Original Article

Role of tuberculin skin test in latent tuberculosis infection in HIV patients in a tertiary care hospital of India

Shital Patil, Mukund Phutane[1], Sanjay Mundkar[1]

Department of Pulmonary Medicine and [1]Department of Medicine, MIMSR Medical College, Latur, Maharashtra, India

ABSTRACT

Background: Human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome can affect the natural course of tuberculosis (TB) and pose diagnostic difficulties and may negatively affect the treatment due to frequent drug interactions in the advanced state of disease. Targeted tuberculin skin testing (TST) for latent tuberculosis infection (LTBI) identifies persons at high risk for TB who would benefit by treatment of LTBI, if detected. **Materials and Methods:** A prospective observational study conducted at the Department of Pulmonary Medicine and Department of Internal Medicine, MIMSR Medical College, Latur, India from November 2012 to October 2013 included all HIV-positive patients attending the outdoor department. A total of 100 HIV-positive patients subjected to TST were studied. The clinical presentation, CD4 count and tuberculin test result were studied. Chi-square test was applied to know the test of significance. **Results:** In this study of 100 patients, 48 were male, 52 were female and the male to female ratio was 0.92:1, with majority of the cases in the age group of 31-40 years. The mean age of the patients was 35.89 years. The most common mode of transmission of HIV infection was heterosexual in 93 patients (93%), blood transfusion in four patients (4%) and injections in three patients (3%). Of the 100 patients studied, 56 patients were TST negative (56%), whereas 44 patients were TST positive (44%). Of the 100 patients studied, 48 patients had a CD4 count of <200 cells/mm^3; of these 48 patients, 37 patients were TST negative and 11 patients were TST positive. **Conclusion:** TST reactivity varied directly and that of anergy inversely with absolute CD4 counts. TST should be correlated with CD4 count as indurations to protein purified derivative depend on CD4 count. TST in asymptomatic HIV cases, irrespective of CD4 count, would definitely guide regarding decision of chemoprophylaxis in LTBI. The role of TST in the decision to start chemoprophylaxis in LTBI should be considered cautiously in India, as the prevalence of both HIV and TB is high.

Key words: CD4 count, HIV, LTBI, Tuberculin skin test (TST)

Address for Correspondence:
Dr. Shital Patil,
Head, Pulmonary Medicine,
MIMSR Medical College, Latur,
Maharashtra, India.
E-mail: drsvpatil1980@gmail.com

Access this article online

Website: www.intern-med.com

DOI: 10.4103/2224-4018.141841

Quick Response Code:

INTRODUCTION

Tuberculosis (TB) is the most common human immunodeficiency virus (HIV)-related opportunistic infection in India, and caring for patients with both diseases is a major public health challenge. It is estimated that 60-70% of HIV-positive persons will develop TB in their lifetime.[1] Approximately 50% of the adult Indian population is infected with *Mycobacterium tuberculosis*, and the spread of HIV infection could lead to a potentially explosive increase in the number of cases of TB.[1]

About 1.8 million new cases of TB are occurring annually in India, whereas the pool of HIV-infected individual is quite large (~2.5 million). Therefore, there is always a propensity for deadly synergic interactions between HIV and TB.[2] HIV infections fuel tubercular epidemics in different ways. HIV infection is the most important known risk factor that favors progression to active TB from latent infection by suppressing the immune response against TB. Exogenous re-infection can also occur as HIV-infected individuals fail to contain new infections.

Although the prevalence of HIV infection among patients with TB ranges from 50% to 80% in many settings in sub- Saharan Africa, in other parts of the world it varies from 2% to 15%.[3] Studies from India have reported HIV seropositivity rates varying from 0.4% to 20.1%.[2] On the other hand, approximately 50% of the HIV-infected people in India are co-infected with *M. tuberculosis*, and approximately 200,000 of these co-infected persons will develop active TB each year in association with HIV infection.[4]

