

## Latent Tuberculosis in Psoriasis Patients Planned for Systemic Therapy – A Prospective Observational Study

### Abstract

**Background:** India has a high prevalence of tuberculosis and latent tuberculosis infection (LTBI) is common in the general population. LTBI can progress to active tuberculosis in almost 10% patients and the risk increases with immunosuppression. This predisposes patients of psoriasis on systemic therapy for the development of active tuberculosis. **Aims:** To find the prevalence of LTBI in patients with psoriasis planned for systemic therapy. **Methodology:** It was a prospective observational study conducted in a tertiary care center during period Jan-Dec 2019. Patients older than 18 years with chronic plaque psoriasis planned for systemic therapy and willing to be part of the study were included. Baseline clinical data were collected. Radiograph of chest and tuberculin skin test (TST) was performed in all patients. Detailed evaluation including sputum examination and computed tomography of the chest and abdomen were performed in patients with TST >10 mm. **Results:** A total of 105 patients met the inclusion criteria of the study, with the mean age of patients being  $29.5 \pm 2.12$  years. Out of these patients, 58 were males and 47 females. The mean duration of psoriasis was  $2.95 \pm 1.3$  years. The mean PASI score was  $16.71 \pm 4.384$ . Mantoux was positive (>10 mm) in 33 (31.42%) patients. Two patients were found to have features of active tuberculosis based on imaging and microbiological investigations. Totally, 31 (29.5%) patients had LTBI and were treated with isoniazid and rifampicin for three months while 2 (1.9%) patients were treated with four drugs antitubercular regimen. **Limitations:** Small sample size, convenience method of sampling and study population limited to those visiting medical college hospital are its major limitations. **Conclusion:** LTBI is common in study population and screening for LTBI should be performed in all patients of psoriasis planned for systemic therapy. A thorough search for active tuberculosis should be performed. Timely detection of LTBI helps in the prevention of development of active tuberculosis in the patients on immunosuppressive treatment.

**Keywords:** Latent tuberculosis infection, LTBI, psoriasis, systemic therapy

### Introduction

Latent tuberculosis (LTBI) is defined as a state of the persistent immune response to stimulation by Mycobacterium tuberculosis antigens with no evidence of clinically manifest active TB. The diagnosis of LTBI is based on tuberculin skin test (TST) or interferon-gamma release assay (IGRA) with the absence of symptoms of active tuberculosis and signs on the chest radiograph. There is no gold standard test for the diagnosis of LTBI. The prevalence of LTBI has regional and community variation.<sup>[1]</sup> In countries with a low prevalence of tuberculosis, the prevalence of LTBI is approximately 8-10%, while in high endemic zones the prevalence of LTBI is up to 40-45%.<sup>[2]</sup> In health care workers, the prevalence of LTBI is even higher and

pooled prevalence is 57% in one study.<sup>[3]</sup> The detection of LTBI is important as it can progress to active tuberculosis in almost 10% of patients. The risk of progression to active tuberculosis in human immunodeficiency virus (HIV) infected patient is 10% per year.<sup>[4]</sup> Immunosuppressive treatment can result in the transformation of latent tuberculosis to active form and screening for LTBI should be done before initiation of systemic therapy with methotrexate, cyclosporine or biologics. We performed this study to find out the prevalence of latent tuberculosis in patients of psoriasis planned for systemic therapy in a tertiary care center in western Maharashtra.

### Methodology

It was a prospective observational study conducted in a tertiary care center during

**Shekhar Neema,  
S. Radhakrishnan,  
Disha Dabbas<sup>1</sup>,  
Biju Vasudevan**

*Department of Dermatology,  
AFMC, Pune, Maharashtra,  
<sup>1</sup>Department of Dermatology,  
Command Hospital (WC),  
Chandimandir, Chandigarh,  
India*

**Address for correspondence:**  
Dr. Disha Dabbas,  
Department of Dermatology,  
Command Hospital (WC),  
Chandimandir, Chandigarh,  
India.  
E-mail: dishadabbas@gmail.com

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the study period Jan 19 to Dec 19. Institutional ethical committee clearance was obtained. Patients more than 18 years of age with chronic plaque psoriasis planned for systemic therapy and willing to be part of the study were included in the study. Patients with erythrodermic psoriasis where performing Mantoux test was not feasible, patients with HIV infection, patient with previously treated tuberculosis, features of active tuberculosis on history and clinical examination or already on immunosuppressant treatment were excluded from the study.

