

Prevalence of Latent Tuberculosis Infection and Willingness for Preventive Treatment among Household Contacts: A Prospective Observational Study from a Tertiary Centre, Karnataka, India

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ABSTRACT

Introduction: Latent Tuberculosis Infection (LTBI) represents a state in which individuals are infected with *Mycobacterium Tuberculosis* (MTB) but do not exhibit active disease symptoms. Despite the absence of clinical manifestations, LTBI poses a significant public health challenge, as approximately one-quarter of the world's population is estimated to harbour latent infection. Household Contacts (HHCs) of individuals with active Tuberculosis (TB) are frequently exposed to MTB, leading to greater risk of developing LTBI due to shared living environments. Without treatment, 5-10% of individuals with LTBI may progress to active TB during their lifetime. Early identification and management of LTBI are critical to TB control and elimination efforts, highlighting the importance of effective screening and preventive therapy strategies.

Aim: To determine the prevalence of active TB and LTBI among HHCs and to assess their willingness to initiate Tuberculosis Preventive Treatment (TPT), as well as treatment adherence and associated barriers.

Materials and Methods: The prospective observational study was undertaken between April 2023 and January 2025. HHCs of active

TB patients were enrolled after informed consent, and a structured questionnaire was used for data collection. Chest radiography, sputum microscopy, and Tuberculin Skin Test (TST) were carried out for screening. Willingness to initiate TPT, reasons for refusal, and adherence among those treated were documented. Data were analysed using Statistical Package for Social Sciences (SPSS) v20.0, and significance was set at a p-value threshold of 0.05.

Results: A total of 264 HHCs were evaluated. Females were 136 in number, constituting 51.5% of the population. The mean age was 34.55 ± 16.45 years, and the mean Body Mass Index (BMI) was 22.29 ± 4.16 kg/m². Active TB was diagnosed in 2 (0.76%) participants, and LTBI in 43 (16.3%). A total of 213 (81.3%) HHCs showed willingness to initiate TPT, though completion was observed in only 77 (37.2%). The primary reason for non-initiation was misconception about the disease and treatment.

Conclusion: The present study revealed 16.3% LTBI prevalence within the HHCs population and low completion rates of TPT despite high initial willingness, indicating gaps in adherence. Targeted education and strengthened programmatic support are crucial to enhance LTBI management and advance TB elimination efforts.

Keywords: *Mycobacterium tuberculosis*, Tuberculin skin test, Tuberculosis burden

INTRODUCTION

Caused by *MTB*, TB continues to be a leading infectious cause of illness and mortality globally [1,2]. According to recent data by the World Health Organisation (WHO) in 2023, 10.8 million individuals were affected by TB, equating to an new occurrence of 134 cases per lakh population [3]. India accounted for 26% of the global TB burden, highlighting its significant role in the global scale of TB epidemic [4]. While the focus of TB control efforts has traditionally been on the recognition of active disease and its clinical management, the reservoir of LTBI poses a substantial challenge to disease elimination [5].

LTBI refers to a condition where an individual harbours *MTB* but does not display symptoms or clinical evidence of active TB [6]. This condition is identified through a persistent immunological response to mycobacterial antigens, commonly evaluated through the Interferon-Gamma Release Assay (IGRA) or TST, in the absence of bacteriological or imaging evidence suggestive of TB [5,7,8]. Asymptomatic individuals with LTBI may still experience reactivation of the infection, leading to active TB, especially when factors such as immunosuppression, malnutrition, or co-morbidities like diabetes mellitus are present [6,9,10]. It is estimated that 5-10% of individuals harbouring

latent TB infection will experience progression to active disease during their lifetime [11].

Within high-risk populations, HHCs of individuals with pulmonary or extrapulmonary TB face a substantial risk of becoming infected, due to frequent and prolonged exposure within confined living environments [11,12]. Evidence suggests that implementation of TPT can lower the risk of progression of LTBI to active disease by nearly 60% [13]. Despite this, treatment initiation and completion rates remain low, often hindered by factors such as lack of awareness, misconceptions about LTBI, and healthcare system limitations [14].

The LTBI among HHCs of active TB patients remains a major challenge to TB elimination efforts, particularly in high-burden settings like India. While previous studies have explored LTBI prevalence and associated risk factors, few have comprehensively examined both clinical and behavioural determinants, especially in tertiary care contexts [15,16]. Additionally, data on the willingness to initiate and complete TPT remain limited. The present study addresses these gaps by evaluating the prevalence of active TB and LTBI, identifying sociodemographic factors and co-morbidities associated with LTBI, and assessing the willingness to initiate and complete TPT, along with the barriers for treatment among HHCs of active TB cases attending a tertiary care hospital.

