92·3-100·0)	4/15	26·7 (10·9-52·0)	95·7 (85·5-99·2)
12-18 months prior to TB breakdown	20/46	11/20	550 (34·2-74·2)	95·7 (85·5-99·2)	8/20	40·0 (21·9-61·3)	100·0 (92·3-100·0)	7/20	35·0 (18·1-56·7)	95·7 (85·5-99·2)
>18 months prior to TB breakdown	20/46	10/20	50·0 (29·9-70·1)	95·7 (85·5-99·2)	8/20	40·0 (21·9-61·3)	100·0 (92·3-100·0)	4/20	20·0 (8·1-41·6)	95·7 (85·5-99·2)

3. Study of Virologic response and HIV Drug resistance (pre-treatment and acquired) in adults newly initiated on an INSTI-based first line ART regimen in a representative population from Chennai, Tamil Nadu

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Participating Institutes	:	ICMR-NIRT, GHTM-Tambaram
Source of funding	:	ICMR-Intramural
Study period	:	5 years
Category	:	Discovery
Pillar	:	Build

Background

As per recent WHO recommendations, a dolutegravir (DTG)-based ART regimen comprising of tenofovir disoproxil, lamivudine and dolutegravir, was introduced in the National ART program as the first line regimen in 2020. As the use of DTG-based first-line ART is being scaled up in the country, it becomes important to conduct periodic surveys to document the emergence of drug resistance mutations to this new class of drugs (integrase strand transfer inhibitor/ INSTI) drugs that may affect population level treatment outcome.

Objectives

1) To determine the prevalence of baseline HIV drug resistance (HIVDR) in treatment-naive individuals newly initiated on first line ART.
2) To document viral suppression and emergence of HIVDR at one year post-treatment initiation (Acquired Drug Resistance).
3) To investigate the association between viral failure and drug resistance with specific ART regimen, adherence patterns, and other demographic and clinical factors.

Methods

Study Design: Prospective observational study

Study Group: Newly diagnosed HIV positive adults naïve to ART (n=200)

Assays:

1) CD4/CD8 testing at baseline (prior to start of ART) and at 12 months post treatment initiation.
2) HIV Viral load testing at baseline and 12th month.
3) HIV drug resistance genotyping by sequencing at baseline and 12th month.

Study progress

One hundred and fifty eight HIV-1 infected ART naïve participants have been screened and enrolled.

CD4 test and HIV-1 viral load assay were performed for all the participants. Viral RNA extraction and HIV DR genotyping by sequencing of integrase, reverse transcriptase and integrase gene have been completed for 100 participants. Participant recruitment and follow-up are ongoing.

4. Role of Persistent Immune Activation and Systemic Inflammation on accelerated Immune Senescence and Increased Mortality in Successfully Treated and Cured TB patients

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR
Study period	:	2022 – 2025
Category	:	Discovery
Pillar	:	Detect

Background

Although is completely curable, several studies have shown significantly higher rates of mortality among successfully treated and cured TB patients than in the general population. It has been reported that ~20% of post-treatment deaths among those with a history or TB are attributable to co-morbid conditions such as cardiovascular disease and cancer. A number of experimental studies have demonstrated heightened levels of immune activation in TB patients, which declines with anti-TB treatment but does not normalize to levels seen in healthy controls even after complete microbiological sterilization and cure. The present study is based on the hypothesis that accelerated immunosenescence due to persistent immune activation and systemic inflammation despite cure contributes to the accelerated risk for metabolic disorders which contribute to the higher rates of mortality seen in those who have had TB.

Objectives

- To evaluate the levels of systemic inflammation and immune activation by measuring soluble inflammatory molecules and immune activation markers in plasma.
- To examine alterations in the frequency of CD4 and CD8 memory cell subsets and evaluate the cytotoxic potential of terminally differentiated immune cells.
- To assess the extent of mitochondrial dysfunction, telomere length and telomerase activity in immune cells.

Methods

This case-control study involves a one-time point analysis of cured TB cases (Group 1) and matched healthy controls (Group 2). TB patients who completed treatment and were completely cured of TB at least 2 years earlier were recruited into the study. Preliminary socio-demographic data and clinical data were gathered using a structure questionnaire. Blood samples were collected for haematological, biochemical,

immunological and molecular tests, to analyse their haematological parameters, LFT, RFT and lipid profile, and to assess the function and phenotype of immune cell subsets, levels of immune activation, telomere length and telomerase activity, extent of immunosenescence and mitochondrial dysfunction.

Study progress

One hundred and eighty-five participants have been enrolled into the study. Participant enrolment, data collection, and sample processing for downstream analysis are ongoing. Haematological, biochemical and immunological tests have been performed in real time for the recruited participants and samples have been stored for molecular and serological tests.

5. Next-Generation Dual Transcriptomics based approach to investigate the host-pathogen interplay in various forms of Extrapulmonary Tuberculosis using Human Cell Lines

Principal Investigator	:	Dr. V. Umashankar, Scientist E
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR Intramural Grant
Study period	:	2024-2026
Category	:	Discovery
Pillar	:	Detect

Background

The seemingly rising cases of TB over years has encouraged researchers to delve deep into the pathogenesis of various forms of TB other than the commonly occurring form of pulmonary TB. In extrapulmonary TB, the tubercle bacilli invade and infect organs other than lungs. Extrapulmonary TB poses a huge diagnostic challenge due to the need for invasive samples and the poor sensitivity of the routine TB diagnostics to diagnose extrapulmonary disease. Hence it is essential to undertake in-depth analysis of the host-pathogen interplay in various infected cell lines to understand the underlying pathogenic mechanisms and to identify disease-specific biomarkers that can be detected in less invasive samples. The advantage of using cell lines is that they do not display heterogeneity, can be easily maintained and cultured under favourable growth conditions and are non-invasive and cost-efficient.

Objectives

i. To infect various types of cell lines with *M. tuberculosis* H37Rv and perform dual RNAseq to analyse the transcriptomic profile of the pathogen and the host using high

performance computational methods.

ii. To catalogue the landscape of transcriptomics interplay of the host and the pathogen in various kinds of infection milieu.
iii. To investigate and probe into the differential mechanisms of bacterial invasion and host defense.
iv. To host the expression profiles as a knowledgebase for customized meta-analysis.

Methods

Selected cell lines reported to be susceptible to *Mycobacterium tuberculosis* infection will be cultured and infected with standard doses of the bacteria. Post-infection, total RNA will be extracted from the infected cells and subjected to dual RNAseq analysis. Data generated will be analyzed and validated using computational methods. User-friendly computational pipelines will be developed for analysing the high throughput data which will be generated.

Study progress

A computational pipeline which delivers end-to-end dual transcriptomics analysis is under development. So far, a concrete approach for mapping good quality dual RNAseq reads has been established in the pipeline. An article emphasizing the importance of mapping dual RNAseq reads has been submitted for publication in Bioprotocol Journal. Cell culture work is in progress.

6. Evaluation of Immunogenicity of ChAdOx1 nCoV-19 (Covishield) Vaccine in Adults with Diabetes mellitus

Principal Investigator	:	Dr. P. L. Natarajan, Scientist D
Participating Institutes	:	ICMR-NIRT and RGGGH, Chennai
Source of funding	:	Intramural
Study period	:	2021-2024
Category	:	Description
Pillar	:	Build

Background

Diabetic individuals infected with COVID-19 are known to face a significantly higher risk of hospitalization, intensive care unit admission, intubation, or death - a trend that has been observed globally as well as in India. Neutralizing antibodies (NAbs) play a crucial role in protecting against acute viral infections. A preliminary study by Pal et al. (2021) demonstrated impaired anti-SARS-CoV-2 antibody responses in non-severe COVID-19 patients with diabetes mellitus, with neutralizing activity serving as a predictor of survival. Additionally, older diabetics have shown reduced responses to Hepatitis B and CoronoVac vaccines.

Despite WHO's recommendation for a three-dose regimen of Covishield for adults, there is limited data on the immunogenicity of booster doses in diabetic patients, and reinfections among diabetics. The present study is an investigation into the immunogenicity and durability of the vaccine-induced immune response in individual with diabetes.

Objectives

Primary: To compare the kinetics of anti-spike IgG antibody and neutralizing antibody responses to three doses of Covishield SARS-CoV-2 vaccine in diabetic patients and healthy controls.

Secondary:

1. To analyse T follicular helper (Tfh) and B cell responses to Covishield SARS-CoV-2 vaccination.
2. To determine the level of anti-spike IgG antibody induced by the vaccine and correlate it with frequencies of Tfh cells and B cells.

Methods

Study Design and Population: Prospective observational cohort study including 3 study groups:

- Cohort I: Healthy controls receiving three doses of the Covishield vaccine.
- Cohort II: Individuals with diabetes receiving three doses of the vaccine.
- Cohort III: Individuals with breakthrough COVID-19 infections.

Recruitment:

Participants in Cohorts I and II were recruited through random sampling from the COVID Vaccination Center at the Rajiv Gandhi Government General Hospital (RGGGH), Chennai, and those in Cohort III were recruited from the COVID-19 ward with the written informed consent of the participants.

Vaccination Schedule, Blood Sampling, and Follow-up:

After collecting demographic data, vital signs, and information on diabetic status, medication and clinical history, participants received the Covishield vaccine in a three-dose regimen at 0, 3 and 9 months. Blood samples were collected at baseline, 14 and 28 days post-prime dose, as well as at months 3, 4, 6, 9, 10, 12 and 15, and at the time of COVID-19 infection. Participants were followed up bi-weekly via telephone throughout the study period to gather information on COVID-19 infection. The collected blood samples were used for antibody assays and flow cytometric analysis of immune cell frequencies and function.

Study progress

Follow-up is ongoing and scheduled to be completed by the end of this year. Analysis of T and B cell activation markers are being planned and will be performed once adequate number of follow-up samples have been acquired. Serum samples have been stored for measurement of antibody levels.

7. Neutrophil extracellular trap (NET) formation in pulmonary tuberculosis patients with and without diabetes

Principal Investigator	:	Dr. Nancy Hilda J, Scientist C
Participating Institutes	:	ICMR- NIRT, RGGGH, GHTM
Source of funding	:	Intramural
Study period	:	2024-2026
Category	:	Discovery
Pillar	:	Build

Background

Neutophil Extracellular Trap (NET) formation, commonly known as NETosis, is a unique way of cell death, which has been well-documented in diabetes, as well as autoimmune disorders and cancer. Upon immunological trigger, activated neutrophils produce net-like traps consisting primarily of citrullinated histones, DNA expelled from the infected cells and numerous physiologically active cytosolic and antimicrobial peptides released from cellular granules to trap extracellular bacteria and release reactive oxygen species in order to kill them. We hypothesize that neutrophils plays a diplomatic role by assuming both protective and pathogenic roles in individuals with TB and diabetes, and analyze induction of NETs in both conditions, occurring singly as well as together, to test our hypothesis.

Objectives

1) To quantify NET markers (elastase, MPO, extracellular DNA, citrullinated histone) in the plasma.
2) To investigate the correlation between levels of NET markers and other immunological parameters (MMP9, PAD4, cytokines like IL8 and IL6 & complement proteins).
3) To determine variations in NET formation/ clearance by OHA/ insulin and correlate it with time to sputum conversion.
4) To measure changes in NET markers during anti-TB treatment and correlate it with the clinical parameters.

Methods

Study Design: Longitudinal observational study

Study Groups:

1. Healthy Volunteers (n=45)
2. Newly diagnosed TB patients with diabetes (n=45)
3. Newly diagnosed TB patients with diabetes mellitus (n=70)
4. Known diabetics without an history of TB (n=45)

Methods:

1) Neutrophil isolation and cell culture
2) ELISA for quantification of plasma NET markers

3) Flow cytometric analysis of NET markers on neutrophils
4) Estimation of Reactive Oxygen Species (ROS)
5) Neutrophil transcriptomics analysis

Study progress

Procurement of reagents is ongoing. Participant recruitment is yet to be initiated.

8. Complement proteins as prognostic biomarkers in paediatric tuberculosis

Principal Investigator	:	Dr. Nancy Hilda J, Scientist C
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR Intramural
Study period	:	2024-2025
Category	:	Discovery
Pillar	:	Detect

Background

Pediatric TB has always been a diagnostic and prognostic challenge, prompting the urgent need for minimally invasive, non-sputum-based, highly sensitive and specific diagnostic tests that can use easily accessible biological specimens such as blood and urine. An acceptable diagnostic/ prognostic biomarker for TB have to be a pathogen or host marker that is specific to the underlying process of the disease.

While several components of the immune system have highly explored in TB research, the complement system has been comparatively less explored. The complement system is a complex innate immune surveillance system and a predominant player in host homeostasis, inflammation and defense against pathogens.

Objectives

Primary Objective:

To identify complement protein biomarkers/ biosignature for TB detection and monitoring of treatment response children with pulmonary and extrapulmonary TB.

Secondary Objectives:

To evaluate differences in complement protein levels across children with active TB disease, LTBI and other respiratory disorders.

To identify complement protein biomarkers which can serve as surrogate markers for TB diagnosis and correlate them with haematological parameters.

To understand the ability of complement proteins to activate complement receptors.

To correlate levels of significant complement proteins with mycobacterial growth inhibition activity (where data is available).

Methods

Study Design: Longitudinal observational study

Study Groups:

Retrospective component - stored plasma samples) of 400 children (100 children with pulmonary TB, 100 children with extrapulmonary TB, 100 children with Latent TB Infection and with 100 children other respiratory diseases (ORD). For children with TB, plasma samples stored at months 2 and 6 of TB treatment will also be included for the analysis.

Prospective component: Blood will be collected from 20 LTBI negative healthy children at one time point and plasma will be used for biomarker analysis.

Study progress

Procurement of reagents is ongoing. Line listing of retrospective samples has been completed.

9. Role of Interferon Stimulated Genes (ISGs) in the establishment/maintenance of HIV latency

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Co-investigator	:	Dr. Divyadarshini A, Research Associate
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR-RA Fellowship
Study period	:	2022-2025
Category	:	Description
Pillar	:	Build

Background

Therapeutic cure for HIV remains elusive due to the seeding of persistent latent reservoirs that evade current antiretroviral therapies early during HIV infection. HIV is known to persist in long-lived resting CD4 memory cells for many years and rebound upon ART cessation. Interferon-stimulated genes (ISGs) that can suppress viral replication during acute infection, are thought to be down regulated by HIV through its viral proteins resulting in impaired immune surveillance. HIV LTR and ISG expression are both regulated by histone acetyl transferases (HATs) and histone deacetylases (HDACs) in conjunction with transcription factors and repressor molecules. It was hypothesized that down-regulation of ISGs promotes HIV latency via recruitment of HDACs to the HIV LTR promoter. The present study aims to investigate the ISGs down regulated by IFNs that might promote HIV latency.

Objectives

1. To identify critical ISGs induced by Type I/Type II IFNs during the

maintenance and reversal of HIV-1 latency.
2. To establish the role of the identified ISGs in HIV-1 latency reversal through gene knock down studies with siRNA.
3. To investigate the epigenetic mechanisms involved in the establishment/maintenance of viral latency.
4. To correlate the level of epigenetic modifications in target gene expression with the size of the viral reservoir in HIV-infected persons.

Methods

1. Culture and maintenance of J-Lat cells.
2. Reactivation of latent cells by type 1 and type 2 interferon individually and in combination with SAHA in J-Lat cells.
3. Transcriptomic analysis of J-Lat cells treated separately with type 1 and type 2 interferons and in combination with SAHA.

Study progress

Lead ISGs involved in reversing HIV-1 latency have been identified using J-Lat cells as the cell model for HIV latency based on our transcriptomics analysis. The functional assessment of the identified ISGs is currently under progress.

10. Surveillance of Zoonotic Respiratory Viral Infections in animal farms from Thiruvallur District, Tamil Nadu: A model project with a focus on One Health approach

Principal Investigator	:	Dr. N. Sudhakar
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR under PM-ABHIM Scheme
Study period	:	2023-2026
Category	:	Description
Pillar	:	Detect

Background

One Health is a collaborative, multisectoral and transdisciplinary approach to address the complex challenge of zoonotic diseases. One Health is gaining recognition globally as an effective way to fight health issues at the human-animal-environment interface. The present study aims to establish a surveillance system for zoonotic respiratory viral infections among farm animals, animal handlers, and environment for early detection of emerging and re-emerging zoonotic respiratory viral infections.

Objectives

1. To establish a surveillance system for zoonotic respiratory viral infections among farm animals, animal handlers,

and farm environment for early detection of emerging and re-emerging respiratory viral infections.
2. To identify the zoonotic respiratory viruses circulating among farm animals, animal handlers and environment in the given area and to study the effect on climate on the emergence, transmission and outcome of viral infections.

Methods

The study will involve monthly surveillance of zoonotic respiratory viral infections in animals from farms across four taluks in Thiruvallur District over two years, covering both summer and winter seasons. Samples will be collected from livestock (cattle, buffalo, goat, sheep, swine, poultry) and animal handlers, with sample sizes of 920 for livestock, 120 for animal handlers, and 120 for environmental samples. Nasopharyngeal swabs will be screened for Influenza A, B and SARS-CoV-2 using multiplex RT-PCR, followed by subtyping of positive samples. Additional testing will be conducted for RSV, human metapneumovirus, parainfluenza viruses, and bovine RSV using specific RT-PCR assays.

Study progress

The study has received approval from the Animal Husbandry Department, Tamil Nadu, and field visits to Tiruvallur, Ponneri, Ambattur, and Poonamallee are underway in collaboration with the department. Veterinary Animal Surgeons have provided contacts for farm and backyard owners with over 20 animals, and the number of cattle, buffalo, sheep, and goats on each farm has been recorded, though no piggery farm has been identified yet. Primers and probes for detecting zoonotic respiratory viral infections have been finalized and ordered. The project is in progress, with field visits ongoing and wet lab work being planned.

11. Comparing the performance of T-SPOT and QuantiFERON tests for detection of latent tuberculosis infection (LTBI)

Principal Investigator	:	Mr. Anbalagan S
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR Intramural
Study period	:	2022-24
Category	:	Development
Pillar	:	Detect

Background

Detection of latent tuberculosis infection (LTBI) followed by appropriate prophylactic treatment could be instrumental in reducing TB burden. Interferon Gamma Release Assays (IGRA) are reported to have higher specificity than the tuberculin skin test

(TST), and are therefore a more effective option for the diagnosis of latent infection. The present study is aimed at comparing the performance of two IGRA based kits, the T-SPOT.TB test versus the currently used QuantiFERON-TB Gold Plus assay (QFT-Plus).

Objectives

1. To compare the performance of T-SPOT.TB test and QFT-Plus
2. To compare the performance of C-Tb test and QFT-Plus
3. To determine the diagnostic accuracy of T-SPOT.TB and C-Tb in detecting LTBI.

Methods

The study population includes healthy household contacts of smear-positive TB patients (n=100; 70 adults and 30 pediatric), healthy TB healthcare workers (n=50), immunocompromised/ HIV+ individuals (n=50) and community controls (n=80).

Twelve millilitres of blood was collected into lithium heparin blood collection tubes for the T-SPOT.TB test, and QFT-Plus blood collection tubes for the QFT-Plus test. All assays were performed according to the manufacturer's instructions.

C-Tb was administered intradermally and the induration was read after 48h up to 72h by measuring the size of the induration in mm. The diagnostic efficiency will be determined by calculating the sensitivity, specificity, PPV and NPV of the test.

Agreement between tests will be assessed by estimating Cohen's κ coefficient.

Study progress

Initial standardization of the T-SPOT assay has been performed in the laboratory. Awaiting the supply of more T-SPOT test kits for initiating the study.

