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Viewpoint

Resilience strengthening of tuberculosis diagnostic services under national tuberculosis program to withstand pandemic situations

Sarika Jain[1], Monil Singhai[2], Vineet Chadha[3], N. Somashekar[4]

[1]Laboratory Division, National Tuberculosis Institute, Bangalore, [2]Centre for Zoonotic and Arboviral Diseases, National Centre for Disease Control, New Delhi, [3]Public Health Specialist, [4]Senior TB Specialist, National Tuberculosis Institute, Bangalore, Karnataka, India.

ABSTRACT

In the midst of extraordinary challenges, uncertainty, and the rapidly changing scenario of the prevailing COVID-19 pandemic, existing tuberculosis (TB) laboratories worldwide had to gear up on very short notice to face the dual challenge of fulfilling the increasing demands of laboratory testing for COVID-19 while simultaneously continuing the TB services. The brunt of the same fell on routine TB laboratory services, which include diagnostics (microscopy, rapid molecular testing, culture, and drug-susceptibility testing), and activities of training, quality assurance, and research pertaining to TB worldwide. With the sudden eruption and rapid spread of the global pandemic of COVID-19, TB diagnostic services were affected or disrupted especially where laboratories lacked adequate infrastructure and adequate resources for safe handling of specimens. The human resource challenges such as panic and apprehensions among laboratory workers to deal with newer pathogens, particularly those performing direct smear microscopy, along with staff shortage due to deployment in COVID-19 management duties and the pressure of continuing TB services with enhanced biosafety practices were difficult to handle. We also experienced decline in specimen workload at our national reference laboratory for TB diagnosis by 31% in 2020 as compared to pre-COVID period (2019). This is worrisome as undiagnosed TB as well as improper follow-up of those on TB treatment during the peak of COVID-19 pandemic could be associated with enhanced community transmission of TB and poorer patient outcomes. As the COVID-19 pandemic stretched out untiringly in the country and world over, we rapidly need to adapt and find ways to effectively sustain TB diagnostic services, training and research activities. In this perspective, we document current challenges of TB laboratories and suggest robust ways to address them including biosafety concerns. The safe integration of diagnostic services for TB and where required newer airborne pathogens, to ensure uninterrupted TB services, must be the utmost priority in the face of ongoing and any future unprecedented pandemics.

Keywords: COVID-19, Tuberculosis, Tuberculosis laboratories network, Laboratory biosafety, Tuberculosis diagnostics services

INTRODUCTION

The COVID-19 pandemic with enormous devastation to human lives, health system, and economy was a huge challenge to handle. The case fatality rate of COVID-19 has been reported to range from 0.13% to 6.22% in a cross-country comparison.[1] At the same time, tuberculosis (TB) still remains a global infectious disease killer.

The impact of COVID-19 pandemic on TB case notification was seen as a steep decline by 25–30% in three high TB burden countries – India, Indonesia, and the Philippines.[2]

To meet the immediate enormous demand for ramping up of SARS-CoV-2 diagnostic testing, the World Health Organization suggested countries to leverage on TB laboratories network for utilizing existing specimen transportation mechanisms and molecular diagnostic platforms toward COVID-19 response as well.[3,4] TB laboratories under national programs worldwide had to therefore gear up on a very short notice to face the unforeseen travail of fulfilling the increasing need of COVID-19 testing while ensuring continuation of essential TB services. Further, as both the diseases spread primarily through aerosol transmission,[5,6] the advent of COVID-19 posed a dual challenge of ensuring biosafety in low-risk TB laboratories such as microscopy and nucleic acid amplification test (NAAT) centers while processing direct specimens.

We discuss here the challenges encountered by TB laboratories in India during COVID-19 pandemic and the plausible long-term interventions to effectively deal with future such events while ensuring laboratories biosafety [Table 1].