Tuberculin skin testing (TST) using protein purified derivative (PPD) has a lower sensitivity in diagnosing TB in patients with HIV infection than in other populations. Because the TST loses sensitivity with progressive immune suppression, induration of greater than or equal to 5 mm is considered positive in HIV-infected individuals. In one study, only 14% of HIV-infected drug users had a reaction of at least 5 mm induration to PPD, whereas 25% of HIV-seronegative drug users had a reaction of at least 10 mm induration. In addition, the sensitivity of the TST declines as CD4 cell levels fall. However, even in the setting of advanced HIV disease, almost half of the patients with active TB have a positive PPD, and the test maintains a high positive predictive value for the diagnosis of TB.[5]

Targeted tuberculin testing for latent tuberculosis infection (LTBI) identifies persons at high risk for TB who would benefit by treatment of LTBI, if detected. Persons at a high risk for TB have either been infected recently with *M. tuberculosis* or have clinical conditions that are associated with an increased risk of progression of LTBI to active TB.[6] Treatment of LTBI substantially reduces the risk of developing active TB in HIV-infected patients and has also been shown to reduce the mortality. The protection offered lasts for 2.5-3 years.[2]

There is lack of data regarding tuberculin testing and its application for the detection of latent TB in HIV-positive patients in developing countries. The present study is carried out to correlate TST reactivity and anergy with CD4 count so that it can be used for the early detection of TB in HIV-positive patients such that development of active TB can be prevented.

MATERIALS AND METHODS

The present study was a prospective, observational study conducted in the Department of Pulmonary Medicine and Department of Medicine, MIMSR Medical College, Latur, India from November 2012 to October 2013 to evaluate the role of the TST in HIV patients and to study its correlation with CD4 count. The study included 100 HIV-positive patients after satisfying the inclusion and exclusion criteria. Ethical committee approval was taken and the research project was approved by the Institutional Review Board.

Inclusion criteria

HIV positive without active TB or with prior history of TB and willing to participate in the study were enrolled in the study.

Exclusion criteria

HIV-negative person, patients having active TB, patient not willing to participate for study.

All the 100 HIV-positive patients fulfilling the inclusion criteria were studied and a detailed medical history of every patient included in the study was taken. History of fever, cough, breathlessness, weight loss, headache and oral and genital ulcer was taken. Detailed physical general examination and systemic examination of the patients were performed. Baseline data laboratory investigations like hemoglobin percentage (Hb%), total leukocyte count (TLC), differential leukocyte count (DLC), erythrocyte sedimentation rate (ESR), chest X-ray posterior-anterior (PA) view, serum bilirubin, alanine amniotransferase, serum creatinine, blood sugar and CD4 count were carried out.

Tuberculin test

The recommended method for the TST, the Monteux method, is performed by the intradermal injection of a standardized, stabilized dose of two tuberculin units of PPD. The PPD used in our study is prepared by the BCG Laboratory, Guindy, in Chennai, India, from a freeze-dried form of PPD RT23 with Tween 80 received from Staten's Serum Institute (SSI), Copenhagen. TST was carried out on the 1st visit with the help of a tuberculin syringe. The skin was prepared with an alcohol swab. With the needle bevel upward, the skin was punctured shallowly and 2 TU of PPD RT23 with Tween 80 and 6-10 mm tense wheal was raised upon injection of 0.1 mL intradermally into the flexor aspect of the left forearm and the site was marked with a pen. The patients were instructed not to wash the left forearm thoroughly with water and were advised to visit within 48-72 h for reading of the test. It was the induration that was measured, not the erythema, with the help of a vernial caliper. The extent of induration was measured 48-72 h later. Results were measured in millimeters, with >5 mm considered positive and <5 mm as negative.

The American Thoracic Society (ATS)/CDC guidelines (2000) for interpretation of the TST results state that a 5 mm induration is considered a positive result for individuals with HIV infection or other comparable

immunosuppression. In our study, we considered similar criteria to interpret TST in the participants.

Written consent was taken from all the study cases.

Statistical analysis was performed using the chi test.