12. Characterizing the molecular mechanism of Protease Inhibitor resistance in HIV-1 infected individuals

Principal Investigator	:	Lucia Precilla K
Participating Institutes	:	ICMR-NIRT an GHTM, Tambaram
Source of funding	:	Intramural
Study period	:	2023-2026
Category	:	Description
Pillar	:	Build

Background

HIV-1 Protease Inhibitors (PIs) are key drugs that are extremely important in salvage therapy for patients who fail initial treatment regimens. PIs are competitive inhibitors that bind to the active site of the HIV protease enzyme. HIV-1 protease is an enzyme which cleaves its substrate, the Gag polyprotein, into its respective components namely, matrix, capsid, SP1, NC, SP2 and P6 to produce a mature infectious virion.

Blocking the cleavage of Gag makes the virion non-infectious. This makes HIV-1 protease a promising drug target. Although both the natural substrate (Gag) and inhibitor (PIs) bind to the same active site on the protease, it has been observed that drug resistance emerges in such a way that the variant enzyme does not bind inhibitors well, but allows its natural substrate to bind and get processed by the enzyme. Some studies have demonstrated that protease genotypic resistance does not always agree with virological outcomes. Hence, the main goal of this project is to better understand the underlying mechanisms of HIV-1 drug resistance in protease inhibitor-treated individuals and to develop strategies to combat resistance.

Objectives

1. To characterize HIV-1 PI resistance mutations occurring in the protease and gag genes among individuals on PI-based, second-line anti-retroviral treatment.
2. To study the substrate (Gag) and inhibitor (PI) binding affinity towards Protease enzyme.
3. To perform conformational sampling of the mutant Protease structures using molecular simulation study.
4. To perform phenotypic analysis of viral fitness, infectivity and PI drug susceptibility of viruses from responsive and non- responsive groups.

Methods

Study Design: Retrospective cohort study with two observational time points (at baseline and >6 months of treatment on a PI-based regimen). Participants will be categorized into two groups: virological responders (Group I) who respond to treatment and reduce their viral load to less than detectable levels, and virological non-responders (Group II) who do not respond to treatment and continue to have high circulating viral load.

Assays:

1) HIV-1 RNA extraction from plasma, PCR amplification and Sanger sequencing of protease and gag genes.
2) Cloning, expression, and purification of patient specific protease and gag genses.
3) Binding affinity assay
4) Bioinformatics analysis
5) Phenotypic analysis for infectivity and PI drug susceptibility.

Study progress

A line list of HIV positive individuals on PI-based second line ART was obtained from the ART CoE at the Government Hospital of Thoracic Medicine, Chennai, and a group of 100 responders and 53 non-responders were identified for inclusion in the present study. The demographic and clinical details of each participant were captured in the data collection form. Stored plasma samples of the identified cases were retrieved from the sample repository. Sanger sequencing is currently in progress.

13. Development of a simple and affordable assay for screening of Dolutegravir (DTG) resistance in HIV-1 infected persons

Principal Investigator	:	S. Manohar Nesakumar, Technical Officer B
Participating Institutes	:	ICMR-NIRT
Source of funding	:	ICMR-Intramural
Study period	:	3 years
Category	:	Development
Pillar	:	Detect

Background

Drug resistance mutations (DRMs) are linked to reduced efficacy of antiretroviral drugs. Currently, HIV drug resistance genotyping is not routinely available in the national ART program due to limitations such as the absence of Sanger/NGS sequencing infrastructure and high costs. To address this, a "targeted genotyping" method using modified real-time PCR has been developed to detect drug-specific mutations, particularly for (N)NRTI-based regimens. However, no method other than sequencing exists for detecting DRMs to the integrase inhibitor dolutegravir (DTG), which has recently been added to the National ART program as a first-line drug. In India, where subtype-C HIV prevalence is high and data on integrase inhibitor resistance is lacking, it is crucial to screen for DTG resistance mutations before initiating a DTG-based regimen.

Objectives

1) To develop a real time PCR-based assay for detection and identification of HIV-1 drug resistance mutations at four important drug resistance associated codons that are markers of various HIV-1 integrase class of inhibitors including Dolutegravir.
2) To design various sets of primers and probes and carry out standardization experiments.
3) To evaluate the performance of the qualified primers and probes set in the initial standardization further using synthetic templates and NGS characterized drug resistant EQAPOL QC panel samples.

Methods

Study Design: Laboratory assay development and validation

Assays:

1) Bioinformatics analysis for primer and probe design
2) Real time PCR
3) Sanger sequencing

Study progress

During the reporting period, several key activities were planned and executed:

1) Based on the results of previous experiments, two sets of primers and

one set of probes have been designed to advance assay development.

2) A Material Transfer Agreement was finalized and signed between NIRT-ICMR and Duke University, facilitating the import of EQAPOL genetic diversity and EQAPOL drug-resistant virus panels for validation of the newly developed assay. The samples were received in July 2023.
3) Synthetic gBlocks gene fragments containing known polymorphic mutations in the probe binding regions, as well as specially modified primers and probes required for validation experiments, have been indented.

Completed studies

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
1	Indian Catalogue of *Mycobacterium Tuberculosis* Mutations and their association with Drug Resistance, Version 2.0	Dr. V. Umashankar, Scientist E	ICMR-Intramural	Development	This catalogue presents a comprehensive collection of MTB-specific mutations classified into five groups based on their link to TB drug resistance. Derived from 8,894 MTBC isolates across India, Version 2.0 includes 52 new mutations compared to v1.0, with **rpoC** contributing the most (25). New genes such as *ndh*, *ubiA*, *rrl*, and *fabG1* are also featured for the first time. Serving as a national reference for interpreting drug resistance mutations, this updated catalogue supports TB control strategies and public health initiatives. The soft copy is available at: **https://nirt.res.in/pdf/mutation_catalogue_v2.pdf**
2	CoHRPICA (Cohorts for HIV resistance and prevention in Indian children and adults)	Dr. Luke Elizabeth Hanna, Scientist F	DBT & ICMR	Development	The study, completed in February 2023, involved collecting longitudinal samples from HIV-exposed uninfected cohorts (MSM, TG, IDU), exposed sero-negatives (ESNs), and HIV-infected individuals, including early HIV cases and those with/without co-morbidities. Samples are stored in a central biorepository with an associated database containing detailed demographic, clinical, and laboratory data.
3	Role of Neutrophils and Neutrophil Extracellular Traps (NETs) in the pathogenesis of TB in individuals recently infected with SARS-Cov-2	Dr. Nancy Hilda J, Scientist C	Intramural	Discovery	Past SARS-CoV-2 infection did not appear to impair the ability of neutrophils to produce NETs in individuals newly diagnosed to have TB. A manuscript on the above-mentioned finding is in the pipeline.

SNo.	Title of project	Name of PI with designation	Source of funding	Category	Outcome
4	Construction and characterization of Infectious Molecular Clones (IMCs) of Transmitted/Founder (TF) HIV-1 viruses	Dr. Luke Elizabeth Hanna - Scientist F, Mr. Aanand Sonowane - SRF	ICMR Intramural	Development	Sixteen full length infectious molecular clones of T/F viruses have been developed and characterized genotypically and phenotypically. A manuscript has been written and is currently under review.
5	Cloning, expression, purification and characterization of HIV-1 Tat in *Lactococcus lacits*	Dr. Luke Elizabeth Hanna Scientist F, Mr. Deepak Selvam - SRF	ICMR Intramural	Development	The study optimized the conditions for expression of the highly toxic HIV-1 Tat protein in *L. lactis* as it is difficult to express in the *E. coli* system due to the formation of inclusion bodies and contamination with endotoxin. A manuscript has been published in *Protein Expression and Purification 2024; 217:106443.*
6	Introduction and Evaluation of Point mutation in Gag region of HIV-1 using Adenosine Deaminase acting on RNA (ADAR)	Balakumaran S, SRF (ICMR)	ICMR Intramural	Development	HIV-1 Gag and Rev specific gRNA cassettes were developed and tested in concert with ADAR for their efficiency to edit HIV-1 mRNA. However, the editing efficiency that was obtained was very insignificant.
7	Analysis of genetic variability between transmission pairs and inheritance of broadly neutralizing antibody (bNAb) imprinting ability	Dr. Luke Elizabeth Hanna, Scientist F	ICMR Intramural	Development	The study included 4 transmission pairs, and examined 22 parameters, including 18 neutralization and 4 binding reactivities, but did not find a direct correlation between bNAb imprints and the genetic diversity in the envelope sequences of the transmission pairs. Future research focused on sequential characterization of neutralization response and envelope signatures of transmission pairs to identify bNAb-imprinting strains may provide useful information for HIV vaccine design.

NIRT LIBRARY

The Library and Information System at NIRT is designed to provide comprehensive access to health-related information, supporting research and intellectual development while adapting to the evolving needs of its users. The library maintains an extensive collection of print and digital resources, including books, journals, databases, CD-ROMs, theses, WHO publications, photographs, reprints, slides, video cassettes, and other gratis materials.

In line with its mission, the NIRT Library delivers high-quality resources in a timely manner through a robust digital platform. Its electronic collection is particularly strong in the field of respiratory health, offering unique access to journals, books, and archival materials that significantly support scientific research.

Now functioning as a hybrid library, it is progressively moving towards a fully integrated electronic platform.

Value-Added Services (VAS)

The NIRT Library also offers a wide range of value-added services, ensuring excellence and commitment to delivering high-quality information support to researchers and scholars.

Access to Digital Resources: The Digital Library serves as an essential gateway foraccessing our electronic resources:

- **Digital Library** *(established in 2001)* Portal has been updated with
  - Annual Reports *(NIRT)*
  - Catalogue *(OPAC)*
  - E-Books
  - E-Journals (*including Archives*)
  - Library Forms
  - E-Office interlink for File Management System *(Firefox)*
  - ICMR e-Consortium
  - *(Journals)* Impact Factor (*by Clarivate Analytics- a Web of Science Group)*
  - **Institutional Scholarship Repository** *(it keeps getting updated/uploaded with full-text publications with copyright policy)*
  - IRINS *(Indian Research Information Network System),*
  - iThenticate *(plagiarism software)*
  - NIH Library *(Resource Sharing)*
  - Open Access Resources
  - Predatory Journals

- Science Citation Index
- Specialized Databases
- STHIRA *(a tool for NIRT staff)*
- Tamizh Books
- *(Pointing)* International Tuberculosis organizations

- **Archives**: Our institutional scholarship archive *(scholarly database)* offers access to all research publications since 1958, ensuring a comprehensive collection of our research contributions over the years;

- **Circulation**: Electronic Check-in and Check-out services since 2002;

- **C**urrent **A**wareness **S**ervice (**CAS**) – Daily Service**:**
  This service helps researchers and scholars stay up-to-date about the latest information and development without having to actively search for new content themselves. It savesthem time and effort by delivering relevant content directly to them, allowing them to focus on their work without missing any important updates. Our library offering the following CAS services:

- **Digital Information Alert Services** on

  - Press Clippings in particular on Tuberculosis and HIV *(and COVID)*; and health in general
  - New Article(s) Alert on Tuberculosis and HIV
    - Online First Article
    - Accepted Manuscript(s) online
    - Ahead of Print
    - In Press
    - High Impact Articles
  - Table of Contents
  - Weekly Updates
  - Monthly Updates

- Information about Awards, Conferences, Seminars, Workshops, Webinars etc.

- **Historical Slides:** A collection of 'slide(s)' presentations predating the era of PowerPoint, crafted by our esteemed scientists, remains archived in the library to serve as a valuable resource for historical research;

- **Open Access Support:** Our Library support open access publishing and repository, whichenhance the visibility to the research output at the global level and increase the citation;

- **Photographic References:** We maintain an accessible repository of photographs, providing a visual reference for research purposes and preserving moments that have shaped our institution's historical journey;

- **Website:** For over two decades, the library was holding the responsibilities for the Designing, Hosting, and Maintenance (2003-2020) of the NIRT website;

- **Reference Manager:** The library uses and assists the scientist in organizing and styling ofcitations using the tool viz., EndNote;

- **Remote Access:** The library offers off-campus researchers and scholars the ability to remotely access NIRT research publications spanning from 1958.

- **S**elective **D**issemination of **I**nformation (**SDI**) Service**:** SDI services enhance the overall experience for library patrons and contribute to the community's research needs; particularly useful for researchers who need to stay current in their field(s). It will help patrons stay informed about the latest developments, research findings, publications, and other relevant content without having to actively search for it themselves. The library extends the following SDI services:

  - Information Resources/Journal Articles Published [*on Tuberculosis, COVID-19(during COVID) and HIV*]
  - Digital Document Delivery Service *(DDDS)*
  - Literature search
  - Reference Assistance (*Face-to-face, Telephone, E-Mail*)
  - Resource Sharing (*NIRT-ICMR Institutes and Medical Institutions*)

  These services collectively enhance the research experience for scholars and researchers by providing the necessary tools, resources and expertise for their impactful research.

E-PUBLICATIONS

To effectively fulfill the SDI and CAS Services, the library employs a combination of these resources called publications. This will leverage modern technology and tools to process collecting and disseminating relevant information to users who have expressed interest in specific topics or fields of research. The NIRT Library publishes the following three publications to fulfil the patrons' needs:

- **TB Alert** *(Fortnightly)*
- **HIV Monitor** *(Fortnightly)*
- **News Bulletin** *(Weekly)*

CONTRIBUTION TO NATIONAL PROGRAMME

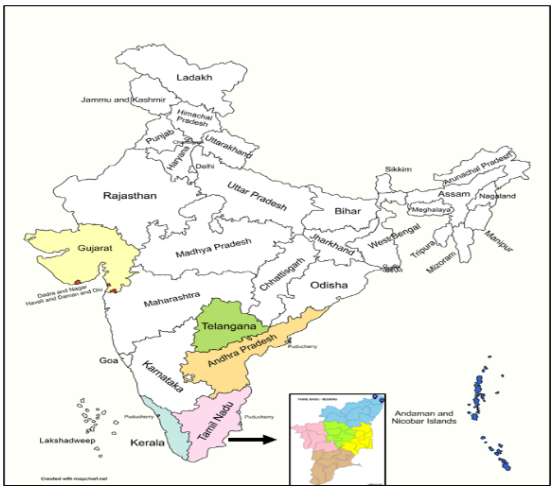
S.No	Name of programme	National/ State	Type of Support
1	*Wings of support*	*Tamil Nadu state NTEP*	*Provided psycho-social care and support to approximate 1000 patients and care givers in TB in-patient and outpatient facilities in Chennai and Kancheepuram.*
2	*Ni-kshay Mitra support*	*Tamil Nadu state NTEP*	*Nutritional support to 110 patients in the district of Chennai, Tiruvallur and Tuticorin.*
3	*Motivation and Orientation Session for Health Care Providers, NTEP, Chennai*	*Tamil Nadu state NTEP*	*Department of Social and Behavioral Research (DSBR), ICMR-NIRT, in collaboration with the NTEP and Greater Chennai Corporation, hosted a Motivation and Orientation Session for Health Care Providers of NTEP, Chennai attended by Senior Treatment Supervisors (STS) and Senior Tuberculosis Laboratory Supervisors (STLS). This session aimed at motivating and orienting healthcare providers, empowering them to make a meaningful impact in the fight against tuberculosis and thus contributing towards the National Tuberculosis Elimination Programme.*

NTEP ACTIVITIES IN NATIONAL REFERENCE LABORATORY, NIRT, CHENNAI (2023-2024)

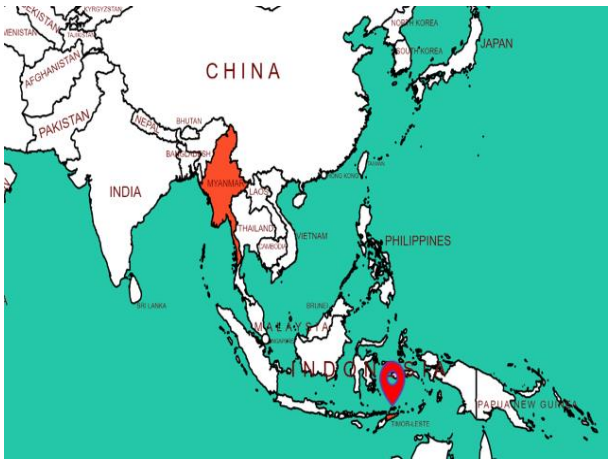
Contact person : *Dr.* S. Siva kumar, Scientist E
(Email: shanmugam.sk@icmr.gov.in)

Source of Funding : Central TB Division, Ministry of Health & Family Welfare, New Delhi

National Institute for Research in Tuberculosis (NIRT), Chennai is one of the National Reference Laboratory (NRL) closely monitors five states and five UT's for NTEP activities in India and as an SNRL extends its arms upon supporting Timor-Leste and Myanmar indicated in the below figure.



Andhra Pradesh, Gujarat, Kerala, Tamil Nadu, Telangana states and five Union territories-Sri Vijaya Puram, Puducherry, Lakshadweep, Daman & Diu and Dadra & Nagar Haveli



SNRL extends support to Timor-Leste and Myanmar

NRL Microbiologists/Biotechnologists along with Senior Lab technicians and a Biomedical Engineer visits each state for 5 days and 3 days for UTs for onsite evaluation (OSE) and monitoring EQA activities of smear microscopy, culture and DST by both phenotypic and genotypic methods as per the NTEP protocol. During OSE visit, NRL Microbiologist/ Biotechnologist provides technical support for establishing quality assured smear microscopy, Culture and Drug susceptibility (C&DST) services for the rapid diagnosis of MDR/XDR TB. NRL also undertakes yearly proficiency testing of IRL and C&DST labs as part of the certification process under NTEP

Biomedical engineer supports in monitoring C&DST equipment, calibrating minor equipment and maintaining quality management systems across states and UT's. NRL biomedical engineer helps in providing inputs on critical issues identified on

infrastructure maintenance and indeed supports on developing laboratory layouts in new laboratories across states and UT's. Nine IRLs and eleven C&DST labs catering for diagnosis of DR-TB patients from aforementioned states. During 2023-2024, the Institute conducted the fifteenth round of proficiency testing for 25 labs including five NRLs in India, with panel of 20 cultures for susceptibility testing for both first- and second-line anti-TB drugs by genotypic and phenotypic methods. First round of Whole genome sequencing EQA panel comprising of 5 strains was sent to NTI (Bengaluru), NITRD (New Delhi) IRL Ahmadabad, Sir J.J. Group of Hospitals and NDTB Center, New Delhi (WGS sites). NRL, NIRT supported self-assessment of IRLs using standardized laboratory grading by CTD with the support of USAID's IDDS team visited IRL Ahmadabad, Chennai and Puducherry. As an expert group members NRL participated in the final review of the TB biosafety manual as well as the QSP document for use in NTEP diagnostic facilities.

A total of 11936 samples were received for DR-TB diagnosis of which 9334 (DX) and 2603 samples received for follow-up cultures from six districts of Tamil Nadu. As part of NRL EQA activities, On-Site Evaluation (OSE) of sputum microscopy and C&DST conducted by NRL Microbiologists for five states (Andhra Pradesh, Gujarat, Kerala, Tamil Nadu and Telangana) and 4 UTs (Sri Vijaya Puram, Daman & Diu and Dadra & Nagar Haveli and Puducherry) for on-site evaluation of sputum microscopy and 1,150 panel slides were used to assess the proficiency of 230 laboratory personnel for smear microscopy. Additionally, for unsatisfactory scores on CBNAAT and TrueNAT EQA conducted by NTI, post-EQA visit were performed at districts in Andhra Pradesh, Gujarat and Telangana. LPA and LC-DST training has been provided for 93 participants across States and UTs at onsite and at NIRT. State level Induction training conducted for LTs and STLS across Tamil Nadu at the Institute of Public health, Poonamalli for 324 participants in 8 batches.

