Section: Miscellaneous

Original Research Article

PREVALENCE OF LTBI (LATENT TUBERCULOSIS INFECTION) AMONG PATIENTS RECEIVING IMMUNOSUPPRESSANT DRUGS FOR VARIOUS SKIN CONDITIONS IN SKIN DEPARTMENT IN TERTIARY CARE HOSPITAL

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Abstract

Background: Latent tuberculosis infection (LTBI) is a critical reservoir for future active TB cases. Patients suffering from chronic skin conditions, receiving immunosuppressive therapy, are likely to have reactivation of latent TB infection (LTBI). However despite India's high tuberculosis burden, data on the prevalence of LTBI among patients receiving immunosuppressive therapy for dermatological conditions remain limited. **Materials and Methods:** A descriptive study was carried out in the outdoor patient department of Skin, V.D and Leprosy of a tertiary care hospital. Over a period of 12 months, patients on immunosuppressant drugs for ≥3 months were enrolled consecutively (n=160), out of which 150 completed the follow up. Active TB was excluded via chest X ray and sputum analysis. The Mantoux skin test (2 TU PPD) was used for assessing LTBI, interpreted between 48 and 96 hours. Indurations ≥15 mm were considered positive. Information was collected on demographic details, BCG status, comorbidities, substance and viral infections. We used descriptive statistics and multivariable logistic regression for our analyses (SPSS v21). **Result:** Out of the 150 patients (mean age 47.1 ± 13.0 years; 80 males, 70 females), 42 (28%) were positive for LTBI. 30% of boys and 25.7% of girls had it. Multivariable analysis showed an increasing risk for LTBI with every increasing year of age (AOR 1.24; 95% CI 1.02–1.51; p=0.032), substance use (AOR 1.86; 95% CI 1.12–3.09; p=0.041) presence of comorbidities (AOR 1.92; 95% CI 1.15–3.21; p=0.028), HIV/HBsAg/HCV infection (AOR 2.45; 95% CI 1.28–4.68; p=0.012). A BCG scar decreased the risk of LTBI by 55% (AOR 0.45; 95% CI 0.25–0.82; p=0.008). Clinical symptoms were uncommon, signifying the latent nature of infection. **Conclusion:** About 1/3rd of the dermatology patients on immunosuppressants at this tertiary care facility have LTBI. It is recommended that all patients, especially older age groups, patients with co-morbidities, viral infections, substance abusers, and patients undergoing immunosuppressive therapy should be routinely screened for LTBI before or during treatment for timely prophylaxis and decrease chances of progression to active tuberculosis.

INTRODUCTION

Latent tuberculosis infection (LTBI) represents a significant global health challenge, particularly among immunocompromised individuals. The World Health Organization defines LTBI as a state of persistent immune response to Mycobacterium tuberculosis antigens without evidence of clinically manifest active tuberculosis.[1] It is estimated that approximately one-quarter of the world's population is affected by LTBI, making it a substantial reservoir for potential active TB cases.[2]

The management of patients receiving immunosuppressant therapy for dermatological conditions presents a unique challenge in tuberculosis control. These patients face an elevated risk of LTBI reactivation due to their compromised

immune status, similar to what has been observed in other immunocompromised populations.[3] The interaction between immunosuppressive therapy and tuberculosis is complex, with evidence suggesting that altered monocyte function and impaired cell-mediated immunity may contribute to increased susceptibility to both TB infection and reactivation.[4] Recent global estimates indicate that the risk of progression from LTBI to active TB is significantly higher in immunocompromised individuals compared to the general population. According to Houben and Dodd's mathematical modeling study, while the lifetime risk of LTBI reactivation in immunocompetent individuals is approximately 5-10%, this risk increases substantially in those receiving immunosuppressive therapy.[5] This heightened risk necessitates careful screening and monitoring protocols for patients initiating or maintaining immunosuppressive treatment for dermatological conditions.

The prevalence of LTBI among patients receiving immunosuppressant therapy for dermatological conditions in India remains poorly documented, despite the country's high TB burden. Understanding the prevalence and risk factors associated with LTBI in this specific patient population is crucial for developing targeted screening and prevention strategies. This is particularly relevant in the context of tertiary care settings, where complex dermatological cases requiring long-term immunosuppressive therapy are managed.

This study aims to address this knowledge gap by investigating the prevalence of LTBI among patients receiving immunosuppressant drugs for various skin conditions in a tertiary care hospital setting. Additionally, we seek to identify specific risk factors and clinical characteristics associated with LTBI in this population, which could inform screening protocols and preventive strategies in dermatological practice.

Aims & Objectives

To find out prevalence of latent TB infection among patients among patients receiving immunosuppressant's drugs at Skin OPD.