Baseline clinical data were recorded. The severity assessment was performed with PASI and, history of tuberculosis in past or family were recorded. History of active tuberculosis (cough, fever, night sweats, and weight loss), diabetes, hypertension, harmful use of alcohol was noted. As a part of protocol we perform complete blood count, erythrocyte sedimentation rate, radiograph of chest and Mantoux test, renal and liver function test, blood sugar fasting and post-prandial, hepatitis B, C, and HIV serology in all patients prior to starting systemic therapy. Computed tomography scan of chest and abdomen was advised to rule out active tuberculosis in patients with Mantoux positivity.

Mantoux test was performed with 0.1 ml (5 unit) of purified protein derivative (PPD), intradermally in the volar aspect of left forearm with the help of tuberculin syringe to produce a wheal of 6–10 mm in diameter. The reaction is measured in mm of induration, across the forearm (perpendicular to the long axis) after 48-72 hours. A measurement of 10 mm or more was considered positive. Latent tuberculosis was diagnosed based on Mantoux positivity and absence of features of active tuberculosis on clinical examination and radiography of chest. Isoniazid and rifampicin were administered in an appropriate dosage to patients with LTBI for three months.

The data was entered in Microsoft Excel™. The categorical data is presented as percentage and quantitative data as mean or median depending on skewness of data. SPSS ver 24 was used for analysis, Chi-square analysis and t test were performed where appropriate. *P* value of less than 0.05 was considered statistically significant.

## Results

A total of 105 patients met the inclusion criteria of the study, with the mean age of patients being  $29.5 \pm 2.12$  years. Out of these patients, 58 were males and 47 females. The mean duration of psoriasis was  $2.95 \pm 1.3$  years. The mean PASI score was  $16.71 \pm 4.384$ . Baseline clinical features have been tabulated in Table 1. Baseline characteristics including co-morbidities seen in patients diagnosed as LTBI is compared with non-LTBI group and is tabulated in Table 2. The 2 patients diagnosed as active tuberculosis have been omitted from either group for analysis.

Mantoux was positive (>10 mm) in 33 (31.42%) patients. HIV serology was negative in all patients. Radiograph

**Table 1: Basic clinical parameters and investigations in study population**

Parameter	Value (n=105)
Age (mean±SD)	29.5±2.12 years
Sex (M:F)	1.23 (58:47)
Duration of disease	2.35±1.3 years
Psoriasis assessment severity index (PASI)	16.71±4.384
TST positive (>10 mm)	33 (31.42%)
Abnormal chest X ray	5 (4.3%) (1- active tuberculosis; 4 - old, healed infection)

**Table 2: Baseline characteristics of patients**

Parameter	LTBI group (n=31)	Non- LTBI group (n=72)	<i>P</i>
Age (mean±SD) years	43 (±6.3)	44 (±7.7)	0.737
Sex (M:F)	17:14	39:33	
BMI (kg/m <sup>2</sup> )	24.73 (±5.3) kg/m <sup>2</sup>	26.64 (±0.5)	0.86
PASI (mean±SD)	16.4 (±6.43)	16.74 (±4.38)	0.95
Diabetes	3	11	0.44
Hypertension	2	8	0.48
Alcohol abuse	3	13	0.28