Laboratory indicators from 1403 TrueNAT sites, 381 CBNAAT sites, 7151 smear microscopy sites and 20 laboratories for LPA & LC-DST were collected monthly, verified by the NRL consultants and data analyst. The lab performs LPA-based NTM speciation for the states of Tamil Nadu, Kerala and Telangana with the M. abscesses as predominantly identified strains. The lab offers whole genomic sequencing, targeted Next-Generation sequencing for 50 patients from the states of Andhra Pradesh, Telangana, Kerala, New Delhi and Gujarat. NRL-NTEP also extended support for DST for newer drugs upon request to difficult to treat TB patients across states.

The ICMR-NIRT EDP division plays a crucial role in supporting all research activities at NIRT by providing essential IT and data management services. The comprehensive IT and data management support enables ICMR-NIRT to contribute effectively to the National TB Elimination Program through its research activities.

The Population Attributable Fractions (PAF) estimated from the National TB Prevalence Survey, highlighting that individuals with a history of past tuberculosis treatment, undernutrition, advanced age, smoking habits, and diabetes constitute roughly 30% of the population but are responsible for 70% of tuberculosis cases, underscore critical areas for intervention within the National TB Elimination Program. This evidence suggests that targeted strategies, including intensified preventive measures, comprehensive diagnostic services, effective treatment regimens, and long-term follow-up, should prioritize these high-risk groups. Moreover, it is essential that these interventions are designed with an equitable focus on both sexes to ensure comprehensive care.

The study ‘Cost-effectiveness of implementing the Cy-Tb test to screen latent tuberculosis infection in India’ has provided a scientific evidence-based findings on LTBI screening tests (Cy-Tb and TST), the policy brief was prepared and sent to Department of Health Research for incorporation in NTEP policy level decision making. The paper was also published in International Health journal, making it more authentic.

The study ‘Cost-effectiveness of BPaLM/BPaL regimen for multi-drug resistant, rifampicin resistant tuberculosis, India’ was completed and provided a scientific evidence based findings on shorter BPaLM/BPaL regimens for MDR/RR-TB compared to current practice, the policy brief was prepared and sent to Department of Health Research for incorporation in NTEP policy level decision making.

Developed a Policy document on Cost-effectiveness analysis for implementation of smoking cessation strategies at primary health care settings

Regional Reference Lab for the National AIDS Control Organization:

(Contact person: Dr Luke Elizabeth Hanna, Scientist F)

The Department of Virology and Biotechnology has been serving as a Regional Reference Lab for NACO for HIV-1 viral load testing for the National ART Program and molecular diagnosis of HIV infection for the National EID Program.

For the EID program, the lab received and tested a total of 3,600 DBS samples from the states of Tamil Nadu, Kerala, Pondicherry, Andhra Pradesh, Orissa and Telangana during the period of report. For the National ART program, the lab has received and tested a total of 19,623 samples for HIV-1 viral load from various districts of Tamil Nadu as well as from Andamans during the period of report. Further details are provided in Table 2 below.

Table 2: Testing Details for HIV-1 Viral load and HIV-1 TNA PCR for 2023-24

HIV-1 Viral Load testing details		**HIV-1 TNA PCR testing details**	
Total samples tested	19623	Total DBS received	3881
<1000 copies/ml	1798	No. of samples tested	3600
>1000 copies/ml	1114	Confirmed positives	125
Not Detected	16711	Not Detected	3475
No. of Proficiency panels participated	1	No. of Proficiency panels participated	1(Sep-2023)
Proficiency scoring	100%	Proficiency scoring	100%

BUILDING COHORTS, BIOREPOSITORY AND LABORATORY CAPACITY

Establishing the metabolomics facility:

Tuberculosis (TB) is a complex infectious disease that manipulates host metabolic pathways to enhance its survival. Understanding these metabolic changes across various stages of infection can serve as a powerful tool for biomarker discovery. Recognizing this need, the Department of Biochemistry at ICMR-NIRT has initiated the establishment of a state-of-the-art Metabolomics Facility to support research in metabolomics, lipidomics, and drug/nutrient analysis across diverse biological samples.

As a significant step forward, an LC-MS/MS instrument has been successfully installed, and the procurement of supporting equipment is underway. Recruitment for skilled human resources is in progress. Once fully operational, the facility will cater to both intra- and inter-institutional collaborative research.

Strengthening Laboratory Quality - ISO 15189: 2022 Accreditation

To ensure international standards in laboratory testing, the department has actively pursued accreditation under ISO 15189:2022 through the National Accreditation Board for Testing and Calibration Laboratories (NABL). The application process is complete, and all staff members are trained and certified under the updated standards. This accreditation will significantly enhance the reliability and global acceptance of test reports generated by the laboratory.

AI-ready chest X-ray dataset development

The Department of Epidemiology has developed the IN-CXR dataset, a comprehensive chest X-ray dataset in DICOM format, compatible with all standard DICOM viewers. This resource is intended to support the development of machine learning (ML) and deep learning (DL) models in radiology, especially for tuberculosis. The dataset serves as a valuable tool for researchers and developers aiming to advance AI-driven diagnostic applications.

Establishment of the TB Vaccine Immunology Laboratory (TBVIL) at NIRT

Purpose:
With support from the Bill & Melinda Gates Foundation (BMGF), NIRT has secured approval to establish the TB Vaccine Immunology Laboratory (TBVIL). This facility will perform validation assays for novel TB vaccines, assessing both immunogenicity and effectiveness.

Plan of Action:

The project will be executed in two phases

- Phase I: Planning and preparation.
- Phase II: Validation and execution.

Currently, we are in the process of obtaining the necessary administrative approvals to initiate this laboratory capacity-building project.

Model Rural Health Research Unit (MRHRU) - Madurai

Establishment of a Model Rural Health Research Unit (MRHRU) at Thoppur, Madurai, was sanctioned by DHR, Govt of India in March 2024.This unit will work towards research for the local programmatic needs in close collaboration with local state government authorities including Directorate of Public Health and, Tamilnadu and Directorate of Medical Education and Research, Tamilnadu. ICMR-NIRT will be the mentoring Institute, Dr.S.Ramesh Kumar, Scientist F being the Nodal Officer. Madurai Medical College is the affiliating Govt Medical College.

Adverse Drug Reaction Monitoring Centre (NIRT-AMC)

Recognized by the **Indian Pharmacopoeia Commission (IPC)** in April 2022, ICMR-NIRT functions as an **ADR Monitoring Centre (AMC)** under the **Pharmacovigilance Programme of India**. As a TB research leader, NIRT collects and analyzes adverse drug reactions (ADRs) to anti-TB drugs using standard forms. These reports undergo **causality assessment** by the institute's dedicated committee and are uploaded to **Vigiflow**, contributing to India's national ADR data and the WHO database.

An exclusive, fully equipped AMC office has been established at NIRT, Chennai. By March 2024, over **70 ADRs** were reported. Notably, a case series on **Ethambutol-induced optic neuropathy** was published in an international journal. The center has also conducted **CMEs, sensitization programs, and quiz competitions** to educate healthcare providers on ADR reporting.

- **Coordinator**: Dr. S. Ramesh Kumar, Scientist F
- **Deputy Coordinator**: Dr. Syed Hissar, Scientist E

1. Central Biorepository for TB Specimens - Phase II

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Participating Institutes	:	ICMR-NIRT
Source of funding	:	DBT (GoI)
Study period	:	2023-2026
Category	:	Development
Pillar	:	Build

Background

The RePORT India Central Biorepository was established at ICMR-NIRT and became operational since April 2017. In February 2024 the Biorepository moved into a large, newly constructed Composite Lab facility at NIRT's Thiruvallur campus. The biorepository stores large volumes of high-quality biospecimens of various types collected from cohorts of TB patients and their household contacts recruited and followed up at the different RePORT India Clinical Research Sites, and serves as a very valuable resource for TB researchers to undertake cutting edge research in TB.

To ensure the quality of the peripheral blood mononuclear cells stored in the Biorepository for immunological studies, ICMR-NIRT has been implementing an in-country PBMC External Quality Assessment (EQA) program, which administers quarterly surveys to assess the quality of the cells prepared and stored at the clinical research sites of the RePORT India Consortium.

Objectives

Central Biorepository:

1. To undertake long term storage of biological specimens collected and shipped from the RePORT India Clinical Research Sites.
2. To distribute archived samples to TB researchers with approved protocols.

In-Country PBMC EQA Program:

1. To assess the performance of laboratories preparing PBMC for long term storage in the Biorepository.
2. To enable prompt responses to poor performance and offer laboratories opportunities for improvement.
3. Provide data to networks for choosing labs and / or specimens for studies.

Methods

The Central Biorepository receives and stores biological samples from the participating Clinical Research Sites in Chandigarh, Chennai, Hyderabad, Mumbai, Puducherry, Pune, Shillong, and Vellore. Samples include MTB isolates, whole blood for DNA, Paxgene RNA, sputum, nasopharyngeal aspirate, gastric lavage, saliva, oral swabs, extra pulmonary specimens, urine, stool, PBMC and QuantiFERON supernatants collected from well characterized longitudinally followed cohorts. All samples, except PBMCs, are stored in

ultra-low deep freezers at -80°C; PBMCs are stored in the vapor phase of liquid nitrogen.

The In-Country PBMC External Quality Assessment (EQA) program caters to six clinical research sites: CMC, MVDRC, JIPMER, BJMC, BMMRC, and NIRT. The viability and recovery of PBMC prepared by the participating sites are assessed by the trained team at the Central Biorepository and results are shared with the sites to maintain their approved status. Refresher trainings and support for corrective and preventive action are provided by the Biorepository staff for sites with suboptimal performance scores.

Study progress

Both activities are ongoing. Details of samples stored in the Biorepository for this project are detailed in Table 3.

Table 3: Samples stored in the Central Biorepository during the period April 2023-March 2024

Details of Cohorts	No. of samples stored
RePORT India Phase II Cohort A	5197
RePORT India Phase II Cohort B	144
RePORT India Phase II Dx Cohort	621
Total	5962

2. The Regional Prospective Observational Research for TB (RePORT) India - Common Protocol Phase II

Principal Investigator : Dr. P. K. Bhavani, Scientist E
Participating Institute : ICMR-NIRT
Source of funding : DBT (GoI)
Study period : 2022-2025
Category : Development
Pillar : Build

Background

RePORT India Common Protocol is currently in Phase II of its operations with two additional sites and one additional cohort. At ICMR-NIRT participants are recruited into two cohorts – a Diagnostic cohort comprising of presumptive TB cases and Cohort A comprising of confirmed TB cases.

Objectives

ICMR-NIRT under RePORT India Phase II Common Protocol is involved in three specific scientific aims:

1. To evaluate novel diagnostics and biomarkers of diverse states of Mtb infection.
2. To identify TB treatment response biomarkers
3. To identify markers of lung injury associated with unfavourable TB treatment outcomes.

In addition to the research objectives, the study undertakes storage of longitudinally collected well characterized biospecimens from the recruited participants.

Methods

The Department of Virology and Biotechnology processes and stores various types of samples including whole blood, serum, plasma, PBMC and Paxgene samples for this study. At regular intervals the samples stored in the site freezer are shipped to the Central Biorepository at Thiruvallur for long term storage.

Study progress

Participant recruitment and follow-up are ongoing.

Details of the samples collected and stored as part of this study during the period of report is listed in Table 4.

Table 4: RePORT Phase II sample inventory

Cohort A specimens							
Visit Type	**Plasma**	**Plasma Antibody**	**Whole blood DNA**	**NAT**	**Paxgene**	**Micro-nutrient**	**PBMC**
BL	185	19	57	37	19	0	20
M1	270	0	0	0	30	270	30
M2	261	27	0	0	27	0	28
Unsched M2	45	5	0	0	5	0	5
EOT	218	24	72	48	24	0	24
Unsched M2	18	2	6	4	2	0	2
Tx F/R/W	9	1	3	2	1	0	1
Total	1006	78	138	91	108	270	110

Diagnostic Cohort specimens				
Visit Type	**Plasma**	**Plasma Antibody**	**Paxgene**	**Whole blood DNA**
BL	36	4	8	12
M2	90	10	20	0
Total	126	14	28	12

3. CoHRPICA (Cohorts for HIV resistance and prevention in Indian children and adults) Regional Biorepository

Principal Investigator	:	Dr. Luke Elizabeth Hanna, Scientist F
Participating Institutes	:	ICMR-NIRT
Source of funding	:	DBT (GoI)
Study period	:	2017-2023
Category	:	Development
Pillar	:	Build

Background

Longitudinal cohort studies carried out across the globe have been instrumental in spurring research on the genetic, immunologic and viral factors that alter susceptibility/resistance to HIV infection in a sub-group of HIV-infected/exposed persons. Such well-characterized cohorts are non-existent in the country. This multicentric study is an attempt to build such cohorts and store longitudinally collected biospecimens as well as linked data for them the cohort participants for future research.

Objectives

1. To build well-characterized cohorts of high-risk HIV-exposed seronegative individuals, as well as HIV-infected adults and children.
2. To collect longitudinal clinical and socio-demographic data as well as biological specimens from enrolled participants for undertaking studies aimed at answering pertinent questions with regard to HIV transmission, genetic susceptibility / resistance and pathogenesis.

Methods

The targeted enrollment for this study was 1050 HIV-exposed uninfected individuals from key high-risk populations (350 each of MSM/TG, PWID and FSW), 250 HIV-infected adult participants (including 100 individuals without co-morbidities and 150 with/at-risk of co-morbidities like TB, cardiovascular disease and diabetes mellitus), and 100 HIV-infected children (including 50 mother-child transmission pairs). Biological specimens and linked socio-demographic as well as clinical and laboratory data were obtained from the enrolled participants using well-standardized templates and procedures that were harmonized across the participating sites.

Study progress

ICMR_NIRT contributed to the collection of 175 MSM participants and 100 HIV-infected participants with and without comorbidities for this study. ICMR-NIRT also serves as the Regional Biorepository for the study. Details of the samples stored in the NIRT Biorepository for this study are listed in Table 5. Collection of data and biological specimens from enrolled participants is as per well-standardized templates and procedures that have been harmonized across the participating sites.

Longitudinal samples were collected from HIV-exposed uninfected cohorts (MSM, TG, IDU) including exposed sero-negatives (ESNs) and HIV-infected adults and children including those with early HIV infection (EHI) as well as those with and without co-morbidities and stored in a central biorepository.

Table 5: Biospecimens stored at Regional Biorepository at ICMR-NIRT for CoHRPICA study

Cohort	Serum	Plasma	PBMC
HIV Infected Adults	393	1899	751
HIV Infected Children	0	0	198
EHI	8	56	22
HIV uninfected at risk	539	1178	868
Total	940	3133	1839

4. Virus Research and Diagnostic Laboratory (VRDL)

Principal Investigator : Dr. Luke Elizabeth Hanna, Scientist F
Participating Institutes : ICMR-NIRT
Source of funding : Department of Health Research (GoI)
Study period : 2021-2026
Category : Development
Pillar : Build

Background

A medical college level VRDL has been established at the NIRT Thiruvallur site and operationalized.

Objectives

i. To create infrastructure for timely identification of viruses and other agents causing epidemics or morbidity significant at the public health level.
ii. To develop capacity for identification of novel and unknown viruses and other organisms, and develop diagnostic kits.
iii. To provide training to health professionals.
iv. To undertake research for identification of emerging and newer genetically active/ modified agents.

Methods

The goal of this project is to establish mechanisms and systems for dealing with outbreak infections and emerging epidemics of public health importance.

Study progress

VRDL facility has been set up at the NIRT Thiruvallur unit. Collaborations have been initiated with the Microbiology Department of the Thiruvallur GH and Medical College. Sample collections have been ongoing for the dengue virus project from Thiruvallur GH. Field work has been initiated for the One Health project.

TRANSLATIONAL VALUE OF RESEARCH PROJECTS

ICMR-National Institute for Research in Tuberculosis

The translational research undertaken by the institute focuses on bridging the gap between scientific discovery and public health impact, with a strong emphasis on tuberculosis (TB). By integrating laboratory innovations, clinical studies, community-based interventions, and policy-relevant evaluations, the institute transforms research findings into practical tools, diagnostic methods, and treatment strategies that directly benefit patients and the national TB control program. This includes the development of cost-effective diagnostic assays, AI tools, community health modules, drug resistance profiling techniques, and public health models—demonstrating the institute's commitment to applying scientific advancements to real-world health challenges, particularly in resource-limited and high-burden settings.

Key Translational Research Highlights:

- In-house Targeted Next-Generation Sequencing (tNGS) for Drug Resistance Developed by *Dr. Sivakumar Shanmugam*, this method allows rapid and comprehensive detection of drug-resistant TB, supporting personalized treatment approaches.

- Standardization of Stool-Based LPA for TB Diagnosis *Dr. Priya Rajendran* has standardized an in-house protocol to extract DNA from stool specimens for LPA-based detection of *Mycobacterium tuberculosis* and its drug resistance patterns—offering a non-invasive diagnostic tool for pediatric and extrapulmonary TB cases.

- Critical Breakpoints for Newer TB Drugs *Dr. V. N. Azger Dusthackeer* identified new MIC thresholds for Bedaquiline, Clofazimine, and Delamanid, contributing to improved interpretation of susceptibility testing.

- Lineage-specific MIC Observations Notably, Lineage 1 strains were found to have higher MIC values for Pretomanid, suggesting a need for lineage-based treatment decisions.

- AI Tool for LPA Interpretation An artificial intelligence-based platform is under development to aid automated and accurate interpretation of LPA results.

Ongoing Translational Studies:

- Point-of-Care Estimation of Vitamin D and CRP in TB Contacts This study aims to enhance TB screening efficiency in household contacts using simple biochemical markers. The approach is expected to reduce the number of unnecessary confirmatory tests, resulting in substantial cost savings.

It is highly adaptable to other high-risk settings such as tribal populations and prisons.

- Nanopeptide Therapeutics for Residual Lung Injury A completed study has developed a novel nanocarnosine formulation to address post-TB lung injury. The formulation has demonstrated promising anti-inflammatory and biocompatible properties and is being prepared for preclinical testing and IPR filing.

Diagnostic and Surveillance Innovations:

- A newly developed HPLC-UV method enables simultaneous quantification of first-line TB drugs in FDC tablets. This low-cost method is ideal for routine quality control in resource-limited settings.

- Findings from both National and Sub-National TB Prevalence Surveys underscore the high prevalence of subclinical TB cases. These cases, often undetected, play a major role in sustaining community transmission. The research emphasizes the need for improved early detection strategies and has significant implications for public health interventions.

- The surveys also revealed low health-seeking behavior among symptomatic individuals. The findings underscore the urgent need for targeted Information, Education, and Communication (IEC) efforts and robust active case finding (ACF) initiatives to enhance early diagnosis and reduce transmission.

Policy-Influencing Economic Evaluations:

- Cost-Effectiveness of Cy-Tb for LTBI Diagnosis Research demonstrated that Cy-Tb is a cost-effective alternative to the traditional Tuberculin Skin Test (TST), particularly for early detection and prevention of active TB through targeted TB preventive therapy (TPT). Strategic procurement can enhance affordability in low-resource settings.

- Economic Impact of BPaLM/BPaL Regimens for MDR/RR-TB Evidence from economic modeling indicates that BPaL/BPaLM regimens are more cost-effective and clinically beneficial compared to the current standard of care. Their adoption under NTEP could significantly improve patient outcomes and reduce national treatment costs.

- Smoking Cessation Strategies in Tamil Nadu Comparative analysis revealed that combining intensive counseling with Nicotine Replacement Therapy (NRT) and Bupropion offers better health and economic outcomes than

standard practices. The findings advocate for the integration of these strategies into primary health care for greater impact.