MATERIALS AND METHODS

Study Design: Hospital-based cross-sectional study

Study Setting: Skin, V.D & Leprosy OPD Guru Govindsingh Hospital, Jamnagar. Almost 150 -160 patients visit the skin department OPD of the Hospital.

Study Population: patients under immunosuppressant for various skin conditions with of duration of more than 3 months were enrolled in the study

Ethical statement: This study was approved by the M P Shah Govt. Medical College, Jamnagar Institutional Ethical Committee. All patient details were de-identified upon preparation/ publication of the project. All procedures were followed following the Helsinki Declaration of 1975.

Inclusion & Exclusion Criteria

Patients under immunosuppressant for various skin conditions with of duration of more than 3 months were included in the study patients of active Tuberculosis (positive on X-ray or sputum), were excluded study. Severely ill patients or patients who do not wish to participate were excluded from the study.

Study Duration: 1 year

Sample Size Calculation: By using the following formula sample size came to 96. Considering high death rates, migration rate, and loss of follow up we enrolled all the patients on immunosuppressants for various skin conditions visiting the skin department opd of GGG Hospital, Jamnagar. Thus, the Universal sampling technique was used and all patients fulfilling inclusion criteria were enrolled in the study.

Estimate a proportion in finite population

$$n \geq \frac{NZ^2_{1-\alpha/2}p(1-p)}{d^2(N-1)+Z^2_{1-\alpha/2}p(1-p)}$$

Alpha (a) =0.05

Estimated proportion (P) = 0.4 [10]

Absolute error (d) = 10%

Data collection tool: Pretested semi-structured proforma was used to collect data. It contains information about socio-demographic variables, results of x-ray and sputum analysis, baseline investigation, and other routine investigations as per the protocol

Procedure: After collecting information in the data collection tool, all patients were screened for active tuberculosis using x-ray and sputum analysis, those patients who tested positive on x-ray/sputum were excluded and a Tuberculin test was not conducted on those patients to detect Latent TB infection.

Technical details of Tuberculin test: Product and Dosage: 0.02 PPD RT in 0.1 ml of diluents with Tween 80 makes 1 TU (stored at 2-80C). In our study, we used 2 TU in all subjects. Air-tight 1 ml disposable tuberculin syringe graduated to hundred of mm to facilitate exact measurement of 0.1 ml fitted with 26 G needle sized half an inch length and 20 bevels providing airtight administration of test solution are used.

Administration of test: The test is given on the mid-polar aspect of the forearm. The test site water was cleaned using soap and water and dried. The skin area chosen should be free of scars, veins, and areas of inflammation. The skin is slightly stretched and the needle point inserted with its bevel facing upward into the superficial layers of skin 0.1 ml of tuberculin is injected slowly. If the test is unsatisfactory then

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another injection is given on the other forearm and a second test is recorded as appropriate.

Reading of test: TST result between 48-96 hours after test in good daylight keeping forearm flexed by carefully palpating the site of injection using one finger. The transverse margin of indurations is marked with a ballpoint pen and the maximum diameter is measured in millimeters (mm) with a transparent ruler.

Interpretation of Tuberculin Test

Size of Induration	Interpretation
15 mm and above	Signifies infection with tubercle bacilli, irrespective of BCG vaccination status
10-14 mm	Cross sensitivity induced by environmental mycobacteria BCG induced sensitivity Infection with Mycobacterium tuberculosis
5-9 mm	Majority of such reactions are attributable to cross-sensitivity induced by environmental mycobacteria and/or BCG vaccination Could be attributable to infection with tubercle bacilli in the presence of immunosuppressive conditions
Less than 5 mm	Indicates absence of any type of mycobacterial infection except in individuals with a severe degree of immunosuppression.

Statistical Analysis: The statistical analysis was performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were calculated for all variables, with continuous data presented as mean ± standard deviation and categorical data as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess the normality of continuous variables. Comparisons between groups were performed using Student's t-test for normally distributed continuous variables and Mann-Whitney U test for non-normally distributed continuous variables. Chi-square tests or Fisher's exact test were used for categorical variables as appropriate. Univariate analysis was conducted to identify potential risk factors for LTBI, and variables with p-values < 0.10 were included in the multivariable logistic regression analysis. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. Statistical significance was set at $p < 0.05$ for all analyses.

RESULTS

Table 1: Study Population Distribution.

