Comparison of Sensitivity of QuantiFERON-TB Gold Test and Tuberculin Skin Test in Active Pulmonary Tuberculosis

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ABSTRACT

Objective: To compare the sensitivity of tuberculin skin test (TST) and quantiFERON-TB gold test (QFT-G) in active pulmonary tuberculosis.

Study Design: Analytical study.

Place and Duration of Study: Department of Pulmonology, Fauji Foundation Hospital, Rawalpindi, from July 2011 to January 2012.

Methodology: QuantiFERON-TB gold test (QFT-G) was evaluated and compared it with tuberculin skin test (TST) in 50 cases of active pulmonary tuberculosis, in whom tuberculous infection was suspected on clinical, radiological and microbiological grounds. Sensitivity was determined against positive growth for Mycobacterium tuberculosis.

Results: Out of 50 cases, 43 were females and 7 were males. The mean age was 41.84 ± 19.03 years. Sensitivity of QFT-G was 80% while that of TST was 28%.

Conclusion: QFT-G has much higher sensitivity than TST for active pulmonary tuberculosis. It is unaffected by prior BCG administration and prior exposure to atypical mycobacteria. A positive QFT-G result can be an adjunct to diagnosis in patients having clinical and radiological data compatible with pulmonary tuberculosis.

METHODOLOGY

It was an analytical study, carried out in the Department of Pulmonology, Fauji Foundation Hospital, Rawalpindi, on cases of active pulmonary tuberculosis, in whom tuberculous infection was initially suspected on clinical, radiological and microbiological grounds. Sample size was calculated by WHO sample size calculator. Considering the sensitivity (SN) of quantiFERON-TB gold as 92.3% in tuberculosis and 89.8% agreement between a strongly positive tuberculin skin test and a positive QFT-G assay using the sensitivity calculator, and an absolute precision 0.08, the sample size was found to be 50. Hence 50 patients were inducted by non-probability consecutive sampling from July, 2011 to January, 2012.

If, in a patient, either smear (sputum/bronchial washings stained with Ziehl Neelson) was positive or AFB culture (by Lowenstein Jensen Medium) grow Mycobacterium tuberculosis, he was defined to have active pulmonary tuberculosis.

Patients of either gender aged 13 years and above who had active (smear or culture, sputum or endobronchial washings positive) pulmonary TB and radiographic evidence suggestive of tuberculosis and who had taken medication for ≤ one week were included in the study. Following a written informed consent from all participants, demographic and clinical data were collected.

Past history of TB treatment, smear/culture negative pulmonary TB, extrapulmonary or disseminated TB, HIV positive patients, patients on chemotherapy or renal replacement therapy were excluded from the study.

The QFT-G test was performed in two stages. First, whole blood was collected into each of the QFT-G blood collection tubes, which include a Nil Control tube, TB antigen tube and an optional mitogen tube. The tubes were incubated at 37°C as soon as possible, and within 16 hours of collection. Following a 16 – 24 hours incubation period, the tubes were centrifuged, the plasma removed and the amount of INF-gamma (IU/mL) measured by ELISA method.

Immediately after the sample for QFT-G was drawn a TST was performed by an experienced nursing staff on the volar side of the forearm using 2 tuberculin units of purified protein derivative. Induration was measured after 48 – 72 hours. A positive result was regarded as ≥ 10 mm of induration, regardless of the BCG vaccination.

Statistical Package for Social Sciences (SPSS) version 16 was used for statistical analysis. Mean values were calculated for age. Sensitivity for QFT-G and TST were calculated using the following formula:

\[ \text{Sensitivity} = \frac{a \times 100}{a + C} \]

where \(a\) = patient with active TB and a positive test result and \(c\) = patient with active TB and a negative test result.

RESULTS

Forty patients were females (86%) and 7 were males (14%). Their mean age was 41.84 ± 19.035 years ranging from 14 – 84 years. Out of 50 patients, 24 (48%) of patients were smear (sputum/bronchial washings) positive while rest of patients (26 i.e 52%) were smear negative, 42 (84%) had culture confirmed tuberculosis, 8 (16%) were culture negative. All the patients who were sputum negative were confirmed as active tuberculosis on AFB culture received after 6 weeks as shown in Table I.

Table I: Demographic characteristics of the cases.