SEVERELY AFFECTED TB LABORATORY ACTIVITIES DURING LOCKDOWN/PEAK OF COVID-19 WAVES

Sample collection and transportation (SCT)

- There was decline in passive TB case finding of presumptive TB patients and referral for presumptive TB

***Corresponding author:** Sarika Jain, Laboratory Division, National Tuberculosis Institute, Bangalore, India. sarika.jainagrawal@gmail.com

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Table 1: Suggested strategies for long-term sustenance of TB laboratory services during pandemic/disaster situations.

Key areas for improvement	Suggested strategies
Human resource apprehensions and resource mobilization	• Boosting morale of TB program staff and HCW is required firstly, who have executed functions effectively despite difficult field conditions • Health system to ensure continuous supply of appropriate PPE to HCWs (quality and quantum) • Annual preventive health check-up program for TB laboratory workers for TB screening (Symptoms, chest X-ray, and IGRA) • Provision for psychosocial support and counseling for staff to promote mental health • Periodic refresher/updation trainings for TB program and general health staff on standard precautions, proper use of PPE, biosafety measures, disinfection protocol, BMW management, and hand hygiene practices. • Setting up of national level real time occupational health surveillance reporting system to report laboratory or health care acquired infection.
TB laboratories diagnostic capacity (public and private)	• During non-disaster times, review of district for adequacy and functional status of existing TB laboratory infrastructure, test equipment, manpower and patient accessibility for TB diagnosis for ZN/fluorescence microscopy, rapid molecular diagnosis of drug resistance, culture, and DST under the TB program and in private sector • Review of TB testing facilities for coverage of population in hard to reach areas, hilly terrains, and tribal population in the district • Review of functional private sector laboratories in the district for engagement and UDST • Review the adequacy and accessibility of current patient referral facilities in the district and establish a more effective and efficient patient referral system to reduce patient overload and risk of specimen deterioration at the few sample collection centers • Consider upscaling of diagnostic facilities, testing platforms where needed • Establish system in place for arranging sample pick up and transportation to nearby TB laboratory having adequate resources for testing and sharing workload in case of equipment breakdown or laboratory shut down during disaster • Formal agreement with private sector TB labs for referral of samples for TB diagnosis in case of emergency.
SCT mechanisms	• SCT need to be patient centric to avoid patient dropouts • Robust, reliable, and active sample transportation mechanism should be built with a clear and regular schedule for transportation to avoid batching of samples at collection centers • Integrated sample transportation with other disease programs (TB, HIV, dengue, and cancer) – Hub and Spoke Model in districts • Local innovations required in remote and hard to reach areas – (use of Postal services, mobile collection centers, drones, and motorcycle dispatch riders) • Sample transportation time may be included as processing indicator in TB program • Include operational costs for SCT in the district health budget to sustain system.
Laboratory biosafety	• Re-visit biosafety measures in existing and new TB laboratories for compatibility with high-risk activities involving MTB and any newer respiratory pathogens • Risk assessment of all TB laboratories and enhancement of biosafety measures where needed.
Uninterrupted direct smear microscopy services	• Review of microscopy centers for efficient ventilation (Natural/mechanical ventilation) • Proactive approach for devising engineering controls for mechanical ventilation in microscopy centers to allow air to flow past the technician, across the work area and safely exhaust outside the room • Preferred use of biosafety cabinet (class 1) for smear preparation if feasible (due to possible presence of MDR/XDR TB strain or SARS-CoV-2 or unknown respiratory pathogen) • Pre-treatment of sputum with disinfectant (e.g., phenol) during smear preparation to render it non-infectious for laboratory technician • Strict emphasis on implementation of airborne infection control practices in microscopy centers as these have potential of becoming source of COVID/other infections for presumptive TB patients, HIV-TB coinfected patients visiting health facilities to deposit sputum samples.
Logistics and supply chain management	• Early forecasting of the rise in demand for laboratory consumables • Regular review of inventory and monitoring of optimal utilization of laboratory reagents/consumables as per expiry • Strategic planning, strengthening of procurement process, and monitoring of supply chain for essential laboratory items • Ensure at least 3 months of buffer stock of essential items in laboratory • Ensure optimal storage area (space and storage conditions) for buffer stock • Ensuring timely maintenance and calibration of critical equipment to prevent breakdown.