Category	Number of Patients	Percentage
Total registered patients	160	100%
Excluded - Discontinued/Migrated	6	3.75%
Lost to follow-up	4	2.5%
Final study population	150	93.75%

Table 2: Socio-demographic Variables & LTBI Prevalence

Variables	Female (n=70)	Male (n=80)	Total (n=150)
Age (Mean ± SD)	45.3 ± 12.8	48.6 ± 13.2	47.1 ± 13.0
Weight (Mean ± SD)	58.4 ± 9.7	67.2 ± 10.3	63.1 ± 10.8
LTBI Status			
Positive	18 (25.7%)	24 (30%)	42 (28%)
Negative	52 (74.3%)	56 (70%)	108 (72%)
Socio-Economic Status			
Lower	42 (60%)	45 (56.3%)	87 (58%)
Middle/Upper	28 (40%)	35 (43.7%)	63 (42%)
Education			
Illiterate	25 (35.7%)	20 (25%)	45 (30%)
Literate	45 (64.3%)	60 (75%)	105 (70%)
BCG Scar			
Present	52 (74.3%)	58 (72.5%)	110 (73.3%)
Absent	18 (25.7%)	22 (27.5%)	40 (26.7%)
Tobacco/Smoking/Alcohol			
Present	8 (11.4%)	35 (43.8%)	43 (28.7%)
Absent	62 (88.6%)	45 (56.2%)	107 (71.3%)
Positive Contact H/O			
Present	12 (17.1%)	15 (18.8%)	27 (18%)
Absent	58 (82.9%)	65 (81.2%)	123 (82%)
Comorbidity			
Present	28 (40%)	34 (42.5%)	62 (41.3%)
Absent	42 (60%)	46 (57.5%)	88 (58.7%)
HIV/HBsAg/HCV Infection			
Positive	4 (5.7%)	6 (7.5%)	10 (6.7%)
Negative	66 (94.3%)	74 (92.5%)	140 (93.3%)

Table 3: Clinical Presentation of Patients

Symptoms	No	Yes	Percentage (Yes)
Cough	122	28	18.7%
Breathlessness	135	15	10%

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Fever	128	22	14.7%
Chest Pain	138	12	8%
Anorexia	125	25	16.7%
Other symptoms	130	20	13.3%

Table 4: Laboratory Parameters

Parameters	Mean	Std. Deviation	Minimum	Maximum
Hemoglobin (g/dL)	11.09	1.82	8.2	14.5
Creatinine	1.2	0.45	0.6	2.8
Urea	35.6	12.4	15.0	75.0
Sodium (Na)	138.5	4.2	128.0	145.0
Potassium (K)	4.2	0.6	3.2	5.8
TIBC	245.8	52.3	150.0	380.0
Ferritin	393.35	285.6	85.0	1250.0

Table 5: Risk Factors Analysis for LTBI

Variables	Total (n=150)	Univariate Analysis	Multivariable Regression
Age (Mean ± SD)	47.1 ± 13.0	0.032	1.24 (1.02-1.51)
Weight (Mean ± SD)	63.1 ± 10.8	0.245	0.98 (0.94-1.02)
BCG Scar Present	110 (73.3%)	0.008	0.45 (0.25-0.82)
Tobacco/Smoking/Alcohol Present	43 (28.7%)	0.041	1.86 (1.12-3.09)
Comorbidity Present	62 (41.3%)	0.028	1.92 (1.15-3.21)
HIV/HBsAg/HCV Positive	10 (6.7%)	0.012	

[Table 1] Study Population Distribution

The study initially enrolled 160 patients receiving immunosuppressant drugs for various skin conditions. Throughout the study period, 6 patients (3.75%) were excluded due to discontinuation of treatment or migration, while 4 patients (2.5%) were lost to follow-up. The final analysis included 150 patients, representing a retention rate of 93.75%. This high retention rate strengthens the validity of our findings and suggests effective patient engagement throughout the study duration.

[Table 2] Socio-demographic Variables & LTBI Prevalence

The study population comprised 70 females and 80 males, with a mean age of 47.1 ± 13.0 years. The overall LTBI prevalence was 28% (42/150), with a slightly higher prevalence in males (30%) compared to females (25.7%). Socioeconomic analysis revealed that 58% of participants belonged to lower socioeconomic status, while 42% were from middle/upper classes. Educational status showed that 70% of participants were literate, with higher literacy rates among males (75%) compared to females (64.3%). BCG vaccination coverage, as evidenced by scar presence, was 73.3%. Notably, substance use (tobacco/smoking/alcohol) was significantly higher among males (43.8%) compared to females (11.4%). Comorbidities were present in 41.3% of the study population, and 6.7% were positive for HIV, HBsAg, or HCV infection.

[Table 3] Clinical Presentation of Patients

Analysis of clinical symptoms revealed that cough was the most common presentation (18.7%), followed by anorexia (16.7%) and fever (14.7%). Breathlessness was reported by 10% of patients, while chest pain was the least common symptom (8%). Additional symptoms were noted in 13.3% of patients. The relatively low prevalence of clinical symptoms supports the latent nature of the TB infection in the study population and highlights the importance of screening in asymptomatic immunosuppressed patients.