Emerging Biomarkers and Molecular Tools:

- A set of soluble biomarkers has been identified, with the potential for developing a point-of-care test to identify individuals at high risk of progressing to active TB.
- A ddPCR-based assay has been standardized for detecting circulating cell-free Mtb DNA, especially useful in diagnostically challenging cohorts.
- A rapid diagnostic assay is under development to detect INSTI drug resistance mutations among HIV patients, facilitating timely ART initiation.
- Version 2.0 of the India-specific MTB Mutation Catalogue has been published, offering a comprehensive reference for understanding genetic resistance profiles among *M. tuberculosis* strains in India.

Community-Centered Interventions for Psychosocial Support and TB Case Detection

- The department of social and behavioral research has developed and implemented a participatory intervention module aimed at holistically addressing the psycho-social needs of TB patients and their caregivers. This module is currently being adapted in three districts—Chennai, Kanchipuram, and Thiruvallur—under the National Tuberculosis Elimination Programme (NTEP). The module has also been disseminated through the *Tamil Nadu Journal of Public Health,* contributing to wider public health outreach.
- An intervention study conducted in the tribal district of Senapati, Manipur, aimed at improving TB case detection, led to the development of a training manual for community volunteers. This manual, designed to enhance local engagement in case finding and treatment support, is now being used by the district TB program in Senapati.

This robust portfolio of translational research at ICMR-NIRT is shaping TB diagnostics, treatment, and public health interventions at the national level. By bridging laboratory science and field implementation, these initiatives support the overarching goal of tuberculosis elimination and improved health outcomes across vulnerable populations.

INNOVATIONS AND PATENTS

SNo.	Name of Technology/Product	Area	Patent status	Tech transfered/ Commercialized
1	A CRISPR-Cas13-Based Tool for Rapid Detection of Mycobacterium Tuberculosis	Communicable Disease: TB	Application No.202311071943 (Filed)	NA
2	A patent titled, "Carnosine Nanopeptides for Drug Delivery System (6457IN361)" is filed by Intellectual Property Rights Unit, Innovation & Translational Research Division, ICMR, New Delhi	Nanodelivery	Yet to be granted	NA
3	A paper disc-based method for determining the drug susceptibility of *mycobacterium tuberculosis"* partnering ICMR and IIT Kharagpur. Application number: 6457IN020	TB Diagnostics	Patent No:471729, Date of grant: 22.11.2023	NA

APPENDICES

LIST OF PUBLICATIONS

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Department of Clinical Research				
1	Ethambutol-induced optic neuropathy: should we mandate ophthalmic examination in TB treatment?	S. Ramesh Kumar, Syed hissar, C. Padmapriyadarsini	International Journal of Tuberculosis and Lung Disease	Jan 2024	4.0
2	Inadequate Lopinavir Concentrations with Modified 8-Hourly Lopinavir/Ritonavir 4:1 Dosing during Rifampicin-based Tuberculosis Treatment in Children Living with HIV.	Syed Hissar, Bency Joseph, P K Bhavani, G Prathiksha, D Baskaran, , N S Gomathi, V Mythily, Hemanth Kumar, Silambu Chelvi, L Sekar, Luke Hanna, A Gunasundari, G Mangalambal, Valarmathi Nagarajan, Shakeela Shankar, R Selvi, S Vaishnavi, Krishna Yadav, R Supriya, Hema Giranab, A Seetha, Stella Mary, S Gopika, S Rohini, M Revathy	The Pediatric Infectious Disease Journal	Jul 2023	3.2
3	Role for Linezolid in Drug Sensitive Tuberculosis.	Ramesh Kumar S, Narendran G, Padmapriyadarsini C	Journal of Infection and Public Health	Jan 2024	6.7
4	Obesity and Outcomes of Kawasaki Disease and COVID-19–Related Multisystem Inflammatory Syndrome in Children.	Aishwarya Venkataraman	JAMA network open	Dec 2023	13.35

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
5	Kawasaki Disease in the Time of COVID-19 and MIS-C: The International Kawasaki Disease Registry.	Aishwarya Venkataraman	Canadian journal of cardiology	Jun 2023	6.2
6	Abstract 15506: Pattern of Use of Anakinra for Patients With Kawasaki Disease versus Multisystem Inflammatory Syndrome in Children Associated With COVID-19.	Aishwarya Venkataraman	AHA ASA Journals	Nov 2023	39.9
7	Pediatric COVID-19 and MIS-C–Lessons Learnt and the Way Forward.	Aishwarya Venkataraman	Indian Pediatrics.	May 2023	2.3
8	Alterations of adipokines, pancreatic hormones and incretins in acute and convalescent COVID-19 children.	Aishwarya Venkataraman, Nathella Pavan Kumar	BMC Pediatrics	Apr 2023	2.4
9	Levels of Complement Components in Children With Acute COVID-19 or Multisystem Inflammatory Syndrome.	Aishwarya Venkataraman, Nathella Pavan Kumar	JAMA Network Open	Mar 2023	13.35
10	Addressing the challenges in implementing airborne infection control guidelines and embracing the policies.	Bella Devaleenal Daniel, Abinaya Baskaran, Baskaran D, Hephzibah Mercy, Padmapriyadarsini C	Indian Journal of Tuberculosis	Apr 2023	1.483

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
11	Holistic Approach to Enhance Airborne Infection Control Practices in Health Care Facilities Involved in the Management of Tuberculosis in a Metropolitan City in India - An Implementation Research.	Daniel Bella Devaleenal, Kannan Thiruvengadam, Prathiksha Giridharan, Banurekha Velayudham, Rajendran Krishnan, Abinaya Baskaran, Hephzibah Mercy, Baskaran Dhanaraj, Padmapriyadarsini Chandrasekaran	WHO South-East Asia Journal of Public Health	2023	0
12	Improving treatment adherence among tuberculosis patients through evening DOTS in Chennai, India.	Daniel Bella Devaleenal, Dina Nair, Vasantha Mahalingam, Radhakrishnan R, Binny Priscilla Rebecca, Chandra Suresh, Beena Thomas	National Medical Journal of India	Mar 2024	0.595
13	TB-LAMP (loop-mediated isothermal amplification) for diagnosing pulmonary tuberculosis in children.	Leeberk Raja Inbaraj, Mukesh Kumar Sathya Narayanan, Vignes Anand Srinivasalu, Adhin Bhaskar, Priya Rajendran, Bella Devaleenal Daniel	The Cochrane Library	Sep 2023	8.4
14	QTc Prolongation with Bedaquiline Treatment for drug-resistant Pulmonary TB in a Programmatic Setting.	A Bhaskar, B Ramraj, C Padmapriyadarsini	The International Journal of Tuberculosis and Lung disease	Apr 2023	4
15	Contact screening and yield of tuberculosis from pediatric TB index cases.	Pooranagangadevi Naveneethapandian, Banurekha Velayutham, Mahalakshmi Rajendran	TNJPHMR - Tamil Nadu Journal of Public Health and Medical Research	Apr 2024	0

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
16	Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021.	Leeberk Raja Inbaraj	The Lancet	Jun 2023	202.7
17	Global Burden of Cardiovascular Diseases and Risks, 1990-2022.	Leeberk Raja Inbaraj	Journal of the American College of Cardiology	Dec 2023	24
18	Effectiveness of Adjunctive High-Dose Infliximab Therapy to Improve Disability-Free Survival among Patients with Severe Central Nervous System Tuberculosis: a Matched Retrospective Cohort Study.	Leeberk Raja Inbaraj	Clinical Infectious diseases	Jul 2023	20.9
19	Mortality Estimates of Central Nervous System TB in India.	Inbaraj LR, S Selvaraju	The International Journal of Tuberculosis and Lung disease	Nov 2023	4
20	Effectiveness and safety of Levofloxacin containing regimen in the treatment of Isoniazid mono-resistant pulmonary Tuberculosis: a systematic review.	Leeberk Raja Inbaraj, Vignes Anand Srinivasalu	Frontiers in Medicine	Jun 2023	5

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
21	Leukotriene A4 hydrolase (LTA4H rs17525495) gene polymorphisms and paradoxical reactions in extrapulmonary tuberculosis. Scientific Reports.	Leeberk Raja Inbaraj	Scientific Reports	Mar 2023	4.6
22	Truenat MTB assays for pulmonary tuberculosis and rifampicin resistance in adults.	Leeberk Raja Inbaraj, Priya Rajendran, Adhin Bhaskar, Vignes Anand Srinivasalu, Mukesh KS Narayanan, Muniyandi Malaisamy, Chandrasekaran Padmapriyadarsini	Cochrane Database of Systematic Reviews	Jan 2023	12
23	Antibody Titres in Fully Vaccinated Healthcare Workers with and without Breakthrough Infection during the Delta and Omicron Waves.	Leeberk Raja Inbaraj	Journal of Family Medicine and Primary Care	Jul 2023	1.4
24	Perumal Kannabiran B, Palaniappan NA, Manoharan T, Paramasivam PK, Saini JK, Ansari MS, et al. Safety and Efficacy of 25 mg/kg and 35 mg/kg vs 10 mg/kg Rifampicin in Pulmonary TB: A Phase IIb Randomized Controlled Trial. Open Forum Infectious Diseases. 2024 Mar 1;11(3):ofae034.	Bhavani Perumal Kannabiran, Natarajan Alangudi Palaniappan, Tamizhselvan Manoharan, Paul Kumaran Paramasivam, Balaji Subramanyam, Saravanan Natarajan, Radha Krishnan Ammayappan , Mangalambal Ganesan, Dhanalakshmi Angamuthu, Ponnuraja Chinnaiyan, Padmapriyadarsini Chandrasekaran, Soumya Swaminathan	Open Forum Infectious Diseases	Mar 2024	4.2

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
25	Nutritional supplementation to prevent tuberculosis incidence in household contacts of patients with pulmonary tuberculosis in India (RATIONS): a field-based, open-label, cluster-randomised, controlled trial	Banurekha Velayutham, Basilea Watson	Lancet	2023	98.4
26	Nutritional support for adult patients with microbiologically confirmed pulmonary tuberculosis: outcomes in a programmatic cohort nested within the RATIONS trial in Jharkhand, India	Banurekha Velayutham, Basilea Watson	Lancet Global Health	2023	19.9
27	QTc prolongation with bedaquiline treatment for drug-resistant pulmonary TB in a programmatic setting	Balaji Ramraj, C Padmapriyadarsini	International Journal of Tuberculosis and Lung Diseases	Apr 2023	4.0
	Department of Socio Behavioural Research				
28	Self-driven solutions and resilience adapted by people with drug-resistant tuberculosis and their caregivers in Bengaluru and Hyderabad, India: a qualitative study	Karikalan Nagarajan, Senthil Sellapan Stephen Arangba, Javeed Basha, Pearl Maria Dsouza, Malaisamy Muniyandi	The Lancet Regional Health - Southeast Asia,	2024	5.0

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
29	Wings of Support (Udhavum Siragugal): A Holistic Psycho-Social Intervention for TB Persons and Caregivers in A Tertiary Care Facility in Tamil Nadu, An Implementation Research Approach	Karikalan Nagarajan, Chandra Suresh, Murugesan P, Sellappan S, Dhanalakshmi A, Rani S, Stephen A, Priscilla B, Chandrasekaran Padmapriyadarsini	Tamil Nadu Journal of Public Health	2024	-
30	Economic aspects of shortening the duration of tuberculosis treatment.	M Muniyandi, Karikalan N	Lancet Global Health	2024	19.9
31	Operational Challenges in Conducting a Subnational TB Prevalence Survey in India: Lessons Learned for Resource-Limited, High-Burden Settings.	Giridharan, P., Murugesan, H., Selvaraju, S., Frederick, A., Selvavinayagam, T. S., Nagarajan, K.,	Global health, science and practice	2024	4.0
32	The Predicted Potential Impact of COVID-19 Pandemic on Tuberculosis Epidemic in Tamil Nadu, South India.	M Muniyandi, Karikalan N	Tropical medicine and infectious disease	2024	2.9
33	Improving the measurement of tuberculosis care cascades to enhance people-centred care.	Faust, L., Naidoo, P., Caceres-Cardenas, G., Ugarte-Gil, C., Muyoyeta, M., Kerkhoff, A. D., Nagarajan, K.,	The Lancet. Infectious diseases	2023	34.4
34	Gender differences in COVID-19 knowledge, risk perception, and public stigma among the general community: Findings from a nationwide cross-sectional study in India.	Stephen, A., Nair, S., Joshi, A., Aggarwal, S., Adhikari, T.	International journal of disaster risk reduction	2023	4.2

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
35	Cost of screening, out-of-pocket expenditure & quality of life for diabetes & hypertension in India.	Brar, S., Kaur, G., Muniyandi, M., Karikalan, N., Bano, H., Bhansali, A., Jain, S., Kumari, S., & Prinja, S.	The Indian journal of medical research	2023	4.2
36	Time Elapsed from Onset of Symptoms to Antituberculosis Treatment in Children with Central Nervous System Tuberculosis in a Tertiary Hospital in South India: A Mixed-Methods Pilot Study.	Giridharan, Prathiksha; Rebecca, Priscilla; Devaleenal, Bella; Chelladurai, Elilarasi; Chinnaiyan, Ponnuraja; Malaisamy, Muniyandi.	Indian Journal of Public Health	2023	2.2
37	Improving treatment adherence among tuberculosis patients through evening DOTS in Chennai, India	Devaleenal DB, Jeyabal L, Nair D, Mahalingam V, Radhakrishnan R, Rebecca BP, et al.	Natl Med J India	2023	0.55
38	Factors associated with stigma and Manifestations experienced by Indian Health Care Workers involved in COVID-19 management in India: A Qualitative Study	Beena Thomas, Geetha Menon, Murugesan Periyasamy, Ragini Kulkarni, Ranjan K Prusty, Chitra Venkateswaran,	Cambridge Prisms: Global Mental Health.	2023	4.00
39	Safety and Efficacy of 25 mg/kg and 35 mg/kg vs 10 mg/kg Rifampicin in Pulmonary TB: A Phase IIb Randomized Controlled Trial	Bhavani Perumal Kannabiran, Natarajan Alangudi Palaniappan, Tamizhselvan Manoharan, Paul Kumaran Paramasivam, Balaji Subramanyam, Ramesh P M, Saravanan Natarajan, Radha	Open Forum Infectious Diseases	2024	3.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
		Krishnan Ammayappan, Mangalambal Ganesan, Dhanalakshmi Angamuthu, Ponnuraja Chinnaiyan, Padmapriyadarsini Chandrasekaran, Soumya Swaminathan			
	Department of Bacteriology				
40	Assessing the utility of Truenat in extrapulmonary tuberculosis diagnosis-A NRL's experience.	Rajendran P, Jayabal L, Venkatesan M, Kumar MP, Ramalingam R, Sivaraman P, Fredrick A, Shanmugam S	Journal of Clinical Tuberculosis and Other Mycobacterial Diseases	2024 Feb	2
41	Evaluation of molecular diagnostic test for detection of adult pulmonary tuberculosis: A generic protocol.	Jayaprakasam M, Pandey RM, Choudhary H, Shanmugam S, Sivaramakrishnan GN, Gupta N	. Indian Journal of Medical Research.	2024 Feb	4.2
42	Long-term follow-up of persons diagnosed with multidrug-resistant TB in Chennai, India, 2013–2020.	Surie D, Sathyanarayanan MK, Lavanya J, Smith JP, Shanmugam SK, Tamilzhalagan S, Selvaraj A, Ramesh G, Tripathy S, Khaparde SD, Ho CS	The international journal of tuberculosis and lung disease.	2024 Jan	3.4
43	Recurrence of pulmonary tuberculosis in India: Findings from the 2019–2021 nationwide community-based TB prevalence survey.	Giridharan, P., Selvaraju, S., Rao, R., Rade, K., Thiruvengadam, K., Asthana, S., ...Siva Kumar shanmugam… & Bhargava, B.	Plos one	2023 Dec	3.7

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
44	Molecular Characterisation of M. kansasii Isolates by Whole-Genome Sequencing.	Rajendran P, Padmapriyadarsini C, Nagarajan N, Samyuktha R, Govindaraju V, Golla R, Ashokkumar S, Shanmugam S.	Pathogens	2023 Oct	3.7
45	Comprehensive assessment of invalid and indeterminate results in Truenat MTB-RIF testing across sites under the national TB elimination program of India.	Gopalaswamy, R., Kumar, N., Vashistha, H., Rajendran, P., Kayesth, J., Peravali, C. J & Shanmugam, S.	Frontiers in Public Health	2023	5.2
46	. (2023). Establishing proof of concept for utility of Trueprep®-extracted DNA in line-probe assay testing. *27*(10), 742-747.	Rajendran, P., Saini, S., Kumar, N., Vashistha, H., Thiruvengadam, K., Ramamoorthy, T., . Siva Kumar shanmugam.. & Padmapriyadarsini, C	The International Journal of Tuberculosis and Lung Disease	2023	3.7
47	Genomics-based strategies for advanced drug resistance and epidemiological surveillance of Mycobacterium tuberculosis and other non-tuberculous mycobacteria.	Ghodousi A, Darban-Sarokhalil D, Shahraki AH, Shanmugam S.	Frontiers in Microbiology.	2023 Aug	5.2
48	Genotype MTBDRsl version 2 and phenotypic drug resistance detection of Mycobacterium tuberculosis for fluoroquinolones and aminoglycosides.	Radhakrishnan, R., Prabuseenivasan, S., Hannah, S., Vaishanavee, V., Senthildevi, V., Kannadhasan, T.,& Shanmugam, S.	The International Journal of Mycobacteriology	2023	1.2

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
49	Newer TB diagnostics: An update.	Rajendran P, Padmapriyadarsini C, Nair S, Sivakumar S.	Indian Journal of Tuberculosis	2023 Jul	0.7
50	Case Report: Ocular Tissue Diagnosis of Previously Undiagnosed, Extensively Drug-Resistant Pulmonary Tuberculosis.	Basu S, Murthy SI, Mitra S, Chittiboyina S, Shanmugham S	The American Journal of Tropical Medicine and Hygiene.	2023 May	3.07
51	Resistance Profiles to Second-Line Anti-Tuberculosis Drugs and Their Treatment Outcomes: A Three-Year Retrospective Analysis from South India.	Gopalaswamy, R., Palani, N., Viswanathan, D., Preysingh, B., Rajendran, S., Vijayaraghavan, V., ... & Shanmugam, S.	Medicina	2023	2.6
52	SARS COV-2 and TB co-infection among current tb patients in chennai, NIRT, India,	Bershila Preysingh, Michel Premkumar, Radha Gopalaswamy, Ashok Kumar Shanmugavel, Lavanya J, Jagadeesan M, Asha Frederick, Chandrasekaran Padmapriyadarsini, Sivakumar Shanmugam	Tamil Nadu Journal of Public Health and Medical Research	2024	-
53	Risk assessment and transmission of fluoroquinolone resistance in drug-resistant pulmonary tuberculosis: a retrospective genomic epidemiology study.	Azger Dusthackeer VN	Scientific Reports	2024	3.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
54	New synergistic benzoquinone scaffolds as inhibitors of mycobacterial cytochrome bc1 complex to treat multi-drug resistant tuberculosis,European	Azger Dusthackeer VN	European Journal of Medicinal Chemistry	2024	6.7
55	Testing the efficacy of green synthesized copper Nanoparticles from the aqueous extract of Eucalyptus globulus against Tuberculosis and other opertunistic infections.	Azger Dusthackeer VN, Angayarkanni	Indian journal of natural sciences	2023	2.742
56	Dactylides A−C, three new bioactive 22-membered macrolides produced by *Dactylosporangium aurantiacum.*	Azger Dusthackeer VN	The Journal of Antibiotics	2023	3.3
57	3,5-disubstituted pyridines with potent activity against drug-resistant Mycobacterium tuberculosis clinical isolates (In press)	Azger Dusthackeer VN, B. Angayarkanni	Future Medicinal Chemistry	2024	3.2
58	Molecular Characterization of *M. kansasii* isolates by Whole-Genome Sequencing.	Rajendran P, Padmapriyadarsini C, Nagarajan N, Samyuktha R, Govindaraju V, Golla R, Ashokkumar S, Shanmugam S.	Pathogens.	2023	2.3

