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Comparison of the Quantiferon tb gold assay and tuberculin skin test to detect tuberculosis infection among tuberculosis patient contact

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Abstract

Introduction: Tuberculosis is a communicable disease and therefore TB patient contacts are at higher risk of developing TB infection. So screening and diagnosis of latent TB is done by QFT Gold assay and Tuberculin skin test (TST).
Methodology: A total of 100 TB patient contacts were taken for study, blood was drawn and processed by using the QFT G assay followed by immediate administration of TST solution in subjects forearm. Data were analyzed and results were compared.
Results: QFT G assay detect LTBI with sensitivity of 88.88% and specificity of 90%. TST Sensitivity 68%, Specificity 16%.
Conclusions: QFT G Assay have higher detection rate among TB contact patient.

Keywords: QFT G quantiferon TB Gold, LTBI- Latent tuberculosis infection, TST – Tuberculin skin test

Introduction

Tuberculosis is the most frequent cause of mortality in developing countries. The disease accounts for 1/5 of global prevalence in developing countries like India and its subcontinent [1].

The aim of testing for LTBI is to identify individual at high risk for active tuberculosis& would benefit from treatment should be tested. The first priority for TB control should be diagnosis and treatment of patients who are having active tuberculosis and having LTBI.

Close contacts is defined as all contacts who have minimum of 40 hrs of exposure to their respective index case [2,3]. In other study, it was defined as individuals who had household contacts in the same room with smear positive pulmonary tuberculosis for more than 8 hrs per day.

Close contacts with active tuberculosis patients is one determinant that leads to positive QFT-GIT test results among TST positive subjects due to prolonged close contact with infectious patients causing high rate of positivity of QST-GIT and TST [4].

Mycobacterium tuberculosis infection remains latent initially due to host defense, which can later develop into active tuberculosis in due course of time.

The source of transmission can be reduced by prompt identification & treatment of LTBI thus reducing the risk of development of disease, thus reducing the risk of developing the disease thus promoting positive health of individual and the public.

Two eminent tests for identification of LTBI, tuberculin skin test & IGRA, to assess cell mediated immunity, but neither can distinguish between latent and active tuberculosis. TST basically consists of delayed type of hypersensitive reaction. Small amount of PPD derived from MTB bacteria is injected intra-dermally, there occurs a localized swelling manifesting as induration of skin at intradermal site within 48-72 hrs, which is CMI to tubercles antigens [5,6].

The QFT-IGRA are in-vitro blood tests to assess Cell mediated immunity. This test measures interferon gamma stimulation by antigen specific to MTB early secretory antigenic target 6k (Da(ESTA—[6] protein & the culture filterate 10kDa pathogenic M. bovies strain but absent in BCG vaccine strain &all non – tuberculosis bacteria of clinical relevance.

The TST measures CMI to PPD, which is a polyvalent antigenic mixture of protein derived from M.TB culture. The PPD used in TST is also present in BCG vaccine strain[7].The present study was done to evaluate &compare the TST versus newer QFT-G method in screening for LTBI in various groups at high risk for TB to determine which method is better for use in a resource limited .

The study was explained to all household contacts & written informed consent was obtained prior to study. All available contacts were asked to provide blood samples for LTBI test. All demographic characteristics were also collected from adults & children living as household contacts.

Materials and Method

The present study was conducted at KBNIMS hospital at OPD of Department of TB & chest. 100 subjects were included in the study. Subjects were, all individual at risk of being infected with tuberculosis. Household contacts of index case were identified through medical records of index cases and interviews. All household contacts which included family& friends who lived in the same house with the index case were included in the study. Household contacts that had other medical conditions or serious illnesses that may affect the result of the study were excluded.

Inclusion Criteria:

1. Tb contact –family/neighborhood in contact to patient
2. Health care workers (High risk)

Exclusion Criteria:

1. Sputum negative patients who are on treatment
2. Acutely ill admitted TB patient
3. TB patients on retroviral therapy
4. Pregnant women

Specimen Collection: Whole blood specimen was drawn in heparin tubes from all subjects for testing with QFT-G assay, followed immediately by administration of TST via an intradermal injection at the lateral upper part of subjects forearm. Subjects were instructed not too scratch the area & to return to hospital 72hrs after injection for a reading of induration.