OBSERVATION AND RESULTS

A total of 100 HIV-positive patients were subjected to the TST. The clinical presentation, CD4 count and TST result were studied. In gender distribution of the study cohort, males were 48 (48%) and females were 52 (52%), with a male to female ratio of 0.92:1. The most common age group of HIV infection was 31-40 years, and 38 patients (38%) were in this age group. The second common age group was 21-30 years, and 35 patients (35%) were in this age group, followed by the 41-50 years age group [16 patients (16%)]. One patient was in the age group of 18-20 years and 10 patients were in the age group of 51 years and above. The youngest patient was 19 years old and the oldest patient was aged 62 years. The mean age of the patients was 35.89 years. The most common mode of transmission of HIV infection was heterosexual in 93 patients (93%), blood transfusion in four patients (4%) and injections in three patients (3%).

In 100 study cases with asymptomatic HIV infection, 48% cases were having a CD4 count <200/mm^3, while 52% cases were having a CD4 count >200/mm^3 [Table 1].

In 100 study cases with asymptomatic HIV infection, 23% cases were showing no response to PPD, 33% cases were showing anergy to PPD while 44% cases were having induration more than 5 mm to PPD, i.e. positive TST [Table 2].

X axis — CD4 count/mm^3 Y axis — proportion of study subjects having indurations to PPD and results to it in color shades as shown.

As the CD4 count increases, indurations to PPD increase, and TST was positive in HIV cases with LTBI, while as the CD4 count decreases, HIV cases with LTBI had anergy to PPD and the TST was observed to be negative [Table 3].

The chi-square test was applied and the odds ratio was 0.17 (0.06-0.456), with an SD value of 16.45 at 95% CI. The test was statistically significant, with a *P*-value of 0.0001. In 83% of the cases with a CD4 count of <200, it was likely to get a negative tuberculin test [Table 4].

Table 1: Distribution of patients as per CD4 count

CD4 counts/mm^3	No. of patients (n = 100)	Percentage (%)
<200	48	48
201-300	34	34
301-400	7	7
401-500	4	4
501-600	2	2
>600	5	5

Table 2: Tuberculin skin test (TST) result

Tuberculin skin test induration reading (mm)	Number of patients (n = 100)	Percentage (%)
0 mm - no response	23	23
1-4 mm	33	33
5-9 mm	31	31
≥10 mm	13	13

Table 3: Bar diagram showing the tuberculin skin test (TST) result with CD4 counts

X axis — CD4 count/mm^3 Y axis — proportion of study subjects having indurations to PPD and results to it in color shades as shown

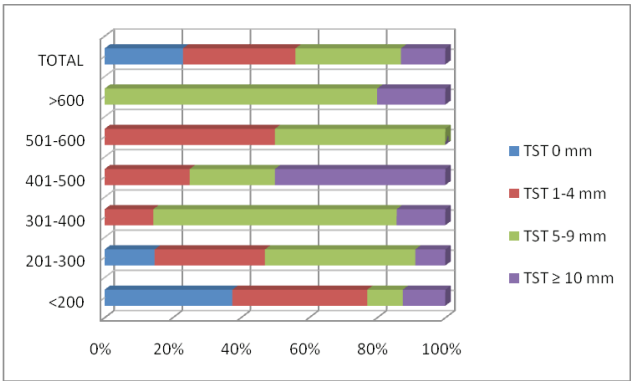

Table 4: Correlation of tuberculin skin test (TST) result with CD4 count

CD4 count/mm^3	TST$^+$	TST$^-$	Total
<200	11	37	48
>200	33	19	52
Total	44	56	100

P < 0.0001

DISCUSSION

There is lack of data regarding TST and its application for the detection of latent TB in HIV-positive patients in developing countries. The present study is carried out to correlate TST positivity with CD4 count so that it can be used for the early detection of TB in HIV-positive patients in order to prevent the development of active TB.

Age and gender distribution of the study cohort

In the present study, of a total of 100 asymptomatic HIV cases, 38 patients (38%) were in the age group

of 31-40 years, 35 patients (35%) were in the age group of 21-30 years, 16 patients (16%) were in the age group of 41-50 years, 10 patients (10%) were in the age group of 51 years and above and one patient was in the age group of 18-20 years. The mean age of the patients in our study was 35.89 years. Among the 100 patients studied, 48 (48%) were male and 52 (52%) were female. The male to female ratio was 0.92:1. MPS Sawhney *et al.*[7] observed that 51.43% of the patients in their study were in the age group of 31-40 years. Torpong Thongngarm *et al.*[8] documented the mean age of their patients to be 35.9 years, with a male to female ratio of 0.58:1, in their study. Peter A. Selwyn *et al.*[9] studied 900 patients with HIV infection and observed that the mean age of their patients was 36 years. S. Swaminathan *et al.*[10] in their study of 175 cases with HIV infection observed that 43% of the male patients in their study were in the age group of 31-40 years, whereas 76% of the female patients were in the age group of 21-30 years, with a male to female ratio of 0.49:1.