[Table 4] Laboratory Parameters

Laboratory findings demonstrated mild anemia among participants with a mean hemoglobin level of 11.09 ± 1.82 g/dL. Renal function parameters showed mean creatinine levels of 1.2 ± 0.45 and urea levels of 35.6 ± 12.4. Electrolyte levels were generally within normal ranges, with mean sodium and potassium values of 138.5 ± 4.2 and 4.2 ± 0.6, respectively. Notably elevated ferritin levels (393.35 ± 285.6) were observed, suggesting underlying inflammation or acute phase reaction in many patients. The wide standard deviation in ferritin levels indicates considerable variability among patients, possibly reflecting different degrees of disease activity or inflammation.

[Table 5] Risk Factors Analysis for LTBI

Multivariable regression analysis identified several significant risk factors for LTBI. Age showed a positive correlation with LTBI risk (AOR: 1.24, 95% CI: 1.02-1.51, p=0.032). The presence of a BCG scar demonstrated a protective effect (AOR: 0.45, 95% CI: 0.25-0.82, p=0.008). Substance use (AOR: 1.86, 95% CI: 1.12-3.09, p=0.041), presence of comorbidities (AOR: 1.92, 95% CI: 1.15-3.21, p=0.028), and HIV/HBsAg/HCV infection (AOR: 2.45, 95% CI: 1.28-4.68, p=0.012) were identified as significant risk factors for LTBI. Weight did not show a significant association with LTBI risk in the multivariable analysis (p=0.245).

DISCUSSION

This cross-sectional study provides important insights into the prevalence and risk factors of latent tuberculosis infection among patients receiving immunosuppressant therapy for dermatological conditions. The overall LTBI prevalence of 28% in our study population aligns with global estimates but

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presents specific concerns in the context of immunosuppressive therapy.

Our findings demonstrate several significant associations with LTBI risk in this population. The protective effect of BCG vaccination, evidenced by scar presence (AOR: 0.45, 95% CI: 0.25-0.82), supports previous research by Romanowski et al., who found similar protective associations in immunocompromised populations.[6] This reinforces the importance of vaccination programs in TB prevention strategies, particularly in regions with high TB burdens.

The higher prevalence of LTBI among male participants (30% vs 25.7% in females) and its association with substance use (AOR: 1.86, 95% CI: 1.12-3.09) aligns with findings from previous studies. As noted by Dobler et al., behavioral and socioeconomic factors often contribute to increased TB risk in specific demographic groups.[7] The significant association between comorbidities and LTBI (AOR: 1.92, 95% CI: 1.15-3.21) emphasizes the complex interplay between multiple health conditions and tuberculosis risk, particularly in immunocompromised individuals.

Laboratory findings in our study, particularly the elevated ferritin levels (mean: 393.35 ± 285.6 ng/mL), suggest an underlying inflammatory state in many patients. This observation is consistent with research by Gibbons et al., who demonstrated altered immune responses in patients with compromised immunity.[8] The presence of mild anemia (mean hemoglobin: 11.09 ± 1.82 g/dL) in many participants may reflect both the chronic nature of their dermatological conditions and the potential impact of immunosuppressive therapy.

The significant association between HIV/HBsAg/HCV infection and LTBI (AOR: 2.45, 95% CI: 1.28-4.68) underscores the importance of comprehensive screening in patients with multiple risk factors. This finding aligns with current WHO guidelines emphasizing the need for enhanced TB screening in populations with overlapping risk factors.[9] The relatively low prevalence of clinical symptoms in our study population (18.7% for cough, and 16.7% for anorexia) highlights the challenges in identifying LTBI through clinical presentation alone.

Our study has several strengths, including a high retention rate (93.75%) and a comprehensive assessment of multiple risk factors. However, limitations include the cross-sectional design, which precludes the determination of temporal relationships, and the single-center nature of the study, which may limit generalizability.

CONCLUSION

This study reveals a substantial prevalence of LTBI among patients receiving immunosuppressant therapy for dermatological conditions, with significant associations identified for multiple risk factors. The findings support the implementation of routine LTBI screening in this patient population, particularly for those with additional risk factors such as comorbidities or viral infections. The protective effect of BCG vaccination and the influence of modifiable risk factors suggest potential avenues for preventive interventions.

Clinical Implications

- Regular LTBI screening should be considered for all patients initiating or maintaining immunosuppressive therapy for dermatological conditions.
- Special attention should be paid to patients with multiple risk factors, particularly those with viral infections or multiple comorbidities.
- The presence of BCG vaccination may provide some protection against LTBI, but should not preclude regular screening in high-risk populations.
- Modification of risk factors, where possible, should be incorporated into patient management strategies.

Future Directions

Future research should focus on:

- Longitudinal studies to assess LTBI progression rates in this specific population
- Evaluation of different screening protocols to optimize early detection
- Investigation of the impact of various immunosuppressive regimens on LTBI risk
- Assessment of preventive therapy outcomes in this patient group

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