chest was abnormal in 5 (4.7%) patients and was reported as normal in rest. The features of active tuberculosis were seen in one patient while in rest it was reported as old infective pathology. After radiograph chest and Mantoux, 32 (30.47%) patients were diagnosed as latent tuberculosis and one (0.95%) patient as active tuberculosis. CT scan chest and abdomen was advised to all patient who had a positive Mantoux test. 26 out of 32 (81%) patients underwent CT scan and positive findings were seen in 8 (30.7%) patients. One patient showed features of active tuberculosis. All 33 patients underwent diagnostic evaluation of sputum for MTB and were found positive in one patient who also had positive findings on chest radiograph. After complete investigations, 2 (1.9%) patients were diagnosed as active tuberculosis based on imaging and microbiology and were treated with antitubercular drugs as per national guidelines. These patients did not have any clinical features of active tuberculosis. (fever, night sweats, cough, and weight loss). 31 (29.5%) patients were diagnosed as LTBI and treated with isoniazid and rifampicin for three months. Serial serum bilirubin and transaminase level were done on day 14, 30, 60, and 90. None of the patient showed any adverse effect requiring treatment termination.

## Discussion

Tuberculosis is an infectious disease caused by Mycobacterium tuberculosis. Tubercle bacilli remain latent in a large percentage of population specially in the high endemic area, which serves as a pool for transformation to active tuberculosis depending on the host factors. Psoriasis patients requiring systemic immunosuppressant

are at higher risk than the general population for the development of active tuberculosis. These patients should be screened for LTBI before starting systemic therapy like methotrexate, cyclosporine or biologic treatment. Tuberculin skin test (TST) is used for screening however, TST is not an ideal test for detection of LTBI as false positive test can be seen with previous BCG vaccination and infection with non-tuberculous mycobacteria (NTM). Interferon-gamma release assay (IGRA) is more specific and does not have these drawbacks, however, it is expensive as compared to TST.<sup>[5]</sup> World Health Organisation (WHO) guidelines suggest either TST or IGRA for the diagnosis of LTBI.<sup>[6]</sup> The cut-off measurement for diagnosis of LTBI varies between different population and considered as 5, 10 or 15 mm in patients with high, intermediate or low risk respectively. We considered cut off of 10 mm as the prevalence of tuberculosis is high in our country and patients with immunosuppressive are at higher risk of developing tuberculosis. TST cut-off of 10 mm also precludes the effect of BCG vaccination or NTM infection. BCG vaccination performed 10 years prior has minimal effect on results of TST.<sup>[7]</sup> In our study, we have included adult patients with psoriasis and since BCG vaccination is performed in infancy in our country; it is unlikely to affect TST positivity rates. National Psoriasis Foundation (NPF) guidelines advise screening for active tuberculosis and LTBI using clinical history, radiograph of chest and TST.<sup>[8]</sup> Centre for disease control (CDC) also recommends chest radiography to rule out active tuberculosis in patient with positive Mantoux test and patient with abnormal radiograph chest finding should undergo diagnostic sputum evaluation.<sup>[7]</sup> There are no clear guidelines on investigations for active tuberculosis in patients who are Mantoux positive. In high burden countries, Mantoux test is not used for diagnosis of active tuberculosis except in children, however, active tuberculosis should be ruled out before starting treatment for LTBI as it can result in incomplete treatment and drug resistance. We advised sputum testing and CT scan of chest and abdomen to rule out active tuberculosis in patients who were Mantoux positive. In our study, we found 2 patients with active tuberculosis out of which one was diagnosed on chest radiograph and sputum microscopy and another patient on CT scan chest. In Spanish psoriasis registry, the prevalence of LTBI was 22.3% and a chest radiograph was positive in 1.1% patients.<sup>[9]</sup> We performed CT scan apart from sputum evaluation as it has high sensitivity and specificity for the diagnosis of pulmonary tuberculosis and also helps in the diagnosis of extra-pulmonary tuberculosis.