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Age mean 41.84 ± 19.035</th>
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<tbody>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14% (n = 07)</td>
</tr>
<tr>
<td>Female</td>
<td>86% (n = 43)</td>
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<tr>
<td>Presenting complaints</td>
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<tr>
<td>Fever</td>
<td>88%</td>
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<tr>
<td>Productive cough</td>
<td>76%</td>
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<tr>
<td>Weight loss</td>
<td>65%</td>
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<tr>
<td>Hemoptysis</td>
<td>35%</td>
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<tr>
<td>Radiological findings</td>
<td></td>
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<tr>
<td>Cavitation</td>
<td>24%</td>
</tr>
<tr>
<td>Consolidation</td>
<td>28%</td>
</tr>
<tr>
<td>Consolidation with cavitation</td>
<td>16%</td>
</tr>
<tr>
<td>Infiltration</td>
<td>22%</td>
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<tr>
<td>Bronchiectasis</td>
<td>10%</td>
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<tr>
<td>Laboratory findings</td>
<td></td>
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<tr>
<td>AFB smear (sputum / bronchial washings)</td>
<td>48% (n = 24)</td>
</tr>
<tr>
<td>AFB culture</td>
<td>52% (n = 26)</td>
</tr>
<tr>
<td>Positive</td>
<td>84% (n = 42)</td>
</tr>
<tr>
<td>Negative</td>
<td>16% (n = 08)</td>
</tr>
</tbody>
</table>

The most common presenting complaints were fever (88%), productive cough (76%), weight loss (65%) and hemoptysis (35%). Radiological findings compatible with tuberculosis included consolidation 28%, cavitation 24% and infiltration 22% consolidation with cavity 16%, bronchiectasis 10%.

Sensitivity of quantiFERON-TB and tuberculin skin test were calculated and found to be 80% and 28% respectively.

DISCUSSION

In this study, QFT-G results were evaluated and compared with TST in active pulmonary tuberculosis cases. Although the diagnosis of pulmonary tuberculosis is established by radiological and clinical data and by detecting tuberculosis bacilli on smear or culture media, it may be problematic if the clinical picture and radiological findings are not typical of tuberculosis.
and when smear microscopy and culture results are negative. Invasive procedures are necessary under these circumstances.

The tuberculin skin test (TST) has been used to diagnose TB infection for about a century. The PPD contains a mixture of more than 200 antigens that are widely shared by mycobacteria other than Mycobacterium tuberculosis, including the vaccinal strain of Mycobacterium bovis bacilli Calmette-Guérin (BCG) and many non-tuberculous mycobacteria (NTM). As a result, individuals sensitized by previous exposure to NTM or BCG vaccine may respond immunologically to PPD. The other main limitation of the TST is its low sensitivity in certain groups of individuals, such as immunosuppressed patients and young children. Moreover, it is painful for the patient and requires a follow-up visit after 72 hours to interpret the results.

QFT-G tests are whole blood assays that use an enzyme-linked immunosorbent assay (ELISA) to detect IFN-γ produced in supernatants by stimulated T-cells. The QFT-G In Tube version (QFTIT), includes a third antigen, TB 7.7. This new antigen is encoded in RD11 and is missing from the BCG strains as well as most common environmental mycobacteria.

Both in vitro tests include a positive control that detects the capacity of T-cells to produce IFN-γ upon stimulation with a mitogen (phytohemagglutinin), in order to distinguish false-negatives from indeterminate results. Numerous studies have explored the utility of the IFN-γ-based tests in contact investigations. In a study conducted in Turkey, QFT-G positivity was 75% and TST positivity was 68.2% in active pulmonary tuberculosis patients and in cases of extra-pulmonary tuberculosis, 76.25 and 62% respectively.

In this study, QFT-G was found positive in 80% and negative in 20%; 54% of TST negative cases showed positive QFT-G. QFT-G was positive in 26% of TST positive cases and in 54% of TST negative cases which imply that QFT-G may further aid in the diagnosis of tuberculosis even when TST is negative in patients with appropriate clinical findings. Furthermore, results could be obtained on the same day and in many studies because of a follow-up visit, QFT-G test is found to be more cost effective as compared to TST. Similarly, for TB culture, besides the high cost, one has to wait for 6 – 8 weeks to get the results.

There were few limitations of the study. First, as this study was performed only in patients with active pulmonary tuberculosis (smear/culture positive) so specificity of QFT-G and TST was neither measured nor compared. Further studies on smear/culture negative patients are required. In addition, future studies on extra-pulmonary disseminated TB and immuno-suppressed patients are needed to further elaborate the utility of QuantiFERON-TB gold. The test is expensive too.

In this study, certain immuno-compromised conditions like HIV, patients on chemotherapy, renal replacement therapy were excluded but diabetic patients and patients on long-term steroids were not excluded. This may be another source of bias as 20% of patients with active pulmonary TB had negative QuantiFERON gold test in this study. Further studies are required that will establish the relationship between diabetes, long-term steroid use and QuantiFERON-TB gold test result.

**CONCLUSION**

Based on this study of active pulmonary tuberculosis cases, the sensitivity of QFT-G was higher than TST. QFT-G has the advantage of easy applicability and high sensitivity. Although it has the disadvantage of being expensive, it gives result on the same day as performed. A positive QFT-G result can be used an adjunct to diagnosis in patients having clinical and radiological data compatible with pulmonary tuberculosis.

**REFERENCES**


14. Schluger NW, Burzynski J. Recent advances in testing for latent TB. *Chest* 2010; 138:1456-63.