Mode of transmission

In the present study, the heterosexual mode was the most predominant mode of transmission of HIV infection observed in 94 (94%) cases. Other modes of transmission were the homosexual mode in three (3%) cases, blood transfusion in two cases (2%) and intravenous drug abuse in one (1%) case. Uzgare *et al.*[11] reported the sexual route of transmission in 93.02% cases, blood transmission in 2.32% cases and other modes in 4.64% cases in their study cases. Christina A. Menezes *et al.*[12] documented the heterosexual route of transmission in 72.6% cases, homosexual route of transmission in 7.7% cases, blood transmission in 5% cases, intravenous drug abuse in 3.3% cases and other routes in 1.4% cases in their study. N. Kumarswamy *et al.*[13] observed the heterosexual route of transmission in 94.8% cases, blood transfusion route in 3.2% cases, intravenous drug abuse route in 0.3% cases and other routes in 1.7% cases in their study. Ajith Sivadasan *et al.*[14] reported the heterosexual route of transmission in 98.7% cases, the homosexual route in 0.43% cases and blood transfusion in 0.86% cases in their study.

Distribution of cases in the study cohort as per CD4 count

In the present study, 48 patients (48%) had a CD4 count less than 200/mm^3, 34 patients (34%) had a CD4 range of 201-300/mm^3, seven patients (7%) had a CD4 range of 301-400/mm^3, four patients (4%) had a CD4 range of 401-500/mm^3, two (2%) patients had a CD4 range of 501-600/mm^3 and five (5%) patients had a CD4 range of more than 600/mm^3. The mean CD4 count was 231.88, with a standard deviation of 109.54. Other studies carried out by different authors have similar findings. Bernard J. Ngowiet *et al.*[15] observed 213 HIV-positive patients not having TB: 72 patients (33.8%) had a CD4 count of less than 200 cells/m^3, 48 patients (22.5%) had a CD4 count of 200-349 cells/mm^3, 36 patients (16.9) had a CD4 count of 350-500 cells/mm^3 and 57 patients (26.8) had a CD4 count of more than 500 cells/mm^3, with a mean CD4 count of 355 cells/mm^3. Ma.de lourdes Garcia-Garcia *et al.*[16] studied 801 HIV-positive subjects: 309 patients had a CD4 count of less than 200 cells/mm^3 and 325 patients had a CD4 count of 200 to less than 500 cells/mm^3, whereas 167 patients had a CD4 count of more than 500 cells/mm^3. Stephen P. Blatt *et al.*[17] subjected 889 HIV-positive patients to delayed-type hypersensitivity testing in their study and found that 64 patients had a CD4 count of less than 200 cells/mm^3, 104 patients had a CD4 count of 201-400 cells/mm^3, 214 patients had a CD4 count of 401-600 cells/mm^3, 241 patients had a CD4 count of 601-800 cells/mm^3 and 266 patients had a CD4 count of more than 800 cells/mm^3. Molebogeng Xheeda Rangaka *et al.*[18] observed asymptomatic 74 HIV-positive patients in their study, and found that 16 patients had a CD4 count of less than 200 cells/mm^3, 27 patients had a CD4 count of 200-349 cells/mm^3 and 30 patients had a CD4 count of 350-499 cells/mm^3, with a mean CD4 count of 392 cells/mm^3. R. Teck *et al.*[19] in their study studied 457 HIV-positive patients of whom 316 patients had a CD4 count of less than 200 cells/mm^3, 97 patients had a CD4 count of 200-350 cells/mm^3 and 44 patients had a CD4 count of more than 350 cells/mm^3.

