Comparison of Xpert MTB/RIF (Xpert) With Liquid Culture System (MGIT 960) For Rapid Detection of Mycobacterium tuberculosis in Non Sputum Specimens

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Abstract: TB diagnosis in extra pulmonary cases have always been challenging due to unavailability of suitable specimens and low sensitivity of widely used smear microscopy, whereas culture is cumbersome and time consuming. This study represents the utility of Xpert over TB culture in non respiratory specimens. A total of 110 specimens were processed by NALC-NaOH method. Processed specimens were tested on Xpert and MGIT. Xpert was found positive in 32.7% (24.26-42.4) cases in comparison of culture positive in 12.7% (7.39-20.7) cases. This report suggests; Xpert as reliable diagnostic tool over TB culture in non sputum specimens.

Key words: Xpert • MGIT 960 • Non Sputum Specimen

INTRODUCTION

Tuberculosis (TB) remains a major public health concern with an estimate of 10.4 million new cases and 1.3 million deaths reported in 2016 [1]. Six countries; India, Indonesia, China, Nigeria, Pakistan and South Africa accounted for 60% of the new cases [1].

The problem of extra pulmonary TB (EPTB) is high, both in developing and developed countries. In India, EPTB accounts 10 to 15 percent of all types of TB, in comparison to 25 percent in France and 50 percent in Canada, partly due to the dual infection of TB with human immunodeficiency virus (HIV) [2, 3]. Diagnosis of EPTB has always been a challenge. It affects virtually all the organs and has a wide spectrum of clinical presentation.

For a definitive diagnosis, it is essential to culture the mycobacterium but it is time consuming. So, newer rapid diagnostic tools are eagerly awaited. In 2013, the WHO [4] endorsed the use of Xpert MTB/RIF assay (Cepheid Inc., Sunnyvale, California) for the diagnosis of pulmonary TB and Rifampicin sensitivity. New recommendations for the diagnosis of EPTB were added in 2014 [5, 6]. The aim of present study was to test the utility of Xpert over TB culture in non-sputum specimens.

MATERIALS AND METHODS

This study was conducted in the Department of Microbiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India. Samples were collected in hospital from the patients attending indoor and outdoor facility during the period of January 2016 to June 2017. Clinicians had made provisional diagnosis for all the patients included in this study. Presumptive TB case was defined as patients having persistent fever more than two-weeks, weight loss /no weight gain/failure to thrive or presenting with symptoms suggestive of extra-pulmonary TB.

A total 110 non duplicate specimens [Lymph node aspirate (LNA)/ Pus-48, cerebrospinal fluid (CSF)-45, others- bronchoalveolar lavage (BAL)-2, pleural fluid-5 and endometrial biopsies-10)] were collected in the sterile condition and transported to the lab. Pus and BAL were processed by N-acetyl-L-cysteine and sodium hydroxide (NALC-NaOH) method as per provisional suggestion for processing of extra-pulmonary specimens by Xpert [7]. Tissue biopsy specimens were first homogenized in sterile single use Beadbug Microtube Homogenizer™ (Benchmark scientific, USA) and then processed as sputum. The sediments were re-suspended in 2 ml PBS.
Table 1: Comparison of Xpert and culture positivity in different specimens

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Cases tested</th>
<th>Xpert positive rate (95% CI)</th>
<th>Rifampicin resistance detected</th>
<th>Proportion of Rifampicin resistance detected (95% CI)</th>
<th>Culture positives detected</th>
<th>Culture positivity rate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>45</td>
<td>17.8% (8.5-32.6)</td>
<td>1</td>
<td>12.5% (0.6-53.3)</td>
<td>4</td>
<td>8.9% (2.9-22.3)</td>
</tr>
<tr>
<td>LNA /pus</td>
<td>48</td>
<td>54.2% (39.3-68.4)</td>
<td>7</td>
<td>26.9% (12.3-48.0)</td>
<td>9</td>
<td>18.7% (9.4-33.3)</td>
</tr>
<tr>
<td>Others</td>
<td>17</td>
<td>11.8% (2.0-37.7)</td>
<td>1</td>
<td>50% (2.67-97.3)</td>
<td>1</td>
<td>5.8% (0.3-30.7)</td>
</tr>
<tr>
<td>Total</td>
<td>110</td>
<td>32.7% (24.26-42.4)</td>
<td>9</td>
<td>25% (12.7-42.5)</td>
<td>14</td>
<td>12.7% (7.39-20.7)</td>
</tr>
</tbody>
</table>

CSF-Cerebro spinal fluid, LNA-lymph node aspirate

RESULTS

A total of 110 presumptive TB cases were enrolled in this study. Of those 79 cases (71.82%, 95% CI 62.3-79.8) were male and 31 (28.18%, 95% CI 20.2-37.7) were female. All the smear were found negative on microscopy. Overall Xpert positive was found in specimen of 32.7% (24.26-42.4) cases, whereas as 12.7% (7.39-20.7) specimens were turn out positive in liquid culture (Table 1).

Further analysis was done to access TB detection on Xpert compared to culture on various specimens (Table 1). Xpert positivity rate was 17.8% (95% CI 8.5-32.6), 54.2% (95% CI 39.3-68.4) and 11.8% (95% CI 2.0-37.7) respectively. However, culture positivity rate was 8.9% (95% CI 2.9-22.3), 18.7% (95% CI 9.4-33.3) and 5.8% (95% CI 0.3-30.7) in respective specimens. Of the total TB positive cases; the proportion of Rifampicin resistance was 25% (12.7-42.5) (Table 1). Remaining 75.0% (95% CI 57.5-87.2) cases were sensitive to Rifampicin.

DISCUSSION

Major bottleneck in prompt TB diagnosis in extra pulmonary cases is related to practical challenges in easily obtaining site specific specimen [8]. The technical limitation of variable sensitivity with smear microscopy makes it further challenging. In the present study Xpert performance on non-sputum specimen was found highly satisfactory. The findings are similar to other studies conducted on Xpert assay on non respiratory specimens [9]. Proportion of valid interpretable results on Xpert under the current study is higher than previous reports from India and Germany [8, 9]. These results demonstrate the feasibility of Xpert testing on alternate types of specimens in extra pulmonary cases compared to other available diagnostic tests. Similar to other studies in India [10] and other countries [8, 11-13] higher positivity was observed in specimens such as CSF, FNAC, Pus, BAL and tissue specimens.

In this study we found over two times of higher TB positive case detection by Xpert than liquid culture system. This study represents 25.0% of Rifampicin resistant of the total TB positive cases; which is alarming. Furthermore, of the 14 culture positive isolates, 9 isolates were resistant to Rifampicin. On the other hand, 23/27 Rifampicin sensitive isolates were culture negative. To understand the possible reasons of presentation of Rifampicin resistant and culture negative results in Rifampicin sensitive cases, all the Xpert positive patients were interviewed retrospectively on telephone. On the conversation 29 of the 36 patients were admits the initiation of first line anti-tubercular treatment (ATT) prior to the bacteriological confirmation of whom 9 patient become resistant. Thus the possible reason of culture negative in Rifampicin sensitive patients was the initiation of ATT prior to TB testing.

CONCLUSIONS

This report suggests that apart from the sputum specimen; Xpert could be the first choice of TB diagnosis in non sputum specimen over liquid culture system.

REFERENCES