Treatment of LTBI prevents up to 60–70% patients from developing active tuberculosis; however, a patient may develop active tuberculosis despite prophylaxis especially with TNF inhibitors and patient should be followed up regularly. American thoracic society recommends 9 months of isoniazid treatment for LTBI.<sup>[10]</sup> WHO recommends

isoniazid monotherapy for 9 months or isoniazid-rifampicin for 3–4 months as an alternative treatment.<sup>[6]</sup> Rifampicin-pyrazinamide combination for the treatment of LTBI is not recommended because of unacceptable liver toxicity. Isoniazid-rifampicin combination is likely to have better compliance, hence we used this combination in our patients. None of our patients had any significant adverse effect to this treatment. The treatment of psoriasis with immunosuppressive systemic therapy should begin at least 1–2 months after starting prophylactic treatment. In patients with active tuberculosis, anti-tubercular treatment should be completed before initiation of immunosuppressive systemic treatment.

Small sample size, convenience sampling and use of Mantoux test for detection of LTBI are some limitations of the study. The study was conducted in a tertiary care center catering to low socio-economic strata that may prevent generalization of these findings.

## Conclusion

Screening for LTBI should be performed in patient planned for systemic therapy for psoriasis. It may prevent development of active tuberculosis in patients who are on long-term immunosuppressive treatment.

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## Conflicts of interest

There are no conflicts of interest.

## References

1. Nuermberger E, Bishai WR, Grosset JH. Latent tuberculosis infection. *Semin Respir Crit Care Med* 2004;25:317-36.
2. Kashyap RS, Nayak AR, Gaherwar HM, Husain AA, Shekhawat SD, Jain RK, *et al.* Latent TB infection diagnosis in population exposed to TB subjects in close and poor ventilated high TB endemic zone in India. *PLoS One* 2014;9:e89524.
3. Kinikar A, Chandanwale A, Kadam D, Joshi S, Basavaraj A, Pardeshi G, *et al.* High risk for latent tuberculosis infection among medical residents and nursing students in India. *PLoS One* 2019;14:e0219131.
4. Salgame P, Geadas C, Collins L, Jones-López E, Ellner JJ. Latent tuberculosis infection--Revisiting and revising concepts. *Tuberculosis (Edinb)* 2015;95:373-84.
5. Auguste P, Tsertsvadze A, Pink J, Court R, McCarthy N, Sutcliffe P, *et al.* Comparing interferon-gamma release assays with tuberculin skin test for identifying latent tuberculosis infection that progresses to active tuberculosis: Systematic review and meta-analysis. *BMC Infect Dis* 2017;17:200.
6. WHO | Latent TB Infection: Updated and consolidated guidelines for programmatic management [Internet]. [Last cited on 2020 Aug 28]. Available from: <https://www.who.int/tb/publications/2018/latent-tuberculosis-infection/en/>.
7. CDC. Guide for primary health care providers: Targeted tuberculin testing and treatment of latent tuberculosis infection. Available from: [www.cdc.gov/tb/pubs/LTBI/pdf/TargetedLTBI05.pdf](http://www.cdc.gov/tb/pubs/LTBI/pdf/TargetedLTBI05.pdf). [Last accessed on 2020 Aug 28].

8. Doherty SD, Van Voorhees A, Lebwohl MG, Korman NJ, Young MS, Hsu S, *et al.* National Psoriasis Foundation consensus statement on screening for latent tuberculosis infection in patients with psoriasis treated with systemic and biologic agents. *J Am Acad Dermatol* 2008;59:209-17.
9. Sánchez-Moya AI, García-Doval I, Carretero G, Sánchez-Carazo J, Ferrandiz C, Ceballos EH, *et al.* Latent tuberculosis infection and active tuberculosis in patients with psoriasis: A study on the incidence of tuberculosis and the prevalence of latent tuberculosis disease in patients with moderate–severe psoriasis in Spain. *BIOBADADERM registry. J Eur Acad Dermatol Venereol* 2013;27:1366-74.
10. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, *et al.* Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of tuberculosis in adults and children. *Clin Infect Dis* 2017;64:111-5.