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
59	Establishing proof of concept for utility of Trueprep extracted DNA in Line Probe Assay testing.	Rajendran P, Saini S, Kumar N, Vashistha H, Thiruvengadam K, Ramamoorthy T, Gopalaswamy R, Kayesth J, Alavadi U, Moore M, Joshi RP, Ramachandran R, Sridhar Anand S, Shanmugam S, Padmapriyadarsini C.	International Journal of Tuberculosis and Lung diseases	2023	4.5
60	Paediatric pulmonary disease-are we diagnosing it right?	Rajendran P, Thomas SV, Balaji S, Selladurai E, Jayachandran G, Malayappan A, Bhaskar A, Palanisamy S, Ramamoorthy T, Hasini S, Hissar S.	Frontiers Pediatics.	2024	4.0
61	Operational Challenges in Conducting a Subnational TB Prevalence Survey in India: Lessons Learned for Resource-Limited, High-Burden Settings.	Giridharan P, Murugesan H, Selvaraju S, Frederick A, Selvavinayagam TS, Nagarajan K, Thiruvengadam K, Krishnan R, Rajendran P, Kumaran P, Kumar M, Chandrasekaran P.	Global Health Science Pract.	2024	2.6
62	Programmatic implications of a sub-national TB prevalence survey in India	G. Prathiksha, S. Selvaraju, K. Thiruvengadam, A. Frederick, H. Murugesan, P. Rajendran, K. Nagarajan, M. Kumar, R. Krishnan, P. Kumaran, T.S. Selvavinayagam, C. Padmapriyadarsini	The International Journal of Tuberculosis and Lung diseases	2024	2.5

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
63	Assessing the utility of Truenat in extrapulmonary tuberculosis diagnosis - A NRL's experience.	Rajendran P, Jayabal L, Venkatesan M, Kumar MP, Ramalingam R, Sivaraman P, Fredrick A, Shanmugam S	Journal of Clinical Tuberculosis and Other Mycobacterial Diseases	2024	2
	Department of Biochemistry				
64	Protein targets in Mycobacterium tuberculosis and their inhibitors for therapeutic implications: A narrative review.	Souparnika Sreelatha, Usharani N, Saravanan Natarajan	Int. J. Biol. Macromol	2023	8.2
65	Biomimetic nanomaterials for pulmonary infections: A prospective view in drug delivery systems	Usharani N, Kanth SV, Saravanan N	Applied Nanoscience	2023	3.7
66	Green synthesis and characterization of water soluble nanocarnosine: A prospective drug delivery system	Usharani N, Naha A, Anbarasu A, Ramaiah S, Kanth SV, Natarajan Saravanan	Applied Materials Today	2023	8.6
67	Safety and Efficacy of 25 mg/kg and 35 mg/kg vs 10 mg/kg Rifampicin in Pulmonary TB: A Phase IIb Randomized Controlled Trial.	Bhavani Perumal Kannabiran et al.	Open Forum Infectious Diseases,	2024	3.8
	Department of Clinical Pharmacology				
68	Development and Validation of a Simple High-Pressure Liquid Chromatography-Ultraviolet Detection	Vilvamani S, Mahalingam S, Nhavilthodi S, Murugesan D, Jeyakumar SM	J Chromatogr Sci.	2024	1.5

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Method for Simultaneous Quantitation of First-Line Anti-Tuberculosis Drugs in Formulations of Fixed-Dose Combination.				
69	Long-Term Intake of Linezolid Elevates Drug Exposure and Reduces Drug Clearance and Elimination in Adults With Drug-Resistant Pulmonary Tuberculosis.	Jeyakumar SM, Bhui NK, Singla N, Vilvamani S, Mariappan MV, Padmapriyadarsini C, Bhatnagar AK, Solanki R, Sridhar R.	Ther Drug Monit.	2023	2.8
	Department of Epidemiology				
70	Prevalence and factors associated with tuberculosis infection in India.	Selvaraju S, Velayutham B, Rao R, Rade K, Thiruvengadam K,	Journal of Infection and Public Health	2023	4.7
71	A novel method for contact tracing for TB at household and community level.	P. Giridharan, B. Devaleenal, K. Thiruvengadam, M. Kaleeswari, Bhavani PK, Ramesh AM	The international journal of tuberculosis and lung disease	2023	4
72	Time Elapsed from Onset of Symptoms to Antituberculosis Treatment in Children with Central Nervous System Tuberculosis in a Tertiary Hospital in South India: A Mixed-Methods Pilot Study	Giridharan P, Rebecca P, Devaleenal B, Chelladurai E, Chinnaiyan P, Malaisamy M.	Indian Journal of Public Health	2023	2.1

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
73	Decreased Legionnaires' disease incidence in the United States during the COVID-19 pandemic, 2020-2022	Reddy Devarajulu	Global Biosecurity	2023	0
74	Linezolid Pharmacokinetics and Its Association with Adverse Drug Reactions in Patients with Drug-Resistant Pulmonary Tuberculosis.	Padmapriyadarsini C, Solanki R, Jeyakumar SM, Bhatnagar A, Muthuvijaylaksmi M, Jeyadeepa B, Reddy D,	Antibiotics	2023	2.1
75	Recurrence of pulmonary tuberculosis in India: Findings from the 2019–2021 nationwide community-based TB prevalence survey	Prathiksha Giridharan, Sriram Selvaraju, Raghuram Rao, Kiran Rade, Kannan Thiruvengadam, Smita Asthana, Rakesh Balachandar, Sampada Dipak Bangar, Avi Kumar Bansal, et al	Plos One	2023	2.9
76	Mortality estimates of central nervous system TB in India.	LR Inbaraj, K Rade, S Selvaraju, R Rao	The international journal of tuberculosis and lung disease	2023	4
77	TB-LAMP (loop-mediated isothermal amplification) for diagnosing pulmonary tuberculosis in children.	Inbaraj LR, Daniel J, Sathya Narayanan MK, Srinivasalu VA, Bhaskar A, Rajendran P, Daniel BD, Epsibha T, Scandrett K, Rose W, Takwoingi Y.	Cochrane Database of Systematic Reviews	2023	8.4

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
78	Operational Challenges in Conducting a Subnational TB Prevalence Survey in India: Lessons Learned for Resource- Limited, High-Burden Settings.	Prathiksha Giridharan, Murugesan H, Sriram Selvaraju,	Global health, science and practice	2024	4
79	Chest x-ray interpretation: agreement between specialist in tertiary care and medical officers from primary health centres in the state tb survey in Tamil nadu	Giridharan P, Selvaraju S, Thiruvengadam K,	Tamil Nadu Journal of Public Health and Medical Research	2024	-
80	Population attributable fraction for under nutrition in TB, in the selected districts of Tamil nadu; the state TB survey.	Giridharan P, Ariarathinam N, Selvaraju S, Thiruvengadam K,	Tamil Nadu Journal of Public Health and Medical Research	2024	-
81	Long-term follow-up of persons diagnosed with multidrug-resistant TB in Chennai, India, 2013–2020	D. Surie, M. K. Sathyanarayanan, J. Lavanya, J. P. Smith,1 S. K. Shanmugam, S. Tamilzhalagan, A. Selvaraj, G. Ramesh, S. Tripathy, S. D. Khaparde, C. S. Ho, P. J. Hall-Eidson, U. D. K. Ranganathan, S. Selvaraju, and P. K. Moonan	The international journal of tuberculosis and lung disease	2024	4

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Department of Health Economics				
82	Muniyandi M, Ramesh PM, Wells WA, Alavadi U, Sahu S, Padmapriyadarsini C. The Cost-Effectiveness of the BEAT-TB Regimen for Pre-Extensively Drug-Resistant TB. Trop Med Infect Dis. 2023 Aug 11;8(8):411. doi: 10.3390/tropicalmed8080411. PMID: 37624349; PMCID: PMC10459879.	Muniyandi M, Padmapriyadarsini C.	Tropical Medicine and Infectious Disease	2023	3.711
83	Brar S, Kaur G, Muniyandi M, Karikalan N, Bano H, Bhansali A, Jain S, Kumari S, Prinja S. Cost of screening, out-of-pocket expenditure & quality of life for diabetes & hypertension in India. Indian J Med Res. 2023 Jun;157(6):498-508. doi: 10.4103/ijmr.IJMR_389_20. PMID: 37530305; PMCID: PMC10466497.	Malaisamy Muniyandi, Nagarajan Karikalan	Indian Journal of Medical Research	2023	4.2
84	Singh M, Bhatia R, Devaraju M, Ghuman MS, Muniyandi M, Chauhan A, Kaur K, Rana M, Pradhan P, Saini S. Cost-	Malaisamy Muniyandi.	Journal of Paediatric Pulmonology	2023	4.09

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	effectiveness of TrueNat as compared to GeneXpert as a diagnostic tool for diagnosis of pediatric tuberculosis/MDR tuberculosis under the National Tuberculosis Elimination Program of India. J Pediatr Pulmonol. 2023;2(1):12-18.				
85	Muniyandi M. Families affected by catastrophic costs due to tuberculosis. Lancet Glob Health. 2023 Oct;11(10):e1492-e1493. doi: 10.1016/S2214-109X(23)00422-9. PMID: 37734785.	Malaisamy Muniyandi.	Lancet Global Health	2023	19.9
86	Vasantha M, Ponnuraja C, Muniyandi M, Bhaskar A, Tamizhselvan M, Vijayalakshmi MM, Venkatesan P. Bayesian Structural Equation Modeling to Identify Factors Influencing Tuberculosis Treatment Adherence. Int J Pulm Respir Sci. 2023;6(4):555691. doi: 10.19080/IJOPRS.2023.06.555691.	Vasantha M, Ponnuraja C, Muniyandi M, Bhaskar A, Tamizhselvan M, Vijayalakshmi MM, Venkatesan P	International Journal of Pulmonary & Respiratory Sciences	2023	1.794

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
87	Giridharan P, Rebecca P, Devaleenal B, Chelladurai E, Chinnaiyan P, Malaisamy M. Time Elapsed from onset of symptoms to antituberculosis treatment in children with central nervous system tuberculosis in a tertiary hospital in South India: A mixed-methods pilot study. Indian J Public Health. 2023 Apr-Jun;67(2):301-304. doi: 10.4103/ijph.ijph_899_22. PMID: 37459028.	Prathiksha Giridharan, Priscilla Rebecca, Bella Devaleenal, Ponnuraja Chinnaiyan, Muniyandi Malaisamy.	Indian Journal Public Health	2023	0.9
88	Thiruvengadam K, Krishnan R, Muniyandi M. The Prevalence of Self-Reported Tuberculosis in the Andaman and Nicobar Islands, India: Evidence from the NFHS-IV and V. Trop Med Infect Dis. 2023 Oct 3;8(10):464. doi: 10.3390/tropicalmed8100464. PMID: 37888592; PMCID: PMC10611087.	Kannan Thiruvengadam, Rajendran Krishnan and Malaisamy Muniyandi.	Tropical Medicine and Infectious Disease	2023	2.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
89	Rosu L, Madan J, Bronson G, Nidoi J, Tefera MG, Malaisamy M, Squire BS, Worrall E. Cost of digital technologies and family-observed DOT for a shorter MDR-TB regimen: a modelling study in Ethiopia, India and Uganda. BMC Health Serv Res. 2023 Nov 18;23(1):1275. doi: 10.1186/s12913-023-10295-z. PMID: 37980524; PMCID: PMC10657602.	Malaisamy Muniyandi.	BMC Health Services Research	2023	2.7
90	Dolla C, Dhanaraj B, Padmapriyadarsini C, Muniyandi M, Kannan T, Menon PA, Krishnan R, Kumaravel P, Devika K, Tripathy SP. Prevalence of tuberculosis infection and disease among homeless persons staying in NGO shelters in Chennai. J Health Manag. 2023;25(4):870-873.	Dolla C, Dhanaraj B, Padmapriyadarsini C, Muniyandi M, Kannan T, Menon PA, Krishnan R, Kumaravel P, Vijayalakshmi R, Devika K, Tripathy SP.	Journal of Health Management	2023	1.0
91	Muniyandi M, Nagarajan K, Mathiyazhagan K, Giridharan P, Thiruvengadam K, Krishnan R. The	Muniyandi M, Nagarajan K, Mathiyazhagan K, Giridharan P, Thiruvengadam K, Krishnan R.	Tropical Medicine and Infectious Disease	2024	2.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Predicted Potential Impact of COVID-19 Pandemic on Tuberculosis Epidemic in Tamil Nadu, South India. Trop Med Infect Dis. 2024 Jan 4;9(1):12. doi: 10.3390/tropicalmed9010012. PMID: 38251209; PMCID: PMC10821053.				
92	Vasantha M, Santhanakrishnan R, Ponnuraja C, Bhaskar A, Muniyandi M, Venkatesan M, Perumal V. Latent factors affecting smoking cessation among TB and HIV patients: Bayesian structural equation modeling approach. Int J Pulm Respir Sci. 2024;7(1):555703. doi: 10.19080/IJOPRS.2024.07.555703.	Vasantha M, Santhanakrishnan R, Ponnuraja C, Bhaskar A, Muniyandi M, Venkatesan M, Perumal V.	International Journal of Pulmonary & Respiratory Sciences	2024	1.794
93	Nagarajan K, Kumarswamy K, Begum R, Panibatla V, Singarajipura A, Adepu R, Munjattu JF, Sellapan S, Arangba S, Goswami A, Swamickan R, Basha J, Dsouza PM, Muniyandi M. Self-driven solutions and resilience adapted by	Karikalan Nagarajan, Senthil Sellapan, Stephen Arangba, Javeed Basha, Pearl Maria Dsouza, and Malaisamy Muniyandi.	Lancet Regional Health Southeast Asia.	2024	5·0

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	people with drug-resistant tuberculosis and their caregivers in Bengaluru and Hyderabad, India: a qualitative study. Lancet Reg Health Southeast Asia. 2024 Feb 21;22:100372. doi: 10.1016/j.lansea.2024.100372. PMID: 38420270; PMCID: PMC10900834.				
94	GBD 2021 Demographics Collaborators. Global age-sex-specific mortality, life expectancy, and population estimates in 204 countries and territories and 811 subnational locations, 1950-2021, and the impact of the COVID-19 pandemic: a comprehensive demographic analysis for the Global Burden of Disease Study 2021. Lancet. 2024 May 18;403(10440):1989-2056. doi: 10.1016/S0140-6736(24)00476-8. Epub 2024 Mar 11. PMID: 38484753; PMCID: PMC11126395.	Malaisamy Muniyandi.	The Lancet	2024	98·4

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Department of Immunology				
95	Downregulation of monocyte miRNAs: implications for immune dysfunction and disease severity in drug-resistant tuberculosis.	Sampath P, Moorthy M, Menon A, Lekshmi Madhav, Aishwarya Janaki, Madhavan Dhanapal, et al.	Frontiers in immunology.	2023 Jun	7.3
96	Plasma chemokines CXCL10 and CXCL9 as potential diagnostic markers of drug-sensitive and drug-resistant tuberculosis.	Sampath P, Anuradha Rajamanickam, Kannan Thiruvengadam, Alangudi Palaniappan Natarajan, Syed Hissar, Madhavan Dhanapal, et al.	Scientific Reports.	2023 May	4.6
97	Plasma Vitamin D levels in correlation with circulatory proteins could be a potential biomarker tool for pulmonary tuberculosis and treatment monitoring.	Kadar Moideen, Pavan Kumar Nathella, Seshacharyulu Madabushi, Rachel Mariam Renji, Srinivasan P, Shaik Fayaz Ahamed, et al.	Cytokine.	2023 Aug	3.466
98	Genomic Characterization of IS6110 Insertions in Mycobacterium orygis.	Ahmed Kabir Refaya, Umashankar Vetrivel, Kannan Palaniyandi.	Evolutionary bioinformatics online.	2024 Jan	2.6
99	Low body mass index is associated with diminished plasma cytokines and chemokines in both active and latent tuberculosis.	Nathella Pavan Kumar, Nancy A, Kadar Moideen, Menon PA, Banurekha VV, Nair D, et al.	Frontiers in Nutrition.	2023 May	5

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
100	Multisystem inflammatory syndrome in children characterized by enhanced antigen-specific T-cell expression of cytokines and its reversal following recovery.	Nathella Pavan Kumar, Abbas KM, Renji RM, Venkataraman A, Nancy A, Poovazhagi Varadarjan, et al.	Frontiers in pediatrics.	2023 Dec	2.6
101	Sex-specific differences in systemic immune responses in MIS-C children.	Anuradha Rajamanickam, Nathella Pavan Kumar, Venkataraman A, Poovazhagi Varadarjan, Elilarasi Selladurai, Thangavelu Sankaralingam, et al.	Scientific Reports.	2024 Jan	4.99
102	Elucidating systemic immune responses to acute and convalescent SARS-CoV-2 infection in children and elderly individuals.	Anuradha Rajamanickam, Pavan Kumar Nathella, Venkataraman A, Chandrasekaran P, Sasidaran Rajendraprasath, Devaleenal BD, et al.	Immunity, inflammation and disease.	2024 Feb	2.493
103	Immune Profiles in Multisystem Inflammatory Syndrome in Children with Cardiovascular Abnormalities.	Kumar NP, Venkataraman A, Nancy A, Selvaraj N, Moideen K, Ahamed SF, et al.	Viruses.	2023 Nov	4.7
104	Whole genome sequencing of bacteriophage NINP13076 isolated against Salmonella enteritidis	Uma Devi Ranganathan,Ramalingam Bethunaickan,Tamilazhagan S,Ashok S	Ecol Genet Genomics	2024 Mar	1.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
105	An Integrated approach for Proteomic and Immunological analysis of Cell wall and Cell membrane proteins of Mycobacterium tuberculosis	Anbarasu Deenadayalan,Madhavan Dhanapal,Magesh Thirumalai,Ramya Arumugam,Varadharajan Sakthivel, Ramalingam Bethunaickan,Uma Devi Ranganathan	Med Res Arch	2023 Dec	-
106	BCG vaccination induces enhanced humoral responses in elderly individuals.	Kumar NP, Padmapriyadarsini C, Rajamanickam A, Bhavani PK, Nancy A, Jeyadeepa B, et al	Tuberculosis	2023 Mar	3.2
107	The need for One Health approach and the way forward	Ramanujam H, Palaniyandi K	One Health	2023 Jun	5
108	Long-term follow-up of persons diagnosed with multidrug-resistant TB in Chennai	U. D. K. Ranganathan	Int J Tuberc Lung Dis	2024 Feb	4
	Department of Statistics				
109	Manikandan P, Durga U, Ponnuraja C. An integrative machine learning framework for classifying SEER breast cancer. Sci Rep. 2023 Apr 1;13(1):5362. doi: 10.1038/s41598-023-32029-1. PMID: 37005484; PMCID: PMC10067827.	Ponnuraja C	Scientific Reports	2023	3.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
110	Sachdeva KS, Bhatnagar AK, Bhaskar A, Singla N, Sridhar R, Ramraj B, Athawale A, Solanki R, Baruah SR, Patel Y, Ramachandran R, Padmapriyadarsini C. QTc prolongation with bedaquiline treatment for drug-resistant pulmonary TB in a programmatic setting. Int J Tuberc Lung Dis. 2023 Apr 1;27(4):329-331. doi: 10.5588/ijtld.22.0406. PMID: 37035973.	Adhin Bhaskar & Padmapriyadarsini C	The International Journal of Tuberculosis and Lung Disease	2023	2.8
111	Padmapriyadarsini C, Solanki R, Jeyakumar SM, Bhatnagar A, Muthuvijaylaksmi M, Jeyadeepa B, Reddy D, Shah P, Sridhar R, Vohra V, Bhui NK. Linezolid Pharmacokinetics and Its Association with Adverse Drug Reactions in Patients with Drug-Resistant Pulmonary Tuberculosis. Antibiotics (Basel). 2023 Apr 6;12(4):714. doi: 10.3390/antibiotics12040714. PMID: 37107075; PMCID: PMC10135341.	Padmapriyadarsini C, Jeyakumar SM, Muthuvijaylaksmi M & Jeyadeepa B	Antibiotics	2023	5.22

