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Letter to the Editor

Serious discordance between MTBC trace positivity by Xpert MTB/RIF ultra and follow up culture

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Sir,

Authors wish to report a major discordance between Xpert MTB/RIF Ultra Trace positivity (GeneXpert, Cepheid) and follow up by liquid culture.

Depending upon the clinical category, WHO in conjunction with the Revised National Tuberculosis Program (RNTCP), India recommends GeneXpert CBNAAT for diagnosis of mycobacterium tuberculosis complex (MTBC). Although, it is desirable that all MTBC detected in GeneXpert is followed up by culture and drug sensitivity testing (DST), anti-tuberculous therapy (ATT) in India is often started based on the GeneXpert reports.[1,2] Subsequently, a new cartridge Xpert MTB/RIF Ultra was introduced with an additional value of Trace. Any report with MTBC detected Trace was automatically reported as rifampicin indeterminate.[3]

From August to December 2019, Authors conducted 2019 tests using Xpert MTB/RIF Ultra of which 439 tested positive (21.7%). Of these 439 positive cases 113 were reported as MTBC detected trace and rifampicin indeterminate. 79 trace samples were cultured in BD BACTEC™ MGIT™ 320 system; 34 remaining samples did not receive a request for culture. Only 6 samples exhibited growth over 23-35 days: 5 MTBC and one non-tuberculous mycobacteria (NTM). Rest of the 73 samples remained culture negative after 42 days of incubation. Overall, 73/79 trace samples remained culture negative (92.4%) leading to a dilemma in starting ATT as rifampicin status remained indeterminate.

In comparison, authors retrospectively analysed 3722 tests using Xpert MTB/RIF cartridge over a period of 8 months (January to August 2019) of which 753 were reported MTBC positive (20.2%). Rifampicin resistance was reported unambiguously.

The aim of reporting this discrepancy is summarised as under:

- Trace positive in Xpert MTB/RIF Ultra mandatorily necessitates culture and DST and/or other confirmatory molecular assays like LPA (Hain Lifescience) for drug susceptibility status.
- In India, initiation of anti-tuberculous therapy (ATT) under the directly observed treatment short-course (DOTS) program is inordinately delayed pending culture and DST. These patients are often lost to follow up.
- Since the semi-quantitative estimation is based on the CT value for the Xpert MTB/RIF Ultra cartridge, it is uncertain as to whether the trace detection occurs due to software-based calculations; presence of NTM or dead tubercle bacilli.
- Worldwide evaluations suggest the Ultra cartridge is more suited for low TB prevalence countries and the chances of false positivity increases two folds in high TB burden countries like India.[4,5]
- In the case of 'Trace" reports being false positive, the patients may be exposed to the toxic effects of ATT especially in pregnant females and those in the pediatric age group.
- In a worrisome MDR/XDR TB scenario, empirical use of ATT may further lead to emergence of resistance that may adversely affect the economics of the DOTS program as newer anti-tuberculous drugs are very expensive.

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