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# Diagnostic performance of non-invasive, stool-based molecular assays in patients with paucibacillary tuberculosis

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**Timely diagnosis of paucibacillary tuberculosis (TB) which includes smear-negative pulmonary TB (PTB) and extra-pulmonary TB (EPTB) remains a challenge. This study was performed to assess the diagnostic utility of stool as a specimen of choice for detection of mycobacterial DNA in paucibacillary TB patients in a TB-endemic setting. Stool samples were collected from 246 subjects including 129 TB patients (62 PTB and 67 EPTB) recruited at TB hospital in Delhi, India. Diagnostic efficacy of stool IS6110 PCR ($n = 228$) was measured, using microbiologically/clinically confirmed TB as the reference standard. The clinical sensitivity of stool PCR was 97.22% (95% confidence interval (CI), 85.47-99.93) for detection of *Mycobacterium tuberculosis* in stool samples of smear-positive PTB patients and 76.92% (CI, 56.35–91.03) in samples from smear-negative PTB patients. Overall sensitivity of PCR for EPTB was 68.66% (CI, 56.16–79.44), with the highest sensitivity for stool samples from patients with lymph node TB (73.5%), followed by abdominal TB (66.7%) and pleural effusion (56.3%). Stool PCR presented a specificity of 95.12%. The receiver operating characteristic curve also indicated the diagnostic utility of stool PCR in TB detection (AUC: 0.882). The performance characteristic of the molecular assay suggests that stool DNA testing has clinical value in detection of TB.**

Tuberculosis (TB), a global health problem, is caused by *Mycobacterium tuberculosis* (*Mtb*) and has two ways of clinical manifestation. Apart from the common pulmonary TB (PTB) manifestation, extrapulmonary TB (EPTB) is identified as a major concern and contributes significantly to the disease burden worldwide. According to the World Health Organization (WHO), 10 million people fell ill with TB in 2018[1]. Although new strategies for diagnosis and treatment over the past decade have led to decline in death rate, it remains inadequate to reach the milestone of the WHO "End-TB" goal[1]. Apart from the diagnostic and treatment difficulties faced in the eradication of PTB, timely diagnosis and treatment of EPTB is considered a bigger challenge. This is due to the diverse, non-specific and paucibacillary presentation of EPTB at remote body sites and requirement of a longer treatment regimen[2]. In 2018, an increase in EPTB incidence was reported in India[3], which is also considered as a TB high-burden country by the WHO. A probable explanation for this rise can be in part due to access to better diagnostic tools that highlight the fact that EPTB burden may have been underrepresented over the years. Thus, accurate and rapid diagnostic tests for PTB and EPTB are key to limit the spread of the epidemic.

In India, diagnosis of TB is done by the Revised National Tuberculosis Control Program guidelines that follow the WHO recommendations (Fig. 1). At present, although the diagnosis of PTB by sputum-smear direct microscopy is considerably established, the diagnosis of smear-negative PTB and EPTB poses serious challenges due to paucibacillary nature of the specimen. Diagnosis of EPTB usually involves sample procurement from the affected body site through invasive and painful procedures that requires clinical expertise. Advent of Xpert MTB/RIF (Xpert), an automated molecular detection system that simultaneously detects TB and resistance to rifampicin,

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