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
112	Adalarasan N, Raji R, Kanimozhi P,Sivashankari V,Vishnupriyan S,Padmanaban S,Ponnuraja Chinnaiyan. Prevalence of cow milk ingestion and ingestion of formula feeds up to 6 months of age inpatients of a tertiary care center. International Journal of Life Sciences Biotechnology and Pharma Research. 2023 Mar 15;12:1065–72.	Padmanaban S & Ponnuraja C	International Journal of Life Sciences Biotechnology and Pharma Research	2023	-
113	Jeyakumar SM, Bhui NK, Singla N, Vilvamani S, Mariappan MV, Padmapriyadarsini C, Bhatnagar AK, Solanki R, Sridhar R. Long-Term Intake of Linezolid Elevates Drug Exposure and Reduces Drug Clearance and Elimination in Adults With Drug-Resistant Pulmonary Tuberculosis. Ther Drug Monit. 2023 Dec 1;45(6):754-759. doi: 10.1097/FTD.0000000000001111. Epub 2023 Jun 5. PMID: 37296501.	Padmapriyadarsini C, Jeyakumar SM & Muthuvijaylaksmi M	Therapeutic Drug Monitoring	2023	2.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
114	Vasantha Mahalingam ,Ponnuraja Chinnaiyan , Muniyandi Malaisamy, Bhaskar Adhin,Tamizhselvan Manoharan , Muthu Vijayalakshmi Mariappan, and Venkatesan Perumal. Bayesian Structural Equation Modeling to Identify Factors Influencing Tuberculosis Treatment Adherence. International Journal of Pulmonary & Respiratory Sciences. 2023 Apr 22;	Vasantha Mahalingam, Ponnuraja Chinnaiyan, Muniyandi Malaisamy, Bhaskar Adhin, Tamizhselvan Manoharan , Muthu Vijayalakshmi Mariappan,	International Journal of Pulmonary & Respiratory Sciences	2023	-
115	Moideen K, Nathella PK, Madabushi S, Renji RM, Srinivasan P, Ahamed SF, Rajkumar H, Bethunaickan R, Babu S. Plasma Vitamin D levels in correlation with circulatory proteins could be a potential biomarker tool for pulmonary tuberculosis and treatment monitoring. Cytokine. 2023 Aug;168:156238. doi: 10.1016/j.cyto.2023.156238. Epub 2023 Jun 3. PMID: 37276815.	Pavan Kumar Nathella, Padmanaban Srinivasan, Shaik Fayaz Ahamed, Ramalingam Bethunaickan	Cytokine	2023	3.7

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
116	Adalarasan N, Thilakavathi K, Ashwin R,SudhaAdalarasan,Padmanaban S,Ponnuraja Chinnaiyan. A study on clinico-biochemical profile and cardiac abnormalities in perinatal asphyxia in tertiary special newborn care unit. International Journal of Life Sciences, Biotechnology and Pharma Research. 2023 Apr 18;12:2595–601.	Padmanaban S & Ponnuraja Chinnaiyan	International Journal of Life Sciences, Biotechnology and Pharma Research	2023	-
117	Chandrasekaran K, Mahalaxmi R, Paulkumaran P,Palaniyandi P, Ponnuraja C. Identification Of Different Forms Of Tuberculosis Spatial Clusters In Tamil Nadu Using Discrete Poisson Model And Log-Likelihood Ratio Test. International journal of creative research thoughts. 2023 May 5;11:580–94.	Chandrasekaran K, Mahalaxmi R, Paulkumaran P,Palaniyandi P, Ponnuraja C	International journal of creative research thoughts	2023	-
118	Inbaraj LR, Daniel J, Sathya Narayanan MK, Srinivasalu VA, Bhaskar A, Rajendran P, Daniel BD, Epsibha T, Scandrett K, Rose W, Takwoingi Y.	Leeberk Inbaraj, Mukesh Sathya Narayanan, Vignesh Srinivasalu , Adhin Bhaskar & Priya Rajendran	Cochrane Database of Systematic Reviews	2023	8.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	TB-LAMP (loop-mediated isothermal amplification) for diagnosing pulmonary tuberculosis in children. Cochrane Database Syst Rev. 2023 Sep 7;2023(9):CD015806. doi: 10.1002/14651858.CD015806. PMCID: PMC10483929.				
119	Kumar AKH, Kadam A, Karunaianantham R, Tamizhselvan M, Padmapriyadarsini C, Mohan A, Jeyadeepa B, Radhakrishnan A, Singh UB, Bapat S, Mane A, Kumar P, Mamulwar M, Bhavani PK, Haribabu H, Rath N, Guleria R, Khan AM, Menon J; METRIF Team. Effect of Metformin on Plasma Exposure of Rifampicin, Isoniazid, and Pyrazinamide in Patients on Treatment for Pulmonary Tuberculosis. Ther Drug Monit. 2024 Jun 1;46(3):370-375. doi: 10.1097/FTD.0000000000001149. Epub 2023 Nov 28. PMID: 38019456; PMCID: PMC11078288.	Agibothu Kupparam Hemanth Kumar, Ramesh Karunaianantham , Manoharan Tamizhselvan, Chandrasekaran Padmapriyadarsin, B Jeyadeepa, Ammayappan Radhakrishnan, Perumal Kannabiran Bhavani & Hemalatha Haribabu	Therapeutic Drug Monitoring	2024	2.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
120	Nithyakalyani Mohan, Anusha Sunder, Kandappa Himakar Reddy,Ponnuraja C. Human Pancreatic Islet Gene View in glucose homeostasis of Diabetic and Non-Diabetic Pancreases in the Indian population. Acta Scientific MEDICAL SCIENCES. 2023 Dec 29;114–21.	Ponnuraja Chinnaiyan	Acta Scientific Medical Sciences	2023	
121	Suganthi P , Divya M,Prabha A,Padmanaban S. Neurological disorders during Pregnancy and puerperium: A focus on obstetric outcome. International Journal of Life Sciences, Biotechnology and Pharma Research. 2023 Sep 25;12:1945–50.	Padmanaban S	International Journal of Life Sciences, Biotechnology and Pharma Research	2023	
122	Perumal Kannabiran B, Palaniappan NA, Manoharan T, Paramasivam PK, Saini JK, Ansari MS, Jayabal L, Aggarwal AN, Garg R, Subramanyam B, Thakur D, Pantula S, P M R, Gs V, Natarajan S, Ammayappan RK, Manpreet B, Ganesan M, Angamuthu D, Chinnaiyan P, Singh M,	Bhavani Perumal Kannabiran, , Natarajan Alangudi Palaniappan, Tamizhselvan Manoharan, Paul Kumaran Paramasivam, Balaji Subramanyam, Saravanan Natarajan, Radha Krishnan Ammayappan, Mangalambal Ganesan, Dhanalakshmi	Open Forum Infectious	2024	4.42

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
	Chandrasekaran P, Swaminathan S. Safety and Efficacy of 25 mg/kg and 35 mg/kg vs 10 mg/kg Rifampicin in Pulmonary TB: A Phase IIb Randomized Controlled Trial. Open Forum Infect Dis. 2024 Feb 2;11(3):ofae034. doi: 10.1093/ofid/ofae034. PMID: 38444824; PMCID: PMC10914527.	Angamuthu, Ponnuraja Chinnaiyan, Padmapriyadarsini Chandrasekaran			
123	Bhatnagar AK, Hemanthkumar AK, Muthu Vijayalakshmi M, Vohra V, Padmapriyadarsini C, Ramesh PM, Taneja G, Chavan VN, Jeyadeepa B, Bhui NK, Solanki R. Effect of Bedaquiline and Delamanid Pharmacokinetics on Sputum Culture Conversion and Adverse Events in Drug-Resistant Tuberculosis. Ther Drug Monit. 2024 Jun 1;46(3):363-369. doi: 10.1097/FTD.0000000000001164. Epub 2024 Jan 1. PMID: 38161267; PMCID: PMC11078291.	Agibothu Kupparam Hemanthkumar , Mariappan Muthu Vijayalakshmi , Chandrasekaran Padmapriyadarsini , Bharathi Jeyadeepa ,	Therapeutic Drug Monitoring	2024	2.8

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
124	Vasantha Mahalingam, Ramesh Santhanakrishnan, Ponnuraja Chinnaiyan, Adhin Bhaskar, Muniyandi Malaisamy, Mythily Venkatesan,Venkatesan Perumal. Latent Factors Affecting Smoking Cessation Among TB and HIV Patients: Bayesian Structural Equation Modeling Approach. International journal of pulmonary and respiratory science. 2024 Feb 15;7:1–10.	Vasantha Mahalingam, Ramesh Santhanakrishnan, Ponnuraja Chinnaiyan, Adhin Bhaskar, Muniyandi Malaisamy & Mythily Venkatesan	International journal of pulmonary and respiratory science	2024	
	Department of Virology and Biotechnology				
125	Experimental models for HIV latency and molecular tools for reservoir quantification-an update.	Angamuthu D, Vivekanandan S, Hanna LE.	Clin Microbiol Rev.	2023	36.8
126	Immune Cell Cross Talk in the Establishment of Human Immunodeficiency Virus-1 Latency.	Rachel G, Hemanathan Vembuli, Kumar G, Luke Elizabeth Hanna.	AIDS research and human retroviruses.	2023	1.5
127	The expression of HIV-1 tat in *Lactococcus lactis*.	Deepak Selvam, Anish D'silva, Arun Panchapakesan, Gohil Y, Singh J, Luke Elizabeth Hanna, et al.	Protein expression and purification.	2024	1.6

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
128	Prevalence and factors associated with tuberculosis infection in India.	Selvaraju S, Velayutham B, Rao R, Rade K, Thiruvengadam K, Asthana S, Balachandar R, Bangar SD, Bansal AK, Bhat J, Chopra V, Das D, Dutta S, Devi KR, Dwivedi GR, Kalliath A, Laxmaiah A, Madhukar M, Mahapatra A, Mohanty SS, Rangaraju C, Turuk J, Menon PA, Krishnan R, Singh M, Sekar K, Robinson A, Turuk A, Krishnan NN, Srinivasan N, Rexy C, Suresh M, Hanna LE, Choudhury AH, Parmar M, Ramachandran R, Kumar N, Joshi RP, Narasimhaiah S, Chandrasekaran P, Khan AM, Panda S, Bhargava B; National TB Prevalence Survey Group.	J Infect Public Health.	2023	4.7
129	QuantiFERON Supernatant-Based Host Biomarkers Predicting Progression to Active Tuberculosis Disease Among Household Contacts of Tuberculosis Patients.	Daniel EA, Thiruvengadam K, Rajamanickam A, Chandrasekaran P, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M, Kulkarni V, Karyakarte R, Shivakumar SVBY, Mave V, Gupta A, Babu S, Hanna LE.	Clin Infect Dis.	2023	8.2

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
130	Antibacterial and Anti-HIV Metabolites from Marine Streptomyces albus MAB56 Isolated from Andaman and Nicobar Islands, India.	Manikkam R, Murthy S, Palaniappan S, Kaari M, Sahu AK, Said M, Ganesan V, Kannan S, Ramasamy B, Thirugnanasambandan S, Dastager SG, Hanna LE, Kumar V.	Appl Biochem Biotechnol.	2023	2.9
131	Plasma chemokines CXCL10 and CXCL9 as potential diagnostic markers of drug-sensitive and drug-resistant tuberculosis.	Sampath P, Rajamanickam A, Thiruvengadam K, Natarajan AP, Hissar S, Ranganathan UD, Babu S, Bethunaickan R.	Sci Rep.	2023	4.997
132	Comparison of Real-time RT-PCR cycle threshold (Ct) values with clinical features and severity of COVID-19 disease among hospitalized patients in the first and second waves of COVID-19 pandemic in Chennai, India.	Natarajan S, Ranganathan M, Natarajan PL, Nesakumar M, Anbalagan S, Lucia Precilla K, Hemalatha H, Kannan M, Narendran G, Mahalakshmi S, Karmegam G, Prakash L, Narayanasamy K, Hanna LE.	J Clin Virol Plus.	2023	1.7
133	Down regulation of Monocyte miRNAs: Implications for Immune Dysfunction and Disease Severity in Drug-Resistant Tuberculosis	Pavithra Sampath, Manju Moorthy Moorthy, Athul Menon, Lekshmi Madhav, Aishwarya Janaki, Madhavan Dhanapal, Alangudi Natarajan Palaniappan, Syed Hissar, Uma Devi Ranganathan, Gopalakrishna Ramaswamy, Ramalingam Bethunaickan,	Front. Immunol.	2023	8.786

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
134	Safety and Efficacy of 25 mg/kg and 35 mg/kg vs 10 mg/kg Rifampicin in Pulmonary TB: A Phase IIb Randomized Controlled Trial.	Perumal Kannabiran B, Palaniappan NA, Natarajan S, Chinnaiyan P, Chandrasekaran P.	Open Forum Infect Dis.	2024	3.8
135	Evaluation of platelet indices as markers of tuberculosis among children in India.	J Nancy Hilda, Aishwarya Venkataraman, Brindha B, Hanna LE	ERJ Open Res.	2024	4.2
136	Potential Hematological Biosignatures as Screening Tools for Tuberculosis Co-Infection among People Living with HIV	Nancy Hilda J , Narendran Gopalan, Banu Rekha VV, Luke Elizabeth Hanna, Ponnuraja C Tamizhselvan M, Dina Nair, Ramesh Kumar S, Poorana Ganga Devi, Narayaniah Cheedarla, Hemalatha Babu, Kannan Muthuramalingam, Mangalambal G, Manimegalai R and Kavidha Chokusamy	J Infect Dis Ther	2024	2.47
137	Genomic Characterization of IS6110 Insertions in Mycobacterium orygis.	Ahmed Kabir Refaya, Umashankar Vetrivel, Kannan Palaniyandi.	Evolutionary Bioinformatics Online	2024	2.6

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
138	Next-Gen Dual Transcriptomics for Adult Extrapulmonary Tuberculosis Biomarkers and Host–Pathogen Interplay in Human Cells: A Strategic Review.	Manohar Nesakumar, Elizabeth Hanna Luke, Umashankar Vetrivel.	Indian Journal of Microbiology	2023	3.0
139	Multilayer precision-based Screening of Potential Inhibitors Targeting Mycobacterium Tuberculosis Acetate Kinase Using in Silico Approaches.	Sneha Subramaniyan, Nagarajan H, Umashankar Vetrivel, Jeyakanthan Jeyaraman.	Computational Biology and Chemistry	2023	3.1
140	RNA-Seq of untreated wastewater to assess COVID-19 and emerging and endemic viruses for public health surveillance.	Stockdale SR, Blanchard AM, Nayak A, Husain A, Nashine R, Dudani H, McClure CP, Tarr AW, Nag A, Meena E, Sinha V, Shrivastava SK, Hill C, Singer AC, Gomes RL, Acheampong E, Chidambaram SB, Bhatnagar T, Vetrivel Umashankar, et al.	The Lancet Regional Health	2023	5.0
141	Structural insights into modelling of hepatitis B virus reverse transcriptase and identification of its inhibitors from potential medicinal plants of Western Ghats: an *in silico* and in vitro study.	Patil VS, Harish DR, Rajitha Charla, Umashankar Vetrivel, Jalalpure SS, Vishwambhar Vishnu Bhandare, et al.	Journal of Biomolecular Structure and Dynamics.	2023	4.4

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
142	Unveiling the therapeutic potential of a mutated paraoxonase 2 in diabetic retinopathy: Defying glycation, mitigating oxidative stress, ER stress and inflammation.	Ravi R, Nagarajan H, Shalini Muralikumar, Umashankar Vetrivel, Bharathidevi Subramaniam Rajesh.	International Journal of Biological Macromolecules	2024	8.2
143	Biochemical and biophysical characterization of biosynthetic arginine decarboxylase from Thermus thermophilus.	Veerapandiyan Malaisamy, Karthika Alagesan, Nagarajan H, Jayaraman M, Umashankar Vetrivel, Jeyakanthan Jeyaraman.	Journal of Biomolecular Structure & Dynamics	2024	4.4
144	Harnessing allosteric inhibition: prioritizing LIMK2 inhibitors for targeted cancer therapy through pharmacophore-based virtual screening and essential molecular dynamics.	Rangaswamy R, Nagarajan Hemavathy, Sneha Subramaniyan, Umashankar Vetrivel, Jeyaraman Jeyakanthan.	Journal of Biomolecular Structure & Dynamics	2023	4.4
145	pH-Dependent conformational stability of SpeB from Thermus thermophilus HB8: insights from molecular dynamics simulation.	Malaisamy Veerapandian, Nagarajan Hemavathy, Alagesan Karthika, Jayaraman Manikandan, Umashankar Vetrivel, Jeyaraman Jeyakanthan.	Molecular Simulation	2023	2.1

Sno.	Title	Authors from ICMR-NIRT	Journal name	Year of publication	Impact factor
146	Structural and functional characterization of 6-phosphogluconate dehydrogenase in Plasmodium falciparum (3D7) and identification of its potent inhibitors.	Alagesan Karthika, Nagarajan Hemavathy, Mathimaran Amala, Sundaraj Rajamanikandan, Malaisamy Veerapandian, Prabhu D, Vetrivel Umashankar.	Journal of Biomolecular Structure and Dynamics	2023	4.4
147	Molecular characterization and re-interpretation of HNF1A variants identified in Indian MODY subjects towards precision medicine.	Babu Kavitha, Ranganathan S, Sundaramoorthy Gopi, Umashankar Vetrivel, Nagarajan Hemavathy, Mohan V, et al.	Frontiers in Endocrino-logy	2023	5.2

WORKSHOPS / SYMPOSIUMS / OTHER EVENTS

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
1	Capacity Building for TB Research under Programmatic Setting" jointly organized by the Indian Council of Medical Research in collaboration with The Union	Workshop	International	NTEP program staff, Researchers	60
2	South-South International collaboration on Research and innovation in TB jointly organized ICMR-NIRT and WHO SEARO	Workshop	International	Members from SEAR countries	45
3	Advanced TB diagnostics A capacity building workshop for countries in the South-East Asian Region" jointly organized by the Indian Council of Medical Research and Mc Gill university	Workshop	International	Researchers, Members from SEAR countries	60
4	Systematic reviews of diagnostic accuracy studies: Introduction to meta-analysis	Workshop	International	Students, Researchers	30

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
5	Systematic reviews of diagnostic Test accuracy" and covered various topics in DTA reviews Organized by India Cochrane affiliate center (ICMR) & Cochrane India network with technical support from ICMR-NIRT	Workshop	National	Students, Researchers	150
6	Advanced TB diagnostics: A capacity building workshop for countries in the South-East Asian Region. Period: 29 January to 2February 2024	Workshop	International	Researchers	50
7	Workshop on "Capacity Building on Sub National Verification of Progress towards TB Free Status" for SEAR Countries (SEAR RRP TB Workshop) funded by PM-ABIM Scheme from 4-8 December 2023.	Workshop	International	Researchers, Members from SEAR countries	51

