Original Article

Tuberculin Skin Test Pak Armed Forces Med J 2013; 63 (2): 231-234

FREQUENCY OF POSITIVE TUBERCULIN SKIN TEST IN BCG-VACCINATED ASYMPTOMATIC ADULTS IN PAKISTAN

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ABSTRACT

Objective: To determine the frequency of positive tuberculin skin test (TST) in BCG-vaccinated asymptomatic healthy Pakistani adults.

Study Design: Cross sectional study.

Place and Duration of Study: The study was carried out in Military Hospital, Rawalpindi in 2008 over six months.

Patients and Methods: One hundred and thirty six individuals fulfilling inclusion and exclusion criteria of study were recruited after consent. They were subjected to TST (Mantoux test) and results were interpreted after 72 hours of injection. Test was recorded as positive if the indurated area was ≥10 mm, and strongly positive if ≥ 15 mm.

Results: All participants were male with the mean age of 26.35±6.164 years. The overall frequency of positive TST was 41.2%. Out of these, 9.6% were strongly positive.

Conclusion: In healthy, BCG-vaccinated adult Pakistani population, TST is found to be positive in high frequency, and even induration of more than 15 mm was seen in significant number. In view of low specificity, TST should not be relied upon for the diagnosis of active tuberculosis (TB).

keywords: Tuberculosis, Tuberculin skin testing, Mantoux Test.

INTRODUCTION

Diagnosis of TB requires clinical suspicion duly supported by detection of acid fast bacilli (AFB) or presence of typical granulomas in the involved tissue. TST has a limited value in clinical work as positive TST is followed infrequently by the disease and a negative TST does not exclude active tuberculosis. After 6-8 weeks of acquiring infection, a person becomes reactive to TST[1]. Majority of infected individuals do not develop active TB, as their immune system contain the mycobacteria. These cases are said to have latent TB infection (LTBI) and have 5-10% risk of developing active TB in their lifetime[2]. Factors that can lead to false positive TST include previous BCG vaccination and infection with Non-tuberculous mycobacteria[3]. Interpretation of TST/ Mantoux test is not merely measuring the induration of the test site. Based on the sensitivity and specificity of the tuberculin skin test and the prevalence of TB in different groups, three cut-off levels of induration have been recommended by the American Thoracic Society and other study groups for defining a positive tuberculin reaction: >5 mm, ≥10 mm, and ≥15 mm of induration. For persons who are at highest risk for developing TB disease, induration of >5 mm is considered to be positive. These include immunosuppressed individuals like HIV infected and those on corticosteroids[4].

In our part of world, situation is quite complicated due to high prevalence of latent infection on one hand and vaccination of majority of population with BCG at birth and high prevalence of infection with atypical mycobacteria. In spite of these serious limitations, Mantoux test/ TST is being advised very frequently and patients are being offered or denied anti-tuberculosis treatment solely on the basis of TST and often in complete disregard to detection of

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Received: 30 Jan 2012; Accepted: 29 Aug 2012

mycobacterium or seeking of histological evidence. This trend needs to be curtailed. Present study is aimed to re-emphasize dubious efficacy of TST in the diagnosis of tuberculosis.

PATIENTS AND METHODS

This study was done in outpatient setting in Military Hospital after approval from ethical committee. Our subjects were only those who were declared medically fit either for induction in army or for United Nation missions abroad by the board of specialists after thorough medical examination and investigations including chest x-ray. One hundred and thirty six subjects, all males within the age bracket of 20-40 years, with the BCG vaccination scar on the skin over deltoid muscle were included in study after informed consent. All the individuals with any sort of respiratory symptoms, history of TB in the past, history of receiving TB treatment in the past, history of close contact with TB patient at home or work place, or evidence of extra-pulmonary TB of any site were excluded. One of the author was trained by consultant microbiologist in the technique of injecting PPD and in measuring the response. All the enrolled subjects were injected with PPD (Tubersol®, Aventis Pastuer Ltd, Toronto, Canada) intradermally in dose of 5 TU (0.1 mL) by Mantoux technique using insulin syringe at appropriate sites on mid-volar aspects of the forearm away from any previous skin lesion, subcutaneous vein and preferably, devoid of hair growth. The selected sites were cleaned with 70% iso-propanalol and allowed to air dry before inoculation. Formation of a clear whitish bleb measuring around 10mm was seen as a result of injection. Instructions were given to the patient to report back after three days for reading of test result. They were allowed to wash the infected site with plain water only. They were asked to avoid scratching of injection site and advised not to take any anti allergy drug for next three days. Results of testing were read after three days of PPD administration using a ballpoint pen method to demarcate area of induration. A calibration tailor's tape was used for the measurement of indurated area and recorded in millimeter (mm). A cut off value of 10 mm was selected for demarcation between positive and negative results. Measurements of 10mm or more were taken as 'Positive Mantoux test'. Measurement more than 15mm was recorded as strongly positive. All tests were performed by a single person to avoid inter-observer variations of test administration and interpretation.