QFT-G assay: All blood samples were evaluated for presence of interferon –gamma. In the laboratory 1ml of aliquots of heparin zed whole were incubated for 16-24 hrs at 37c with 3 drops of saline (nil) phytohemaglutinin (mitogen), ESAT-6 protein, and CFP-10 in costar 24-well micro-titer plates. After incubation plasma samples were harvested & stored at -20c until ELISA analysis of their INF-gamma content done.

The IFN-y levels of the 50µL plasma were determined using the ELISA reagents and protocol provided in the QFT-G assay kit. The 50-µL plasma samples were added to diluted conjugate inflat-bottom micro titer wells and incubated for 2 hours at room temperature. Eight dilutions of INF-y standard (ranging from 0.0 IU/mL to 10.0 IU/mL) were included in each plate. After washing the samples six times, a substrate was added to achieve color development directly proportional of the amount of IFN-y present in each specimen. IFN-y assay results were interpreted as described in the QFT-G product package insert. An IFN-y level > 0.35 IU/mL (TB antigens minus negative control) was considered a positive result [8].

Mantoux TST: Subjects participated were injected with 0.1mL (5 tuberculin units [TU]) of Tuber sol immediately after the blood samples for the QFT-G were drawn by the phlebotomists. The diameter of the resulting wheals reactions were measured 72 hours after puncture. All results obtained were recorded as either positive (if > 10mm) or negative (<10mm) [9]. Test was performed and results were read by highly trained certified nurses.

Statistics: Data was analyzed and follows.

Result were obtained

Results

Table 1: QFT-G

Test	True +ve	True –ve	
QFT-G	40	50	
	5	5	100

Sensitivity = 88.8%

Specificity = 90.9%

Table 2: TST

Test	True +ve	True –ve	
TST	17	63	
	8	12	100

Sensitivity = 68%

Specificity = 16%

Discussion

A total of 100 house hold contact were enrolled in the study to determine the agreement between QFT-G/TST.

Table 1: Shows QFT-Sensitivity is 88.8% and specificity 90.9%.

Table 2: Shows TST sensitivity 68% and specificity 16%.

The role of QFT/TST performed in high risk group (individual exposed to TB patient) to detect the disease. We got the sensitivity of QFT-G- 88% & specificity of 90%. The QFT-G result were similar to the result as study of et al (82% QFT, & 44% TST) [10] as compared to the TST result we got the sensitivity of 68% & specificity 16% as we got in the study as Sohair et al., TST Sensitivity of 66%.The QFT had shown the higher positive detection rate as compared to TST the result were same as study program UNAIDS Geneva [12].

Positive QFT-GIT & negative TST was seen in our study as seen in other study-Faratetal. This is seen in patient with immune suppression & in non MTB infection. But positivity of both tests indicates high probability of tuberculosis.

TST has low specificity and sensitivity due to problem of cross reactivity with other mycobacteria & problem in interpretation & repeat visit to read the test, as we have got in our study.

Conclusions

Both TST and QFT-GIT can be used to detect TB disease or LTBI. Considering that the tests do not measure the same components of the immunological response, they are not interchangeable. The current comparison of TST & QFT-G assay result support that QFT-G assay provides more accurate results than TST in detection of LTBI. The result for the QFT-G assay and the TST in current study inward the overall sensitivity for detect of LTBI among patient.

Both tests should be used in conjugation with risk assessment, radiography and other medical and diagnostic evaluations. The QFT-GIT test can be especially useful and more specific than TST in detecting LTBI in developing countries, which has high BCG vaccination coverage. Screening and treatment of household contacts of active cases of pulmonary M. tuberculosis are important. Further research is necessary to improve the accuracy of QFT-GIT. Given that across most studies more than 95% of persons who

are IGRA positive do not progress to TB disease, emphasizes the need for biomarkers other than interferon gamma for risk prediction, or a combination of interferon gamma with risk factors (e.g. age, contact history, conversion) to enhance predictive value.

Conflict of interest: None declared

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