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
8	National Level Seminar on Role of Health Care Service Providers in Indian Economy	Seminar	National	Students, Researchers	130
9	Infectious Disease Modeling	Workshop	National	Statisticians, Students, Researchers	50
10	Seminar on Siddha, an evidence-based medicine	Seminar	National	Students, Researchers	150
11	Seminar on World TB Day and Women Towards Health and Education	Seminar	National	Students	100
12	Induction Program Siddha Graduates	Seminar	National	Students	50
13	Technical Advisory Meeting Patient Experience Survey	Meeting with Tamil Nadu Health System Research Project, TN	National	Researchers	50
14	Sensitization Meeting with Corporate Social Responsibility donor for Nikshay Mitra	Meeting with CSR workers	National	CSR employees	15

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
15	Awareness Session on Tuberculosis Burden and Elimination Goals for India for Software Technology Parks of India (STPI), Taramani IT Park.	Seminar	State	IT employees of Software Technology Parks of India (STPI)	50
16	“Wings of Support” First Year Completion & World TB Day Event GHTM, Tambaram	Meeting	State	TB champions & caregivers, medical staff, ICMR-NIRT staff	40
17	World TB Day event at DTC-Pulianthope, Chennai	Meeting	State	Medical Officers and Health Care Workers of the District TB Centre (DTC)	30
18	Nutritional Counselling for TB patients and caregivers & Nikshay Mitra Orientation	Meeting	State	TB patients & caregivers, ICMR-NIRT, NTEP	40
19	Motivation and Orientation Session for Health Care Providers, NTEP, Chennai	Training	State	Senior Treatment Supervisors (STS) and Senior Tuberculosis Laboratory Supervisors (STLS)	42

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
20	World TB Day event and awareness program at Sterling Software, Taramani	Seminar	State	IT employees of Sterling Software	80
21	Sensitization Meeting with Corporate Social Responsibility donor for Nikshay Mitra	Meeting	State	Corporate delegates	15
22	Technical consultation on WHO prequalification requirements for Lateral Flow Mycobacterial Lipoarabinomannan (LAM) tests for TB (TB-LAM) at Lyon France	Invited for Technical consultation	International	Invited for Technical consultation	14
23	Grant Writing Workshop: Building Effective Specific AIIMS at New Delhi	Workshop at Gupta-Klinsky India Institute October 13th 2023	National	-National delegates	
24	Oral presentation titled Multicentric field validation of the proof of concept for utility of Trueprep extracted DNA for Line Probe Assay testing at Union conference 2023 held at Paris	Union conference at Paris November 15th -18th 2023	International	International delegates	

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
25	Poster presentation on Diagnostics developed by NIRT towards TB elimination at	India International Science Festival 2023, Faridabad 17th to 20th January 2024	National	Researchers, Students, National delegates	
26	Oral presentation tiled "Assessing the utility of different biological samples (urine, stool and respiratory specimens) for pediatric pulmonary tuberculosis detection"	Asia Pacific Region Conference (APRC at Taipei, Taiwan April 26th 29th 2024	International	International delegates	
27	Health System Costing	Workshop	National	Researchers and Doctors	30
28	Infectious Disease Modeling	Workshop	National	Researchers, Doctors and Students	52
29	Role of Health Care Service Providers in Indian Economy	Seminar	State	Students	131
30	Immune Responses to Oral Vaccines in Early Life	Seminar	National	Researchers and Students	65

SNo.	Title	Type (Seminars / Conferences / Meetings / Workshops / Training)	State / National / International	Nature of participants (researchers / students / state officials / National / international delegates	Number of Participants
31	Workshop on Basic statistics and data science using python	Workshop	State	Students	34
32	Workshop on Basic statistics and data science using python	Workshop	State	Students	41
33	Workshop on Basic statistics and data science using python	Workshop	State	Students	66
34	Workshop on polychromatic flow cytometry (Basics)	Workshop	National	Researchers and students	14
35	Workshop on biorisk management and building a sustainable consortium of excellence in Tamil Nadu	Workshop	National	Researchers	20

AWARDS, RECOGNITIONS AND HONOURS

S.No	Name of Award/s	National/International	Name of Recipient
1.	Best research papers (Oral) for “Targeted NGS for rapid drug resistance profiling of newer and repurposed anti-tuberculosis drugs by portable ONT device”	National	Dr. Sivakumar Shanmugam
2.	Member WHO Advisory group on Tuberculosis Diagnostics and Laboratory Strengthening	International	Dr. Sivakumar Shanmugam
3.	Travel award for presenting the study titled “Assessing the utility of different biological samples (urine, stool and respiratory specimens) for pediatric pulmonary tuberculosis detection”	International	Dr. Priya Rajendran
4.	Indian National Science Academy (INSA)Research associate fellow-2023 (Under the category of Health Science)	National	Dr. N. Pavan Kumar
5.	Travel award to attend the International Vaccinology Course at Seoul, South Korea (11-15 September 2023)	International	Dr. Nancy Hilda J
6.	Travel award to attend the ADVANCE Leadership Development Programme (LDP) meeting at Entebbe, Uganda (11-13 October 2023)	International	Dr. Sudhakar N

STAFF LIST

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS, CHENNAI -31

STAFF LIST AS ON 31/03/2024

S.No.	Name	Designation
1	Dr C. Padmapriyadarsini, MBBS, DNB, MS, Ph.D.	DIRECTOR
2	Dr P. Paul Kumaran, MBBS, MPH	SCIENTIST F
3	Dr D. Baskaran, MBBS, PGDTCD	SCIENTIST F
4	Dr Luke Elizabeth Hanna, M.Sc., Ph.D.	SCIENTIST F
5	Dr G. Narendran, MBBS, DTRD, DNB	SCIENTIST F
6	Dr S. Ramesh Kumar, MBBS, MPH	SCIENTIST F
7	Dr C. Ponnuraja, M.Sc., Ph.D.	SCIENTIST F
8	Dr K. R. Uma Devi, M.Sc., Ph.D.	SCIENTIST F
9	Dr S.M. Jeyakumar,M.Sc., M.Phil., Ph.D.	SCIENTIST F
10	Dr V.V. Banu Rekha, MBBS, PGDPH, MPH	SCIENTIST E
11	Dr. B. Ramalingam, M.Sc., Ph.D.	SCIENTIST E
12	Dr. V. Umashankar, M.Sc.,M.Phil.,PGDBI.,Ph.D.	SCIENTIST E
13	Dr P. Kannan, M.V.Sc., Ph.D.	SCIENTIST E
14	Dr Aishwarya Venkataraman, MBBS, DCH(UK), MRCPCH(UK), PG DIP PID(UK)	SCIENTIST E
15	Dr R Balaji, MBBS, MD	SCIENTIST E
16	Dr A Newtonraj, MBBS, MD	SCIENTIST E
17	Dr I Leeberk Raja, MBBS, MD	SCIENTIST E
18	Dr K. Rajendran, M.Sc., Ph.D.	SCIENTIST E
19	Dr P.K. Bhavani, MBBS, PGDPH, MPH	SCIENTIST E
20	Dr N. Saravanan, M.Sc., M.Phil., Ph.D.	SCIENTIST E

S.No.	Name	Designation
21	Dr S. Syed Hissar, MD(Russia), MPH	SCIENTIST E
22	Dr Dina Nair, MBBS, PGDPH, MPH	SCIENTIST E
23	Dr D. Bella Devaleenal, MBBS, PGDOL, MPH	SCIENTIST E
24	Dr S. Sriram, MBBS, MPH	SCIENTIST E
25	Dr M. Muniyandi, M.A., M.Phil., MPS, Ph.D.	SCIENTIST E
26	Mrs. B. Swarna Deepa, ME, MBA	SCIENTIST D
27	Dr N. Poorana Ganga Devi, MBBS, PGDPH	SCIENTIST D
28	Dr M. Makesh Kumar, MBBS,MPH	SCIENTIST D
29	Dr S. Sivakumar, M.Sc., Ph.D.	SCIENTIST D
30	Dr. V. N. Azger Dusthackeer, M.Sc., Ph.D.	SCIENTIST D
31	Dr. S. Devarajulu Reddy, M.B.B.S.	SCIENTIST D
32	Mrs R. Mahalakshmi, M.Sc., M. Phil	SCIENTIST D
33	Mrs. Basilea Watson, M.Sc.	SCIENTIST D
34	Dr R. Priya, M.Sc., Ph.D.	SCIENTIST D
35	Dr. P. L. Natarajan, MBBS, Ph. D	SCIENTIST C
36	Dr N Pavan Kumar, M.Sc., Ph.D.	SCIENTIST C
37	Dr N. Karikalan, B.S.M.S., MPH	SCIENTIST C
38	Dr Nancy Hilda, M. Sc., Ph. D	SCIENTIST C
39	Dr G. Prathiksha, M.B.B.S, MD	SCIENTIST C
40	Dr N. Sudhakar, M.Sc., M.Phil., Ph.D.	SCIENTIST C
41	Dr Adhin Bhaskar, M. Sc., Ph.D.	SCIENTIST C
42	Dr. A. Stephen, M.A., Ph.D.	SCIENTIST C
43	Mr. Rupam Mukhopadhyay	SCIENTIST C
44	Dr S Vignes Anand, MBBS	SCIENTIST B
45	Dr S Mukesh Kumar, M.B.B.S	SCIENTIST B

S.No.	Name	Designation
46	Dr S Souparnika, M.Sc., Ph.D	SCIENTIST B
47	Mr. S. Padmanaban, M.Sc.	SCIENTIST B
48	Dr E. Thiruvalluvan, M. A., Ph. D	Senior Technical Officer (3)
49	Mrs. Chandra Suresh, M. A.	Principal Technical Officer
50	Mr. B. K. Kirubakaran, M.Sc.	Senior Technical Officer (3)
51	Ms. G. Mangalambal, M. Sc.	Senior Technical Officer (2)
52	Mr. P. Murugesan, M. A., PGDC., BDA	Senior Technical Officer
53	Ms. K. Silambu Chelvi, M. Sc, M. Phil	Senior Technical Officer
54	Dr K. Ramakrishnan, M. Sc, Ph. D	Senior Technical Officer (2)
55	Ms. A. Komathi, M. Sc	Senior Technical Officer (2)
56	Ms. A. Gunasundari, M. Sc.	Technical Officer-C
57	Mr. S. Vijayaraj, M.Sc., MLIS, PGDCA	Technical Officer-C
58	Ms. K. Devika, M. Sc.	Technical Officer-C
59	Ms. Lucia Precilla, M. Sc., M. Phil	Technical Officer-C
60	Mr. S. Anbalagan, M. Sc.	Technical Officer-C
61	Dr. M. Vasantha., M. Sc., M. Phil., Ph. D	Technical Officer-C
62	Ms. D. Saraswathi, M. Sc. M. Phil. LT	Technical Officer-C
63	Dr. M. Harishankar	Technical Officer-C
64	Mr. S. Rajakumar, M. Sc.	Technical Officer-C
65	Ms. B. Angayarkanni, M. Sc., M. Phil., LT	Technical Officer-C

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66	Mr. V. Thiyagarajan, M. Sc., M. Phil	Technical Officer-C
67	Mr. K. Ramesh, M. Sc.	Technical Officer-C
68	Mr. A. Radhakrishnan, M.Sc.	Technical Officer-C
69	Mr.C.Saravanan	Technical Officer-C
70	Ms. C. Kavidha, B. Sc.	Senior Technical Officer (1)
71	Ms. K. Sureswari, B.A., MBA	Senior Technical Officer (1)
72	Ms. P. Pandeeswari	Senior Technical Officer (1)
73	Ms. M. Rathinam	Senior Technical Officer (1)
74	Ms. P. Kowsalya	Senior Technical Officer (1)
75	Ms. M. Mohana	Senior Technical Officer (1)
76	Ms. R. Saraladevi, M.A.	Senior Technical Officer (1)
77	Mr. K. Senthil Kumar, M.Sc., M.Phil.	Senior Technical Officer (1)
78	Ms. R. Vetrichselvi, M. A	Senior Technical Officer (1)
79	Mr. S. Senthil	Senior Technical Officer (1)
80	Ms. J. Chitra, M. Sc	Technical Officer-B
81	Dr. B. Senthil Kumar	Technical Officer-B
82	Mr. M. Baskaran, B. Sc.	Technical Officer-B
83	Mr. D. Ravikumar, M. Sc., DMLT	Technical Officer-B

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84	Mr. M. Michel Prem Kumar, M. Sc., DMLT	Technical Officer-B
85	Dr M. Tamizhselvan, M. Sc. Ph.D	Technical Officer-B
86	Ms. D. Kalaivani, M.Sc.	Technical Officer-B
87	Mrs. C. Suganthi, M.Sc., D.M.L.T.	Technical Officer-B
88	Mrs. M. Malathi, M.Sc., C.L.T.	Technical Officer-B
89	Ms. A. Deepalakshmi, M. A.	Technical Officer-B
90	Dr S. Balaji, M.Sc., Ph.D	Technical Officer-B
91	Dr D. Anbarasu, M. Sc., M. Phil., Ph. D	Technical Officer-B
92	Mr. S. Murugesan, M. Sc.	Technical Officer-B
93	Mrs. B. Mahizhaveni, M.Sc., D.M.L.T.	Technical Officer-B
94	Mrs. G. Vadivu, M.Sc., D.M.L.T.	Technical Officer-B
95	Mr. Y. John Arokiya Doss, M.Sc., D.M.L.T.	Technical Officer-B
96	Mr. K. Rajaraman, M.Sc., C.L.T.	Technical Officer-B
97	Mr. A. Vasudevan, M.Sc. (Bio-Chem), M.Sc. (Cl.Micro)	Technical Officer-B
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102	Mr. P. Kumaravel, D.M.L.T., M. Sc.	Technical Officer-B
103	Mr. B. Ananda Kumar, M.Sc., M.B.A.	Technical Officer-B
104	Ms. K. Sumathi, M. Sc	Technical Officer-B
105	Mr. S. Govindarajan, M. Sc	Technical Officer-B
106	Ms. S. Rani	Technical Officer-B
107	Mrs. N. Lakshmi	Technical Officer-B

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108	Ms. R. Manimegalai	Staff Nurse
109	Ms. Shakila Shankar	Staff Nurse
110	Ms. K. Porselvi, B. Sc.	Staff Nurse
111	Ms. A. Selvi, B. Sc.	Staff Nurse
112	Ms. S. Stella Mary	Staff Nurse
113	Ms. A. Stella Mary	Staff Nurse
114	Ms. C. Hema Giranab, M. Sc.	Staff Nurse
115	Ms. A. Seetha, M. Sc.	Staff Nurse
116	Ms. S. Gopika, M. Sc.	Staff Nurse
117	Ms. Mumtas Banu Kottayil, B. Sc.	Staff Nurse
118	Mr. Sravan Kumar Adavath, B. Sc.	Staff Nurse
119	Mr. P. Munivardhan, B.Sc.	Technical Officer-A
120	Mr. D. Nithya Kumar, M.Sc.	Technical Officer-A
121	Mr. V. Ramesh Babu, M.Sc, C. R. A.	Technical Officer-A
122	Mr. A. M. Ramesh, M.A.	Technical Officer-A
123	Mr. P. K. Venkataramana, B.Com.	Technical Officer-A
124	Mr. N. Prem Kumar, B.Sc.	Technical Officer-A
125	Mr. S. Venkatesan, M.A., B.Ed.	Technical Officer-A
126	Mr. S. V. Joseph Raj Kumar	Technical Officer-A
127	Mr. T. Thangaraj, M.A., B.Ed.	Technical Officer-A
128	Mrs. R. Vijayalakshmi, M.Sc.	Technical Officer-A
129	Mr. M. Kannan, B.Sc., LT	Technical Officer-A
130	Mr. A. Devanathan, M.Com., M.S.W.	Technical Officer-A
131	Mrs. V. Rani, M.Sc.	Technical Officer-A
132	Mr. P. Balaji, M.A., B.Ed.	Technical Officer-A
133	Ms. B. Pricilla Rebecca, M.S.W	Technical Officer-A

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134	Ms. A. Dhanalakshmi, M. A.	Technical Officer-A
135	Ms. V. Mythily, M. Sc	Technical Officer-A
136	Dr M. Muthu Vijayalakshmi, M. Sc., M.Phil., B. Ed., Ph. D	Technical Officer-A
137	Mr. P. Palaniyandi, M. Sc., M. Phil	Technical Officer-A
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140	Ms. H. Hemalatha, M. Sc., DMLT	Technical Officer-A
141	Ms. Devi Sangamithrai, M. Sc., MLT	Technical Officer-A
142	Ms. K. Jeyasree, M. Sc. DMLT	Technical Officer-A
143	Mr. A. Madheswaran, M. Sc.	Technical Officer-A
144	Mr. S. Manohar Nesa Kumar, M.Sc., PGDMLT	Technical Officer-A
145	Mr. P. Sathyamurthi, M.Sc.	Technical Officer-A
146	Mr. S. Govindaraj	Technical Officer-A
147	Mr. K. Ramesh Kumar	Technical Officer-A
148	Ms. S. Theensuwai, B. A	Technical Officer
149	Mr. Munishwar	Technical Assistant
150	Mr. Siva Kishore S	Technical Assistant
151	Ms. P. Shobana	Technical Assistant
152	Ms. Roja. J	Technical Assistant
153	Ms. S Yasaswany	Technical Assistant
154	Ms. S. Devayani	Technical Assistant
155	Mr. S. Kathirvel	Technical Assistant
156	Mr M. Dilipkumar	Technical Assistant
157	Mr. S Bharathan	Technical Assistant

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158	Dr. K. Arun	Technical Assistant
159	Ms. G Priyanka	Technical Assistant
160	Mr. Sankuru Chinnaiah	Technical Assistant
161	Mr. Bathula Sai Kiran	Technical Assistant
162	Mr. Nilay Bhaskar	Technical Assistant
163	Mr. K. Karthik Raja	Technical Assistant
164	Ms. Vidhi	Technical Assistant
165	Ms. Preethi. R	Technical Assistant
166	Mr. Yadla Sai Madhu	Technical Assistant
167	Ms. Jagriti Gupta	Technical Assistant
168	Mr. Mangalampalli Manikantha Anikumar	Technical Assistant
169	Mr. Maloth Mohan Kumar	Technical Assistant
170	Mr. Gujjala Tarun Manikya Kiran	Technical Assistant
171	Mr .Kothoju Bhaskara Chary	Technical Assistant
172	Mr. A. Amuthan	Technical Assistant
173	Mr. S. Iyappan	Technical Assistant (E/S)
174	Mrs. V. Shailaja Devi	Senior Technician (3)
175	Mr. G. Vasu	Senior Technician (3)
176	Ms. O. R. Vijayalakshmi, M. Sc.	Senior Technician (2)
177	Ms. A. Vijayalakshmi	Senior Technician (2)
178	Ms. A. Poongkodi, B. Sc.	Senior Technician (2)
179	Ms. S. Vaishnavi, B. Sc	Senior Technician (2)
180	Ms. R. Suganthi	Senior Technician (2)
181	Ms. K. Maheswari, B. Sc	Senior Technician (2)
182	Ms. V. Senthamizhselvi	Senior Technician (2)

