Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/mjafi

Editorial

Tuberculosis diagnosis in resource limited settings

Col Sourav Sen

Professor & Head, Department of Microbiology, Armed Forces Medical College, Pune 411040, India

The scourge of tuberculosis (TB), it being first documented in India and China some 3300 and 2300 years ago, respectively, continues globally.¹ Towards the common aim of ending the global tuberculosis epidemic, the End TB Strategy of World Health Organisation (WHO) and the United Nations' (UN) Sustainable Development Goals (SDGs), there are certain specific targets, namely a 90% reduction in TB deaths and an 80% reduction in tuberculosis incidence, which are to be achieved by 2030.²

Tuberculosis, at times a great masquerader, continues to occupy the topmost position worldwide, as a cause of death from a single infectious agent – *Mycobacterium tuberculosis*, with an estimated 1.3 million deaths in human immunodeficiency virus (HIV) negative people and 374,000 deaths among HIV positive people. India has the dubious distinction of accounting for 26% deaths among the combined in HIV negative plus HIV positive people and 33% deaths in HIV-negative people globally. As per the 2014 global estimates, India featured in the top 20 countries with high tuberculosis burden, with the highest incidence of tuberculosis (22%), and multidrug resistant (MDR)-tuberculosis (23.7%), and second highest incidence of tuberculosis/HIV (9.2%). Furthermore, out of the estimated incidence of 10.4 million people with TB in 2016, 56% were from five countries, namely, India, Indonesia, China, the Philippines and Pakistan. In India, there was a gap between the estimated incidence (2.79 million) and notified cases (1.936 million) of tuberculosis. However, it is praiseworthy that, in India, there has been a 37% increase in notifications of new TB cases between 2013 and 2016, which has in turn led to an overall global increase. Lastly, an estimated 88,000 notified pulmonary tuberculosis cases in India were reported to be MDR/Rifampicin resistant (RR).²

Early detection and proper management are two essential pillars in successful management of tuberculosis, thereby, preventing transmission, disease spread and emergence of drug resistance and, and thus, bringing down the overall morbidity and mortality. For detection, the traditional smear

microscopy for acid fast bacilli, though simple, inexpensive and easily implementable, is gradually becoming antiquated because of its low sensitivity,³ and may be replaced by newer cartridge based nucleic acid amplification tests (CBNAAT). However, utility of CBNAATs in developing countries are mired with issues related to high costs, logistics and infrastructure.

Agarwal et al., in this issue of Med J Armed Forces India, have studied the potential of liquid culture system (Manual MGIT) followed by microscopy and immunochromatographic test for MPT 64 antigen detection, along with provision of primary drug susceptibility testing (DST) report, thus decreasing the delay in diagnosis and early initiation of effective treatment. Out of the 1018 consecutive clinical (pulmonary and extra-pulmonary) samples processed in the study, 220 were culture positive by a combination of solid – Lowenstein Jensen (LJ) and/or liquid (manual MGIT) culture methods. While 69.7% were positive by both the methods, an additional 24.2% and 6.1% were MGIT and LJ positive, respectively. The time to positivity (TTP) using manual MGIT was 10.4, 20.2 and 13.8 days for smear positive, smear negative and all smears, respectively, this being roughly 17 days lesser than those observed for LJ medium. Similarly, the over turnaround time from the time of inoculation till DST results was reported to be 23.6 days with manual MGIT as compared 61.2 days with LJ medium.⁴ Higher positivity rates and shorter TTP and DST by MGIT, when compared to LJ medium has been reported by other workers as well.^{5–7} The authors, in the present article, used combined presumptive cord formation and MPT 64 antigen positivity by immunochromatographic test (ICT) to differentiate *M. tuberculosis* from nontuberculous mycobacteria (NTM).⁴ A study by Nerurkar et al have highlighted this importance of liquid culture smear along with MPT 64 testing as well, in differentiating *M. tuberculosis* from NTM, and outlined the role of these two tests in diagnostic algorithm, especially for MPT 64 ICT negative isolates.⁸

E-mail address: sensourav@hotmail.com.

<https://doi.org/10.1016/j.mjafi.2018.06.003>

0377-1237/© 2018 Published by Elsevier B.V. on behalf of Director General, Armed Forces Medical Services.