RESULTS

All participants were male with mean age 26.35 years (SD ± 6.164). The overall frequency of tuberculin skin testing positivity was 41.2% (56 out of the 136 subjects) using the cutt-off value of 10 mm. Out of positive TST, 13 subjects, (9.6% of the total) were strongly positive (skin induration >15 mm).

DISCUSSION

In our part of the world TST has been and is still being used for diagnosis of active TB infection in spite of serious limitations. It is not uncommon to find that treatment has been started just on the basis of positive Mantoux test. Our study manifests that in a large proportion of BCG- vaccinated asymptomatic healthy individuals, TST is positive in the absence of active disease. Though there is large pool of infected cases along with treated and naturally healed cases of TB in our country, but this high frequency of TST positivity cannot be attributed to these factors alone. Other factors like previous BCG vaccination and exposure to NTM must be contributing significantly[5]. One of the limitations of our study is absence of female gender, as we recruited young healthy males. However, our study population is a representative sample of the general male population of that age in Pakistan. Moreover, the tested population came from all parts of Pakistan (urban, semi-urban, and rural) and

from all social strata. There are many studies worldwide on this issue. A similar study done on asymptomatic immigrants to Canada showed prevalence of positive TST of 38%[6], while another study done on Indian population gave prevalence of around 15% positive TST in healthy individuals[7]. The studies done on Hellenic and Italian army recruits gave a figure of 3.9% and 4% positive TST respectively[8,9]. A number of studies have been carried out on BCG vaccinated individuals to see its effect on TST reactivity. In a cross sectional study carried out in hospital employees in Spain, it was found that significant tuberculin reactions were more frequent among BCG-vaccinated (60%) than among non-vaccinated (29%) employees[10]. A meta-analysis of the evidence for the effect of BCG vaccination on tuberculin skin testing in subjects without active tuberculosis was performed. It concluded that immunization with BCG significantly increases the likelihood of a positive tuberculin skin test[11]. Result of TST has to be interpreted keeping in mind immune status of individual as well. Cut off for positive TST for HIV positive individuals differ from that for HIV negative[4] . A study on Ethiopian asymptomatic individuals revealed overall TST positivity of 66.2%, when considered individually it was 68.75% in HIV negative and 40.5% in HIV positive persons[12]. Our study lacks the assessment of sensitivity and specificity of TST in comparison with newer techniques especially Food and Drug Administration(FDA) approved Interferon-γ assay. Such comparisons have been made in many parts of the world. A study was done on children admitted in a rural hospital in India to compare the results of TST with IFN-γ assay and it concluded the IFN- assay was a better indicator of the risk of tuberculosis infection than TST in a BCG-vaccinated population[13]. During medical surveillance, it was found Phoenix firefighters had abnormally high rates of positive tuberculin skin test (TST) results. A study was carried out to evaluate them using IF-γ assay comparing the results to their TST results. IF-γ assay positivity was found to be much lower than TST positivity indicating a considerable false positive TST rate[14]. Another study done on firefighters of Mississippi fire department showed 9% of them to have a positive TST. All of them had a negative test when reconfirmed using IF-γ test. Same individual were again subjected to TST and this time TST positivity was only 2%, again making an unreliable test[15].

CONCLUSION

There is very high TST positivity in healthy, BCG-vaccinated adult Pakistani population, making this test practically ineffective tool in the diagnosis of active tuberculosis in our population.

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