TB: Tuberculosis, HCW: Healthcare worker, PPE: Personal protective equipment, IGRA: Interferon gamma release tests, DST: Drug susceptibility testing, SCT: Sample collection and transportation, HIV: Human immunodeficiency, MDR/XDR: Multidrug-resistant/extensively drug, BMW: Biomedical waste management, UDST: Universal drug susceptibility testing, ZN: Ziehl Neelsen, MTB: Mycobacterium tuberculosis

examination during the pandemic due to repurposing of TB program staff toward the COVID-19 response and non-availability of private courier and transportation services for sample transportation to TB laboratories. Community health workers worked relentlessly during the pandemic to collect sputum specimens from the door-step of presumptive TB patients for TB diagnosis

- There was also decline in diagnosis and notification of extrapulmonary TB (3.3 lakh cases in 2019 vs. 2.4 lakh cases in 2020) and pediatric TB (2.3 lakh cases in 2019 vs. 1.5 lakh cases in 2020)[7] probably due to need for hospital visit or admission for performing gastric lavage and extrapulmonary specimen collection.

Deployment of existing and additional rapid NAAT machines toward COVID-19 testing

- In India, existing Truenat and GeneXpert machines available under National TB elimination program (NTEP) were mapped at biosafety level (BSL)-2 and BSL-3 facilities and were immediately deployed for COVID-19 testing.[7] NAAT machines and laboratory technicians (LTs) were repurposed for COVID-19 testing which helped in sharing the burden of reverse transcription polymerase chain reaction (RT-PCR) laboratories and aided rapid screening of COVID-19
- However, the much needed reallocation of NAAT machines and TB program staff for COVID-19 testing, adversely led to reduction in capacity for TB testing during the pandemic. This impacted the detection and notification of new and recurrent Drug susceptible/drug resistant-TB (DRTB) cases despite upscaling of NAAT machines and rigorous mitigation efforts undertaken by NTEP.

Further, laboratory infrastructure set ups for culture and molecular drug susceptibility testing (DST) by line probe assay (LPA) and its laboratory staff were also engaged in COVID RT-PCR testing

Reallocation of NTEP NAAT machines, laboratory infrastructure, and program staff for COVID-19 testing led to reduced TB testing capacity and overall delayed testing and increased turnaround time for TB diagnostic services.

Potential stigma and panic in laboratory workers

Initially, panic and fear of contracting SARS-CoV-2 even among TB laboratory workers also who routinely handle *Mycobacterium tuberculosis* (MTB) harbored sputum specimens was too high due to missing gaps in transmission dynamics of COVID-19. Direct sputum smear microscopy was halted by laboratory technicians (LT) at designated microscopy centers (DMC) and in private sector citing inadequate personal protective equipment (PPE) and aerosol generation risk involved with smear preparation. This inadvertently led to upfront use of rapid automated NAAT as initial test for TB diagnosis which led to acute shortage of Cartridge Based NAAT (CBNAAT) cartridges in the country. Despite sustained administrative efforts toward strengthening standard precautions and infection control measures at personnel and laboratory levels, apprehension of staff working in laboratories was high, particularly where large numbers of respiratory specimens were being processed. Not only in TB laboratories, a global survey of clinical laboratories also reported that there were restrictions imposed in some laboratories on performing direct microscopy of specimens of patients who were clinically suspected or confirmed positive for COVID-19.[8]

Overburdened TB staff

Reallocation of TB program staff to long-standing COVID-19-related duties along with continuation of essential TB services for over a year further accentuated by absenteeism of coworkers due to COVID-19 infection led to their mental, physical, and emotional exhaustion.

Acute shortfalls of PPE and essential laboratory consumables

There was acute shortfall of Personal protective equipment and critical laboratory consumables for COVID-19 and TB diagnostic testing and research activities due to breakdown of manufacturing and supply chain during the pandemic. Sudden requirement of PPE in such enormity was unwitnessed before the current pandemic. Inappropriate and excessive usage of various PPE by staff further intensified its shortage. Absence of or inadequate PPE was a legitimate cause of fear and anxiety among healthcare workers (HCWs).