Distribution of cases in the study cohort as per the TST result

In the present study, of a total of 100 asymptomatic HIV study cases, 56 (56%) study cases were TST negative and 44 (44%) patients were TST positive. Detailed analyses are as follows: 23 patients (23%) were anergic (no response was found), 33 patients (33%) had TST indurations of 1-4 mm, 31 patients (31%) were TST positive (i.e., indurations of 5-9 mm) and 13 patients (13%) were TST strongly positive (i.e., indurations of ≥10 mm). These finding are similar with other studies. MPS Sawhney *et al.*[7] studied the pattern of TST results in 523 newly diagnosed HIV-positive patients. They found that 349 patients (66.73%) had a TST result of 0-4 mm, 56 patients (10.71%) had a TST result of 5-9 mm and 118 patients (22.56%) had a TST result of ≥10 mm. One hundred and seventy-four patients had a positive TST result whereas 349 patients had a negative TST result. Ma.de lourdes Garcia-Garcia *et al.*[16] found that among 801 HIV-positive subjects, 174 patients (22%) had a PPD cut-off level of more than 10 mm, 261 patients (32.6%) had a PPD cut-off level of more than 5 mm and 296 patients (37%) had a PPD cut-off level of more than 2 mm. Santiago Moreno *et al.*[20] assessed the risk of development of TB among anergic patients infected with HIV. They studied 374 patients and found that 108 patients

(29%) had a PPD-positive result of >5 mm, 154 patients (41%) had a PPD-negative result but no skin anergy and 112 patients (30%) were anergic. Belete Tegbaru *et al.*[21] studied 116 HIV-positive subjects and found that the TST result was positive (>5 mm) in 47 patients (40.5%) and negative (<4 mm) in 69 patients (59.5%).

Correlation of TST result with CD4 count

Of the 100 patients studied, we observed that 48 patients had a CD4 count of <200 cells/mm^3; 18 (37.5%) of them had no response to PPD and the TST results were negative with indurations of 0 mm; 19 (39.5%) of them had TST-negative results with indurations of 1-4 mm to PPD; five (10.4%) of them had TST-positive results with indurations of 5-9 mm to PPD; and six (12.5%) of them had TST-positive results with indurations of ≥10 mm ($P < 0.0001$). Norman Markowitz *et al.*[22] studied a total of 1171 HIV patients without acquired immunodeficiency syndrome (AIDS), and found that the prevalence of anergy increased as the CD4 count decreased; the prevalence of anergy was 25.5% in persons with at least 600 CD4 lymphocytes/mm^3 and 72.0% in those with fewer than 200 CD4 lymphocytes/mm^3 ($P < 0.001$). Stephen P. Blatt *et al.*[17] evaluated the prognostic significance of cutaneous delayed-type hypersensitivity (DTH) skin testing in persons infected with HIV and found that the mean CD4 counts are lower for anergic compared with non-anergic patients and for patients responding to a single control skin test compared with those responding to two or more skin tests ($P < 0.05$). The DTH skin test response at first evaluation was also found to predict progression to AIDS. Ma.de lourdes Garcia-Garcia *et al.*[16] correlated the TST result with CD4 count, and found that among 309 patients with a CD4 count of <200, 47 (15.2%) patients were PPD reactive. B.D. Dalal *et al.*[23] studied the value of TST in HIV-positive patients and co-related it with CD4 count, finding that in patients with TST <5 mm, the mean CD4 count was 163.59 in patients without TB.

Of the 100 patients studied, we observed that 41 patients had a CD4 count in the range of 201-400 cells/mm^3; five (12.2%) of them had no response to PPD and the TST results were negative with indurations of 0 mm; 12 (29.3%) of them had a TST-negative result with indurations of 1-4 mm to PPD; 20 (48.8%) of them had a TST-positive result with indurations of 5–9 mm to PPD; and four (9.7%) of them had a TST-positive result with indurations of ≥10 mm. MPS Sawhney *et al.*[7] examined the pattern of TST results in 523 newly diagnosed HIV-positive patients. They found that the average CD4 count was 229.07 in 41 cases with a TST result of 0 mm, 409.50 in two cases with a TST result of 1-4 mm, 264.50 in eight cases with a TST result of 5-9 mm and 317 in 12 cases with a TST result of ≥10 mm. Ma.de lourdes Garcia-Garcia *et al.*[16] correlated the TST result with CD4 count and found that among 325 patients with a CD4 count in the range of >200 to <500, 120 (37%) patients were PPD reactive. B.D. Dalal *et al.*[23] studied the value of TST in HIV-positive patients and correlated it with CD4 count, and observed that the expected CD4 count range for patients without TB is 75-230 and 230-650 for TST <5 mm and TST ≥5 mm.