The National Strategic Plan (NSP) 2017–2025, launched in March 2017, aims at elimination of tuberculosis in India by 2025. The goal of diagnosis and laboratory services is to further expand and strengthen capacity of laboratories in conducting M. tuberculosis culture and drug sensitivity tests towards achieving universal access to quality tuberculosis diagnosis including drug resistant TB. It has been stated that second line DST using Liquid culture systems are in place and are being scaled up to cover the entire country. Provisioning of rapid molecular tests, such as CBNAAT, for diagnosis will be scaled up.⁹ In May 2018, WHO has released the model list of essential in vitro diagnostics (EDLs) for use in a tiered national health care system, including diagnostics of priority diseases such as tuberculosis being outlined separately, with an intention to provide evidence based guidance for successful diagnosis and management. While microscopy, loop-mediated isothermal amplification (LAMP) and intradermal skin tests have been included as those to be available in primary health care level, additional provisioning of tests such as culture, CBNAAT, line probe assay, DST, Lipoarabinomannan (LAM) antigen detection and interferon gamma release assay (IGRA) have been proposed for health care facilities with clinical laboratories.¹⁰ The implementation and sustenance of such programmes will be dependent on factors such as availability of human resources, training and laboratory infrastructure. Here, it is important to reinforce the fact that while CBNAAT is being introduced in large scale, its utility, on date, is primarily of screening in nature, with an added advantage of simultaneous availability of rifampicin resistance data. Further to this will be the application of a phenotypic method for culture and DST, the better option being liquid based medium such as MGIT, so as to generate a reliable and comprehensive report for tuberculosis diagnosis. In the context of resource limitations, Agarwal et al have demonstrated the feasibility of using manual MGIT in low and medium volume laboratories, as a sensitive method with reduced detection time, when compared to solid culture media.⁴

REFERENCES

1. Barberis I, Bragazzi NL, Galluzzo L, Martini M. The history of tuberculosis: from the first historical records to the isolation of Koch's bacillus. *J Prev Med Hyg.* 2017;58(1):E9–E12.
2. In: *Global tuberculosis report 2017*. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
3. Steingart KR, Ramsay A, Pai M. Optimizing sputum smear microscopy for the diagnosis of pulmonary tuberculosis. *Expert Rev Anti Infect Ther.* 2007;5(3):327–331.
4. Agarwal A, Kumar N, Kishore K. Evaluation of manual Mycobacterial growth indicator tube for isolation and susceptibility testing of *Mycobacterium tuberculosis* for implementation in low and medium volume laboratories. *Med J Armed Forces India.* 2018. xxx-xxx.
5. Rodrigues C, Shenai S, Sadani M, et al. Evaluation of the Bactec MGIT 960 TB system for recovery and identification of *Mycobacterium tuberculosis* complex in a high throughput tertiary care centre. *Indian J Med Microbiol.* 2009;27:217–221.
6. Adjers-Koskela K, Katila M-L. Susceptibility testing with the manual mycobacteria growth indicator tube (MGIT) and the MGIT 960 system provides rapid and reliable verification of multidrug-resistant tuberculosis. *J Clin Microbiol.* 2003;41(3):1235–1239.
7. Siddiqi S, Ahmed A, Asif S, et al. Direct drug susceptibility testing of *Mycobacterium tuberculosis* for rapid detection of multidrug resistance using the Bactec MGIT 960 system: a multicenter study. *J Clin Microbiol.* 2012;50(2):435–440.
8. Nerurkar V, Kattungal S, Bhatia S. Utility of MPT64 antigen test for differentiating mycobacteria: can correlation with liquid culture smear morphology add further value? *Indian J Pathol Microbiol.* 2016;59:185–187.
9. RNTCP National Strategic Plan for TB Elimination in India (2017–2025). Central TB Division, DGHS, MOHFW, Government of India. Available at: <https://tbcindia.gov.in/WriteReadData/NSP%20Draft%2020.02.2017%201.pdf>.
10. In: *World Health Organization Model List of Essential In Vitro Diagnostics* First edition. 2018 Available at: In: http://www.who.int/medical_devices/diagnostics/WHO_EDL_2018.pdf.