SUGGESTED STRATEGIES FOR BUILDING RESILIENCY OF TB LABORATORIES TO PREVENT DISRUPTION OF TB LABORATORY SERVICES DURING ANY CRISIS

[Table 1] summarizes strategies for building system resilience for delivering TB laboratory services.

Health staff

- First and foremost, it is essential to boost morale of TB program staff and other HCW who executed functions effectively during the peak of COVID-19 pandemic despite difficult field conditions
- Health system must ensure continuous supply of appropriate PPE to HCWs both in terms of quality and quantum
- Measures to address human resource apprehensions: Regular training of laboratory staff on standard precautions, rational use of PPEs, hand hygiene practices,

disinfection and infection control policies, and biomedical waste management as per the local regulations is important for their safety and allaying fears of contracting SARS-CoV-2 infection or other respiratory pathogens
- Psychosocial counseling of TB staff: Provision of psychosocial support and counseling for those who need will help to prevent their mental breakdown and build their morale and lead to a safe environment for our workforce
- Retention policies for contractual TB laboratory staff: Administrators should make all possible efforts to fill vacant positions for TB laboratory staff in their districts

Furthermore, the formulation of policies aimed at retention of trained contractual personnel should be the emphasis of national program. Contractual workers' salaries have to be at par with those of private sector workers along with regular increments. A health insurance plan or inclusion as beneficiaries for using empanelled health facilities like permanent government employees should be offered to skilled contractual staff who successfully finish their term. Through an annual health examination, NTEP's contracted laboratory employees should be provided screening for TB and even extend this health benefit up to 2 years after leaving the job since TB is a chronic condition.

- Devising strategy for relieving TB staff from extended duties toward disaster response as early as possible
- Annual preventive health check-up for TB screening (Symptoms, Chest X-ray, interferon gamma release tests [IGRA])

The incidence of TB among laboratory personnel involved in TB diagnostic testing is known to be 3–9 times higher as compared to personnel not working with this agent.[9] This is of serious concern and necessitates a regular preventive health check-up program for health staff for occupational health and safety.[9]

- The administrative authorities must ensure routine screening for comorbidities, active TB disease by symptom screening and chest X-ray, and establish links for treatment if positive. As a high-risk category, TB laboratory workers can also be administered yearly IGRA to test for TB infection. If IGRA is positive and active TB disease is ruled out, the staff can then be offered an appropriate TB preventative treatment to treat latent TB infection[10]
- In addition, the administration must ensure that staff in TB laboratories has adequate access to necessary PPE supplies. Laboratory managers must strictly review PPE stock inventory and monitor consumption while maintaining a 2-month supply of buffer stock to do this. In the event when supply chain is projected to be disrupted, a contingency plan should be created to obtain PPE at short notice. A list of additional suppliers for emergency supply should also be in place.

It is important to do a risk assessment for prioritizing N95 masks and gowns for laboratory employees engaged in medium- to high-risk TB laboratory operations. Utilize N95 respirators for an extended period of time when necessary. Investigate the local supply options for necessary PPE.

- Establishment of national occupational health surveillance reporting system: TB remains one of the most common laboratory acquired infections. However, there are limited such laboratory reports in the literature. Therefore, there is a strong need to establish national occupational health surveillance reporting system and essentially report TB and other infectious diseases in workers to account for and analyze infections acquired in healthcare workers.

Laboratory infrastructure adequacy and functionality

It is important for TB program managers to undertake review of:

- Adequate coverage, accessibility, and functional status of existing TB diagnostic facilities under NTEP and private sector in the districts and need based augmentation of diagnostic facilities, testing platforms or arrangements for patient specimen pick up, and transportation from health-care facilities to nearby NTEP laboratory.
- Establish more effective and efficient patient referral systems –
    a. Educating private providers about the NTEP's high-quality, free diagnostic TB services including DST, and links to DRTB services offered to both patients who visit public sector and those who are referred by the private sector.
    b. Involving private providers through prioritization and one-on-one communication about free TB services such as specimen collection and transport, access to free drugs, including newer drugs, chemoprophylaxis, and free human immunodeficiency virus (HIV) and blood sugar testing and links to their treatment; links for NIKSHAY Poshan Yojana and the provider's direct benefit transfer incentive for notification and reporting treatment outcome
    c. In addition, partnership options for private sector engagement and end to end management can be explored.