Of the 100 patients studied, we observed that 11 patients had a CD4 count in the range of >400 cells/mm^3, two (18.2%) of them had a TST-negative result with indurations of 1-4 mm to PPD, six (54.5%) of them had a TST-positive result with indurations of 5-9 mm to PPD and three (27.3%) of them had a TST-positive result with indurations of ≥10 mm. Norman Markowitz *et al.*[22] studied a total of 1171 HIV-seropositive patients without AIDS, and found that the tuberculin PPD reactivity was lower among HIV-seropositive persons with CD4 levels of fewer than 400 cells/mm^3 than among HIV-seronegative persons ($P < 0.001$). However, the prevalence of tuberculin reactivity in HIV-infected participants with 400 or more CD4 cells/mm^3 was similar to that in persons without HIV infection ($P > 0.2$). Reduction in the prevalence of PPD reactivity was accompanied by a corresponding increase in anergy. Anergy was more prevalent in HIV-seropositive than in HIV-seronegative participants overall ($P < 0.001$). Stephen P. Blatt *et al.*[17] evaluated the prognostic significance of cutaneous DTH skin testing in persons infected with HIV and found that patients with more than 400 CD4 cells/mm^3 were more likely than those having fewer than 400 CD4 cells/mm^3 to respond to at least one (94% compared with 67%, $P < 0.001$) or at least two (86% compared with 45%, $P < 0.001$) DTH skin tests. Ma.de lourdes Garcia-Garcia *et al.*[16] correlated the TST result with CD4 count and found that among 167 patients with CD4 counts of >500, 94 (56%) patients were PPD reactive. B.D. Dalal *et al.*[23] studied the value of TST in HIV-positive patients and correlated it with CD4 count, observing in patients with TST >5 mm a mean CD4 count of 486.50. They concluded that in developing countries, it is difficult to perform CD4 counts due to its cost and unavailability; TST can be utilized as a good marker to check the immunosuppression status and to diagnose TB in HIV-positive patients.

Other important observations during the study

1. During the entire study duration of 1 year, we subsequently followed all the cases of HIV irrespective of CD4 count and TST results, either positive or negative, for the development of active pulmonary TB. We observed that of the total of 100 asymptomatic HIV patients, four cases developed active pulmonary TB during the 1 year follow-up. Earlier, during the TST evaluation of these four cases, we observed that one was anergic to TST and developed military TB, one was

TST negative (<5 mm indurations) and showed bilateral lower lobe TB and two cases showed TST indurations 5-9 mm and had upper lobe TB. Study subjects with TST >10 mm indurations were also re-analyzed and active TB was not observed in any of the cases at the end of the study period. The rationale for not developing active pulmonary TB in those found to be TST positive with indurations >10 mm may be because of preserved immune function, which protects them from developing active disease in such an early phase of HIV infection.

2. We offered them anti tuberculosis treatment (ATT) as per the national protocol and started on four drugs — Isoniazid, Rifampicin, Pyrazinamide and Ethambutol — continued for 6 months; the initial outcome was satisfactory as all of those cases were showing bacteriological smear conversion and radiological recovery at the end of the intensive phase. The final outcomes in the form of cure are awaited, which is to be confirmed by bacteriological smear examination and radiological evaluation.

Issues that need further evaluation and more studies, especially in a high TB–HIV burden setting

Should we consider chemoprophylaxis to all asymptomatic HIV cases irrespective of CD4 count?

Should we start chemoprophylaxis to all asymptomatic HIV subjects with TST results showing indurations >5 mm, as all such cases in the developed world or low TB-HIV prevalence settings receive Isoniazid chemoprophylaxis for LTBI.