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183	Ms. V. Shunmugajyothi, M. Sc.	Senior Technician (2)
184	Mr. A.Ravi	Senior Technician (2)
185	Mr. M. Manogaran	Senior Technician (2)
186	Mr. K. Saravanan	Senior Technician (2)
187	Mr. K. Poongavanam	Senior Technician (2)
188	Mr. A. S. Dayalan	Senior Technician (2)
189	Mr.S.S.Jeganathan	Senior Technician (2)
190	Mr. C. Saravanan	Senior Technician (1)
191	Mr. T. K. Bharath, M.Sc.	Senior Technician (1)
192	Mr. R. David	Senior Technician (1)
193	Mr. K. Thulasingam	Senior Technician (1)
194	Mr. E. A. John Washington	Senior Technician (1)
195	Mr. A. Elangovan	Senior Technician (1)
196	Mr. P. Subbaiah	Senior Technician (1)
197	Mr. B. Suresh Kumar	Senior Technician (1)
198	Mr. K. Jagadeesan	Senior Technician (1)
199	Mr. L. Venkatesan	Senior Technician (1)
200	Mr. P. Sivakumar	Senior Technician (1)
201	Mr. N. Rajan Babu	Senior Technician (1)
202	Mr. V. Babu	Senior Technician (1)
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205	Ms. B. Brindha, M. Sc	Senior Technician (1)
206	Mr. P. Nagarajan, M. Sc., DMLT	Senior Technician (1)
207	Mr. P. Sivaraman, M. Sc., DMLT	Senior Technician (1)
208	Ms. V. Sudha, M. Sc., M. Phil	Senior Technician (1)

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213	Mr. M. Thiyagarajan	Senior Technician (1)
214	Mr. V. S. Senthilkumar	Senior Technician (1)
215	Mr. G. Vasu	Senior Technician (1)
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217	Mr. L. Gunalan	Senior Technician (1)
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219	Ms. R. Selvi	Senior Technician (1)
220	Ms. J. Vanitha	Senior Technician (1)
221	Mr. N. Lokeswaran	Senior Technician (1)
222	Mr. W. Wilkingson Mathew	Senior Technician (1)
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225	Ms. K. Subapriya, B. Sc	Junior Staff Nurse
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228	Mr. P. Vijayakumar	Lab Assistant
229	Mr. A. Annamalai	Lab Assistant
230	Mr. R. Damodharan	Lab Assistant
231	Mr. D. Bose	Lab Assistant
232	Mr. N. Murali	Lab Assistant
233	Mr. M. Jayaraj	Lab Assistant
234	Mr. A. Rajavarman	Lab Assistant

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239	Mr. K. Kuttappan	Lab Assistant
240	Mr. J. Selvam	Lab Assistant
241	Mr. G. Eswaran	Lab Assistant
242	Mr. Keshabraj Paudel	Lab Assistant
243	Ms. H. Ponrose	Lab Assistant
244	Mrs. T. Thilakavathy	Lab Assistant
245	Mr. G. Nithyanandam	Lab Assistant
246	Mr. S. Venkatesan	Lab Assistant
247	Mr. R. Anbulingam	Lab Assistant
248	Mr. M. Mohan Shankar	Lab Assistant
249	Ms. D. Sundari	Lab Assistant
250	Mr. Jayavel Anandan	Lab Assistant
251	Mr. S. Anjaiah	Lab Assistant-1
252	Mr. P. Senthilvelan	Lab Assistant-1
253	Mr. R. Krishna Bahadur	Lab Assistant
254	Mr. R. Purushothaman	Lab Assistant
255	Mr. N. Srinivasan	Lab Assistant
256	Mr. S. Prakasam	Lab Assistant
257	Mr. K. Vasudevan	Lab Assistant
258	Mr. J. Jeeva	Lab Assistant
259	Mr. F. Albert	Lab Assistant
260	Mr. T. D. Ponnusamy	Lab Assistant

S.No.	Name	Designation
261	Mr. E. Duraivel	Lab Assistant
262	Mr. R. Yuvarajan	Lab Assistant
263	Mr. S. Innamuthan	Lab Assistant
264	Mr. S. Karunakaran	Lab Assistant
265	Mr. R. Karunanidhi	Lab Assistant
266	Mr. A. M. Sivakumar	Lab Assistant
267	Mr. R. Narasimhan	Lab Assistant
268	Mr. V. Navalan	Lab Assistant
269	Mr. R. Mohanraj	Lab Assistant
270	Mr. D. Sundramurthy	Lab Assistant-1
271	Mr. P. Kosalaraman	Lab Assistant-1
272	Mr. S. Nagarajan	Lab Assistant-1
273	Mr. E. Poongavanam	Lab Assistant-1
274	Mr. A. Govindaraju	Lab Assistant
275	Mr. B. Venkateswara Rao	Lab Assistant
276	Mr. M. Manikandan	Lab Attendant -2
277	Mrs. R. Sakila	Lab Attendant -2
278	Mr. K. N. Thirumalai	Lab Attendant -2
279	Mr. P. Johnson Kennedy	Technician-A
280	Mr. T. M. Loganathan	Technician-2
281	Mr. M. Kawaskar	Technician-2
282	Mr. Santhana Mahalingam, M. Sc., LT	Technician-2
283	Mr. T. Bharathiraja, B. Sc., LT	Technician-2
284	Mr. S. Mangaiyarkarasi, M. Sc., DMLT	Technician-2
285	Mr. M. Pandidurai, B. Sc. LT	Technician-2
286	Mrs. R. Sathya, B. Sc., LT	Technician-2

S.No.	Name	Designation
287	Mr. Harihara Ganapathi Subramanian	Technician-2
288	Mr. A. Vijayakumar	Technician-2
289	Mr. E. Selvaraj	Technician-2
290	Mr. M. Sathish Kumar	Technician-2
291	Mr. M. S. Mani	Technician-2
292	Mr. M. Sekar	Technician-2
293	Mr. P. Yuvaraj	Technician-2
294	Mr. C. Sivaraman	Technician-2
295	Mr. T. Magesh, B.Sc.	Technician-2
296	Mr. M. Pushparaj	Technician-2
297	Mr. M. Anbalagan	Technician-2
298	Mr. U. Murugan	Technician-2
299	Mr. M. N. Balaji	Technician-2
300	Mr. K. Sridhar	Staff Car Driver Ord. Grade
301	Mr. K. Govindan	Staff Car Driver Ord. Grade
302	Mr. J. Jaya Bharath Veeran	Staff Car Driver Ord. Grade
303	Mr. D. Ganesan	Staff Car Driver
304	Mrs. R. Latha, B.E., M.B.A.	Administrative Officer
305	Mrs. Chithra Sivakumar, B.Sc.	Administrative Officer
306	Mrs. M. J. Nagalakshmi, M.A.	Section Officer
307	Ms. P. Kavitha, MA, MBA	Section Officer
308	Mr. S. N. Babu, B.A., B.L.	Section Officer
309	Mr. R. Senthilnathan, B.C.S.	Section Officer
310	Ms. J. Suguna, B.Com.	Section Officer

S.No.	Name	Designation
311	Ms. T. Sheelaa, BBA	Section Officer
312	Mr. H. Krishna Kumar, B.Com., MBA	Private Secretary
313	Mr. R. Hariharan, B. Com	Assistant
314	Mrs. P. Kowsalya, M.A.	Assistant
315	Mr. A. S. Sivaraj, M.A., D.C.A	Assistant
316	Mrs. A. Uma, B.Com.	Assistant
317	Mr. V. Velmurugan	Assistant
318	Mr. M. Senthil Kumar, B.Sc.	Assistant
319	Mr. T. Vaishakh	Assistant
320	Mr. D. Pukhazendi	Assistant
321	Ms. M. Revathy , M.Com.	Personal Assistant
322	Mr. Mohammed Khaleel Ahamed, B.Com	Personal Assistant
323	Mr. Otturi Venkata Pradeep, B.Com	Personal Assistant
324	Ms. G. H. Jyothipriya, B.E., MBA	Personal Assistant
325	Ms. K. Thiriveni, B. Tech., M. Phil	Personal Assistant
326	Mr. S. Sasi Kumar, BCA	Personal Assistant
327	Mrs. K. Sumathy	Upper Division Clerk
328	Mrs. B. Manjula, M.Com., MCA	Upper Division Clerk
329	Mrs. D. Tamilselvi, BBA, MBA	Upper Division Clerk
330	Mrs. J. Supriya, B.Sc.	Upper Division Clerk
331	Mr. Solomon Priya Kumar, M.A.	Upper Division Clerk
332	Mr. P. Madan Kumar	Upper Division Clerk
333	Ms. S. Sundari, M.Sc.	Upper Division Clerk
334	Ms. R. Cathrin Diviya, B.Sc.	Upper Division Clerk
335	Mr. Durga Mohan Kumar Chenna, B.Com	Upper Division Clerk
336	Ms. K. Sangeetha, B.E.	Upper Division Clerk

S.No.	Name	Designation
337	Mr. S. V. Nantha Kumar, B.Sc.	Upper Division Clerk
338	Mr. D. Rajasekaran	Lower Division Clerk
339	Mr. K. Selvakumar, B.A.	Lower Division Clerk
340	Mr. B. Amavasai	Lab Assistant-1
341	Mrs. J. Rajathi	Lab Assistant-1
342	Mrs. P. Hemalatha	Lab Attendant -2
343	Mr. S. Kathiravan	Lab Attendant -2
344	Mr. J. V. Mohanraj	Lab Attendant -2
345	Mr. M. Raghunathan	Lab Attendant -2
346	Mr. D. Ravichandran	Lab Attendant -2
347	Ms. P. Pandiselvi	MTS
348	Ms. V. Amudhavalli, M. Com, M.Phil.	MTS
349	Mr. J. Dilavar	MTS
350	Mr. M. Bel Bhadur	MTS

LIST OF PHD, POST DOCTORAL AND RESEARCH ASSISTANT AT NIRT

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
1.	B. Priscilla Rebecca	Dr. Prince Annadurai,	University of Madras	PhD	Part time	A study to understand the influence of social capital upon treatment pathways, treatment adherence and, quality of life among persons with TB	NA	Ongoing
2.	Mr. Michel Premkumar	Dr Sivakumar, Bacteriology	University of Madras	PhD	Part-time	Rapid Diagnosis and drug susceptibility testing of Mycobacterium tuberculosis	Intramural	Ongoing
3.	Mrs.K.Silambuchelvi	Dr Sivakumar, Bacteriology	University of Madras	PhD	Part-time	Diagnostic Utility and Implications of Molecular methods for the Drug Resistance Tuberculosis.	Intramural	Ongoing
4.	Mr.C.Manjunath	Dr Sivakumar, Bacteriology	University of Madras	PhD	Full time	Manipulation of Autophage for host directed therapy in *Mycobacterium tuberculosis*	ICMR – JRF	Ongoing
5.	Mrs.B.Angayarkanni	Dr.V.N Azger Dusthackeer, Bacteriology	University of Madras	PhD	Part-time	Novel Anti Mycobacterial agents from Indian Traditional System of Medicine	Intramural	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
6.	Mrs.B.Magizhaveni	Dr.V.N Azger Dusthackeer, Bacteriology	University of Madras	PhD	Part-time	Isolation, stabilization and Encapsulation of Myco-bacterophages for phage therapy	Intramural	Ongoing
7.	Mr.A.Radhakrishnan	Dr.V.N Azger Dusthackeer, Bacteriology	University of Madras	PhD	Part-time	Evaluation of essential oils, volatile chemicals and repurposing of drug for anti TB activity	Intramural	Ongoing
8.	Ms. Silla Varghese	Dr. Priya Rajendran, Bacteriology	Madras University	PhD	Full time	Assessing the utility of different biological samples (urine, stool and respiratory specimens) for pediatric pulmonary tuberculosis detection	DST-INSPIRE	Ongoing
9.	Ms. Radhika Golla	Dr. Priya Rajendran, Bacteriology	Madras University	PhD	Part time	Characterisation of *M. abscessus, M. kansasii, M. avium- intracellulare Complex* - the most common NTM species isolated from presumptive TB patients	Intramural	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
10.	Dr N Usha rani	Dr N Saravanan, Biochemistry	NA	RA	Full time	Completed	ICMR	Completed
11.	Miss Preethi (Reg. No.21PHD0207)	Dr N Saravanan (Co-guide), Biochemistry	Vellore Institute of Technology	PhD	Full time	Inhibition of L-Cysteine biosynthesis using natural anti-tubercular compounds as a novel approach to combat persistent and dormant Mycobacterium tuberculosis	VIT	Ongoing
12.	Dr.Sriram Selvaraju	Natarajan Gopalan. Professor. Head, Department of Epidemiology and Public Health.	Central University of Tamilnadu (CUTN)	PhD	Part Time	Estimation of the Prevalence of Subclinical Tuberculosis and associated factors in India: Analysis from the recent National TB Prevalence Survey in India	Nil	Ongoing
13.	JSV Soundarya	Dr.K.R. Uma Devi, Immunology	University of Madras	PhD	Part time	Attenuated Mycobacterial based vaccine against tuberculosis with a novel strategy for T cell priming	-	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
14.	Venkatesan P	Dr.K.R. Uma Devi, Immunology	University of Madras	PhD	Full Time (Applied for Part Time conversion)	CRISPR Mediated Platform for Diagnosis and Rapid Detection Of Drug Resistance Pattern In Mycobacterium Tuberculosis.	-	Ongoing
15.	Kadar Mohideen	Dr. Ramalingam B, Immunology	University of Madras	PhD	Full Time	Biomarkers and immune responses in pulmonary tuberculosis severity and its treatment monitoring.	ICER	Ongoing
16.	Pavithra Sampath	Dr. Ramalingam B, Immunology	University of Madras	PhD	Full Time	Molecular analysis of monocyte subsets in humans infected with Mycobacterium tuberculosis	DST INSPIRE	Ongoing (Thesis Submitted)
17.	Arul Nancy	Dr. Ramalingam B, Immunology	University of Madras	PhD	Full Time	Characterization of host immune response to unfavourable treatment outcomes in tuberculosis	DBT	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
18.	Harinisri G	Dr. Ramalingam B, Immunology	University of Madras	PhD	Full Time	Evaluation of Inflammatory and Immunological markers among latent TB infection.	CSIR	Ongoing
19.	Dr Ahmed Kabir Refaya	Dr P. Kannan, Immunology	NA	RA	Full time	Insights into the genomic adaptations of Mycobacterium tuberculosis (MTBC) species in cattle	ICMR	Ongoing
20.	Mr.S.Arunkumar	Dr.K.R.Uma Devi, Immunology	University of Madras	PhD	Full-time	Functional study of Drug-resistant Mutation in Mycobacterium tuberculosis	DBT-JRF	Ongoing
21.	Mrs. Ananthi	Dr. P. Kannan, Immunology	University of Madras	PhD	Full time	Study on Mutations Associated with Pyrazinamide Resistance in Mycobacterium tuberculosis	ICMR	Ongoing
22.	Ms. R. Harini	Dr. P. Kannan, Immunology	University of Madras	PhD	Full time	Comparative genomics of Mycobacterium tuberculosis complex isolates from animals	ICMR	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
23.	Palaniyandi P	Dr. C. Ponnuraja, Statistics	Madras university	PhD	Part-Time	GIS for time-to-event survival data	ICMR	Ongoing
24.	N.Selvam	Dr. C. Ponnuraja, Statistics	Madras university	PhD	Part-Time	Frailty Models for time to event survival heterogeneous data	ICMR	Ongoing
25.	Shaik Fayaz Ahamed	Dr. C. Ponnuraja, Statistics	Madras university	PhD	Full Time	Flexible machine learning methods for survival analysis of high dimensional clinical trial health care data	ICMR	Ongoing
26.	Palaniyandi P	Dr. C. Ponnuraja, Statistics	Madras university	PhD	Part-Time	GIS for time-to-event survival data	ICMR	Ongoing
27.	Dr. A. Nusrath Unissa	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	__	RA	Full time	Impact of HIV infection and antiretroviral therapy on premature onset of aging-associated disorders	ICMR	Completed

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
28.	Dr Divyadharshini	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	__	RA	Full time	Role of Interferon Stimulated Genes (ISGs) in the establishment/maintenance of latency in HIV	ICMR	Ongoing
29.	Mr. Deepak Selvam	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Full time	Cloning, Expression, Purification and Characterization of HIV-1 Tat protein in *Lactococcus lactis*	ICMR	Completed
30.	Mr. B. Aanand Sonawane	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Full time	Construction and characterization of infectious molecular clones of HIV-1 transmitted/founder (T/F) viruses	CSIR	Ongoing
31.	Ms. Evangeline Ann Daniel	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Full time	Identification of biomarkers that can predict progression from latent tuberculosis infection to active disease	DST-INSPIRE	Completed

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
32.	Ms. Sandhya V	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Full time	Isolation and characterization of broadly neutralizing antibodies from HIV infected elite neutralizers	DBT	Ongoing
33.	Mrs. K. Lucia Precilla	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Part time	Characterizing the molecular mechanism of protease inhibitor resistance in HIV-1 infected individuals	ICMR	Ongoing
34.	Mr. P. Sathyamurthi	Dr. Luke Elizabeth Hanna, Dept. of Virology & Biotechnology	University of Madras	PhD	Part time	Mechanistic insights into the role of immunosenescense and increased mortality in cured TB patients	ICMR	Ongoing
35.	V Sudha	Hemanth Kumar AK, Biochemistry	Meenakshi Academy of Higher Education and Research (MAHER) Deemed University	PhD	Part-time	Bioavailability of fixed dose combination of first line anti-TB drugs in patients with pulmonary tuberculosis	Intramural	Ongoing

SNo.	Name of the candidate	Name of the guide and department	University affiliation	PhD / Post Doctoral / RA	Part time/Full time	Title of thesis	Source of funding	Ongoing / completed
36.	A Vijayakumar	Hemanth Kumar AK, Biochemistry	Meenakshi Academy of Higher Education and Research (MAHER), Deemed University)	PhD	Part-time	Pharmacokinetics of Linezolid when administered with other second line anti-TB drugs in MDR-TB/Pre-XDR-TB Patients	Intramural	Ongoing

OBITUARY

S. No.	Name	PPO No.	Pensioner/ Family Pensioner	Designation	Date of Death
1	Smt.Uthiramary W/o (L) Shri.Iruthayanathan Ex-Lab Attendant	656	Family Pensioner		22.05.2023
2	Shri.M R.Kamalanaban	1671	Pensioner	Ex- Lab Assistant	05.06.2023
3	Shri.Venkatachala Bhat	1220	Pensioner	Ex-Cook	14.02.2023
4	Smt.E.Suseela W/o (L) Shri.K.P.Ramachandran Ex-Driver	1024	Family Pensioner		03.06.2023
5	Smt.Harikaladevi W/o (L) Shri.Balakrishna Ex- Lab Asst.	2679	Family Pensioner		16.07.2023
6	Smt.Kulanthai Theresa	374	Pensioner	Ex- Attender cum Scout	30.07.2023
7	Smt.K.Ragammal	2971	Pensioner	Ex-Lab Assistant	16.08.2023
8	Smt.Saraswathi Velaiyan w/o (L) Shri.Vellaiyan Ex-Sr. Driver	28	Family Pensioner		09.09.2023
9	Smt.P.N.Kalavathi Chari	1931	Pensioner	Ex- Assistant	20.10.2023
10	Smt.Valasamma	1411	Pensioner	Sr.Technician -II	06.11.2023
11	Smt.Regina W/o (L) Shri.Dr.K.Sadacharam Ex-Scientist E	1810	Family Pensioner		27.12.2023
12	Shri.P.G.Shanmugam	2023	Pensioner	Ex-Technical Assistant	29.12.2023
13	Smt.Victoria Kamalam Jayaraj	1533	Pensioner	Ex-Technical Assistant	07.01.2024

S. No.	Name	PPO No.	Pensioner/ Family Pensioner	Designation	Date of Death
14	Smt.D.Kanniyammal W/o (L) Shri.V.Damodharan Ex- Gestetner Operator	1587	Family Pensioner		07.01.2024
15	Shri.Jagat Bahadur	2447	Pensioner	Ex-Laboratory Assistant	12.02.2024
16	Shri.Patturaj H/o(L) Smt.Vasanthira Patturaj Ex- Sr.Technical Asst.	1479	Family Pensioner		25.02.2024
17	Dr.R.Balambal	2388	Pensioner	Ex-Scientist E	10.03.2024

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