Strengthening of specimen collection and transportation systems

- Consider integrated sample transportation with other disease programs (TB, HIV, Dengue, and Cancer) and adoption of hub and spoke model of sample transportation in districts with proactive approach for local innovations.

Enhancement of laboratory biosafety

- COVID-19 pandemic has provided an opportunity to re-visit biosafety measures in existing and new TB laboratories for compatibility with high aerosol generating activities involving MTB and newer pathogens in future
- As a long-term measure, thorough review of laboratory safety through careful site specific risk assessment of TB laboratories set ups and appropriate scaling up of biosafety measures where safety breach is observed, is the need of hour, in laboratory preparedness for better handling of current situation and any future pandemic
- It is critical to review all microscopy centers for efficient ventilation. If required, provision of mechanical ventilation (exhaust fans to allow frequent air changes) and biosafety cabinet class I may be considered, where feasible, to offer optimum protection to LT. This will help to safely resume direct smear microscopy halted at DMCs due to concerns involved with this pandemic over risk of exposure to aerosols and also keeping in view the unknown presence of multidrug-resistant/extensively drug TB strains in the sputum specimens
- Review of guidelines and robust supervision and monitoring for sputum collection at microscopy centers with strict emphasis on implementation of airborne infection control practices since these centers have potential of becoming sources of COVID/other airborne infections for presumptive TB and people living with HIV patients visiting health facility
- Further, considering the high biorisk in face of current and future pandemics, it is suggested that TB laboratories for culture and DST developed in future may be designed with one health approach for laboratory preparedness and response so that if required, they can be upgraded on short notice for handling Ebola virus, SARS-CoV-1, MERS, SARS-CoV-2, NIPAH virus, and other emerging pathogens of pandemic potential.

Ensuring laboratory logistics

The unforeseen material supply crisis during the pandemic has led to countries working on finding local resources or innovating on cost effective alternatives, optimal utilization of resources, as well as strengthening of procurement and supply chain management systems for laboratories.

- In such times, strategic planning and early forecasting of rise in demand for laboratory consumables such as PPE and diagnostic kits critical for TB case detection and universal drug susceptibility testing (UDST) is critical to prevent any delay and interruption in diagnostic services
- In particular, countries who have replaced direct smear microscopy with rapid NAAT test for all presumptive TB cases require strong monitoring and supply chain management of CBNAAT cartridges and Truenat Kits to keep up with the specimen load.

Use of laboratory infrastructure established for COVID testing

- RT-PCR laboratories: Districts can utilize BSL-2 laboratories equipped with certified biosafety cabinets 2A/2B and its extensively trained staff that were established during COVID-19 pandemic over short-time span in medical colleges at the district level, even in tough terrains[11] for molecular detection of other infectious diseases including LPA testing for TB, where deficiencies of facilities exist
- Genome sequencing set ups (INSACOG laboratories): Whole-genome sequencing infrastructure and trained manpower established for COVID-19 can serve as important resources for determining molecular epidemiology and drug resistance surveillance of other infectious diseases.

CONCLUSION

Safe integration of diagnostic services for TB and where required newer airborne pathogens, must be the utmost priority in ongoing and any future pandemics to ensure uninterrupted TB services.

Coverage and accessibility of rapid TB diagnostic tests should be ensured for presumptive TB population to recover missed TB cases during the pandemic. Innovative and robust approaches are required to strengthen SCT systems. Review of biosafety measures in existing TB laboratories and biosafety enhancement wherever deficiency exists is the need of the hour. Optimum utilization of available infrastructure and resources is essential during the crisis to manage logistics and the supply chain.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

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