If we need to consider Isoniazid chemoprophylaxis for LTBI in asymptomatic HIV subjects, for long a duration should it be given? Should it be a standardized 6-month or extended therapy as given in the Botswana trial for up to 5 years, which was conducted in high-burden settings.

Lastly, if we start Isoniazid prophylaxis in LTBI cases with asymptomatic HIV, is the response uniform in a country like India, because the drug resistance survey (DRS) suggested a prevalence of 10% Isoniazid monoresistance in the community. Also, does it will work as monotherapy? Or, will it worsen the existing Isoniazid resistance in the community with a high TB burden setting like India?

Reasonable explanation for all the above mentioned issues

As India is a high TB disease burden country, the chances of having recent infection is much more common than progression of the underlying LTBI or reactivation of TB. This is a very important issue to consider by all health care professionals as recent infection or recurrent reinfection is the vital mode of development of active pulmonary TB in developing countries, including India, in HIV subjects. The mentioned fact is very rare in the developed world and reactivation of LTBI is the predominant mode of active pulmonary TB in HIV subjects.

Hence, before considering chemoprophylaxis in a high-burden setting, one should consider the duration and dosages of drugs chosen for it. After all, chemoprophylaxis will not provide the maximum best possible protection for TB with established high Isoniazid resistance. The possibility should be considered that subjects with an already immunecompromised status due to HIV infection will again become virgin to catch new tuberculous infection as soon as chemoprophylaxis is completed in countries with a high TB-HIV burden setting like India.

CONCLUSION

TST reactivity varied directly and that of anergy inversely with absolute CD4 counts. Tuberculin testing should be correlated with CD4 count as induration to PPD depends on CD4 count. Tuberculin testing in asymptomatic HIV cases, irrespective of CD4 count, would definitely guide regarding the decision of chemoprophylaxis in LTBI. The role of tuberculin testing in decision to start chemoprophylaxis in LTBI should be considered cautiously in India, as prevalence of both HIV and TB is high. As compared with reactivation, chances of recurrent reinfection is the predominant mode of acquiring infection and development of active pulmonary TB in a high-burden country like India mandates careful interpretation of tuberculin testing and treatment of LTBI accordingly. Always rule out active pulmonary TB by all best possible measures before taking a decision to start chemoprophylaxis for LTBI, as it would decrease both the disease burden and the rising trends of multiple drug resistance.

REFERENCES

1. Swaminathan S, Ramachandran R, Bhaskar R, Ramanathan U, Prabhakar R, DaTSTa M, *et al*. Risk of development of tuberculosis in HIV-infected patients. Int J Tuberc Lung Dis 2000;4:839-44.
2. Sharma SK, Mohan A, Kadhiravan T. HIV-TB co-infection: Epidemiology,diagnosis and management. Indian J Med Res 2005;121:550-67.
3. World Health Organization (WHO) Global tuberculosis control: Surveillance, planning, financing-WHO report 2009. Chapter1, Epidemiology. Document WHO/HTM/TB/2009.411. Available from: hTSTp://www.who.int/tb/publications/global_report/2009 [Last accessed on 2013 Sep 16].
4. Khatri GR, Frieden TR. Controlling tuberculosis in India. N Engl J Med 2002;347:1420-5.
5. Fishman AP, Elias JA. Fishman JA, Grippi MA, Senior RM, Pack AL, Editors. Fishman's Pulmonary Diseases and Disorders. 4th ed. New York: McGraw-Hill; 2008. p. 2490.
6. Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection; American Thoracic Society. MMWR June 09, 2000 / 49(RR06); 1-54.

7. Col SawhneyP, Maj Gen Sharma YK. Significance of Tuberculin Testing in HIV Infection: An Indian Perspective. Med J Armed Forces India 2006;62:104-7.
8. Thongngarm T, Valyasevi AM, Pattanapanyasat K, Udompunturak S. Delayed Hypersensitivity Skin Testing in the Thai Adult Population. J Med Assoc Thai 2006;89 Suppl 5:S195-200.
9. Selwyn PA, Sckell BM, Alcabes P, Friedland GH, Klein RS, Schoenbaum EE. High risk od active tuberculosis in HIV infected drug users with cutaneous anergy. JAMA 1992;268:504-9.
10. Swaminathan S, Ramachandran R, Baskaran G, Paramasivan CN, Ramanathan U, Venkatesan P, *et al*. Risk of development of tuberculosis in HIV-infected patient. Tuberculosis Research Centre, Indian Council of Medical Research, Chengalput, Chennai, India. Int J Tuberc Lung Dis 2000;4:839-44.
11. Uzgare R. Mode of transmission, of HIV in Mumbai (India) as per data collected in a private HIV/AIDS clinic. Int Conf AIDS 2000;13:abstract no. TuPeC3369.
12. Pádua CA, César CC, Bonolo PF, Acurcio FA, Guimarães MD. Self-reported adverse reactions among patients initiating antiretroviral therapy in Brazil. Braz J Infect Dis 2007;11:20-6.
13. Kumarsamy N, Venkatesh KK, Cecelia AJ, Devaleenal B, Lai AR, Saghayam S, *et al*. Spectrum of Adverse Events After Generic HAART in Southern Indian HIV-Infected Patients. Aids Patient Care STDs 2008;22:337-44.
14. Sivadasan A, Abraham OC, Rupali P, Pulimood SA, Rajan J, Rajkumar S, *et al*. High rates of regimen change due to drug toxicity among a cohort of South Indian adults with HIV infection initiated on generic, first-line antiretroviral treatment. J Assoc Physicians India 2009;57;384-9.
15. Ngowi BJ, Mfinanga SG, Bruun JN, Morkve O. Pulmonary tuberculosis among people living with HIV/AIDS attending care and treatment in rural northern Tanzania. BMC Public Health 2008;8:341.
16. García-García ML, Valdespino-Gómez JL, García-Sancho C, Mayar-Maya ME, Palacios-Martínez M, Balandrano-Campos S, *et al*. Underestimation of Mycobacterial tuberculosis in HIV-infected subjects using reactivity to tuberculin and anergy panel. Int J Epidemiol 2000;29:369-75.
17. Blatt SP, Hendrix CW, Butzin CA, Freeman TM, Ward WW, Hensley RE, *et al*. Delayed-type hypersensitivity skin testing predicts progression to AIDS in HIV-infected patients. Ann Intern Med 1993;119:117-84.
18. Rangaka MX, Wilkinson KA, Seldon R, Van Cutsem G, Meintjes GA, Morroni C, *et al*. Effect of HIV-1 infection on T-cell–based and skin test detection of tuberculosis infection. Am J Respir Crit Care Med 2007;175:514-20.
19. Teck R, Ascurra O, Gomani P, Manzi M, Pasulani O, Kusamale J, *et al*. WHO clinical staging of HIV infection and disease, tuberculosis and eligibility for antiretroviral treatment: Relationship to CD4 lymphocyte counts. Int J Tuberc Lung Dis 2005;9:258-62.
20. Moreno S, Baraia-Etxaburu J, Bouza E, Parras F, Perez-Tascon M, Miralles P, *et al*. Risk for developing tuberculosis among anergic patients infected with HIV. Ann Intern Med 1993;119:194-8.
21. Tegbaru B, Wolday D, Messele T, Legesse M, Mekonnen Y, Miedema F, *et al*. Tuberculin Skin Test Conversion and Reactivity Rates among Adults with and without Human Immunodeficiency Virus in Urban Settings in Ethiopia. Clin Vaccine Immunol 2006;13:784-9.
22. Markowitz N, Hansen NI, Wilcosky TC, Hopewell PC, Glassroth J, Kvale PA, *et al*. Tuberculin and anergy testing in HIV-Seropositive and HIV-Seronegative person. Ann Intern Med 1993;119:185-93.
23. Dalal BD, Garg P, Dalal P, Desai H, Sheth S, Patel R. Tuberculin test- A good tool in HIV positive patient. J Allerg Clin Immunol 02/2003;111(1):S 226.

How to cite this article: Patil S, Phutane M, Mundkar S. Role of tuberculin skin test in latent tuberculosis infection in HIV patients in a tertiary care hospital of India. J Transl Intern Med 2014;2:136-42.

Source of Support: NIL, **Conflict of Interest:** NIL.