MATERIALS AND METHODS

The present prospective observational study was conducted between April 2023 and January 2025 in the Department of Respiratory Medicine at Shri BM Patil Medical College, Hospital and Research Centre, BLDE (Deemed to be) University, Vijayapura, Karnataka, India. Prior to enrolment, written informed consent was obtained from each participant in accordance with ethical guidelines. Prior to the initiation of the study, the research protocol was approved by the Institutional Ethics Committee in accordance with ethical guidelines. (IEC No: BLDE(DU)/IEC/873/2022-2023).

Sample size calculation: The study included two hundred sixty-four HHCs of active TB patients. The sample size was calculated based on an anticipated prevalence of LTBI of 22.8% [17], with a 95% confidence level and an absolute precision of 5%.

Inclusion criteria: All HHCs of active TB patients aged above five years who provided informed consent to participate were included in the study.

Exclusion criteria: HHCs with active TB who were already undergoing treatment for TB, pregnant and lactating mothers, children under the age of five, and individuals who did not consent to participate were excluded from the study population.

Operational definition [11]: The index case is defined as the first individual, irrespective of age, diagnosed with either new or recurrent TB within a given household where potential exposure to others may have occurred. An individual was considered a HHC if they had lived with the index case and eaten meals from the same kitchen for no less than three months before the index case's TB diagnosis.

Study Procedure

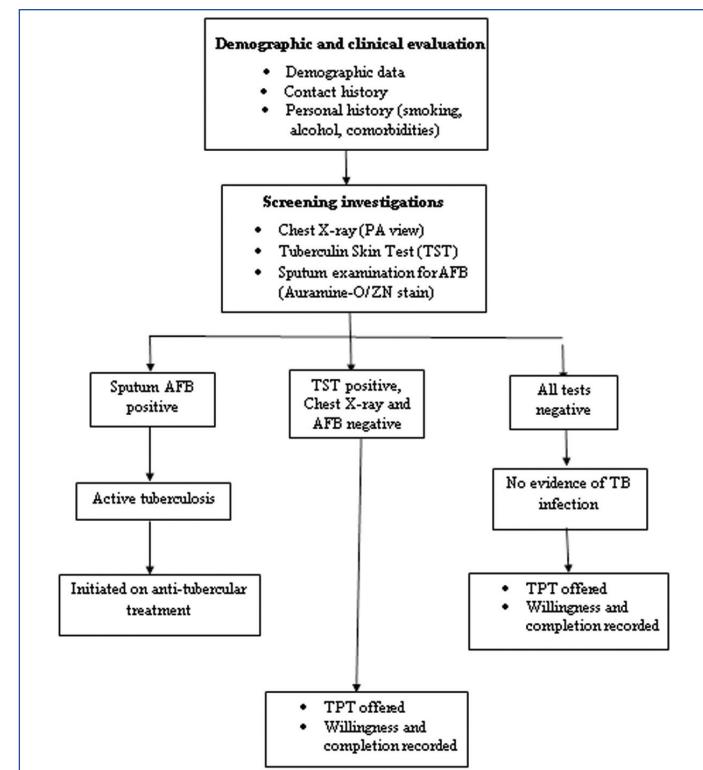
All HHCs of index cases were identified through verbal interviews conducted with the index case. A structured questionnaire was used to document demographic characteristics, clinical symptoms and signs, as well as findings from a basic clinical examination. Information regarding known co-morbidities, tobacco use, and alcohol consumption was also recorded.

Following clinical assessment, all HHCs underwent TST. A skin induration exceeding 10 mm in diameter, evaluated between 48 and 72 hours after administration, was used to define latent TB infection. Contacts were further evaluated using posterior-anterior chest radiographs and sputum examination to assess for active TB disease. Active TB among HHCs was confirmed based on positive sputum smear microscopy results (microbiologically confirmed TB). The number of cases diagnosed as either active TB or latent TB was subsequently analysed to determine their prevalence. Associations between LTBI status and various demographic factors and comorbidities were also assessed.

For all participants without active TB who were eligible for TPT, willingness to accept treatment was assessed. Among those who declined TPT, the reasons for unwillingness were recorded. Treatment adherence was monitored, and completion rates were systematically documented, in participants who were initiated on TPT [Table/Fig-1].

STATISTICAL ANALYSIS

Data were entered and organised using Microsoft Excel 2019, and statistical analysis was performed using SPSS Statistics for Windows, Version 20.0. The demographic and clinical profile of individuals with LTBI, stratified by TST status were summarised through descriptive statistical methods. Categorical variables are presented as absolute numbers and percentages, and were compared using the Chi-square test. Mean±Standard Deviation (SD) was used to describe continuous variables. Logistic regression was applied to examine the relationship between LTBI and potential predictors. Statistical analyses were two-tailed, with a threshold for significance set at $p<0.05$.



[Table/Fig-1]: Algorithm for screening and management of Household Contacts (HHC).

RESULTS

Demographic and health-related characteristics of the study participants

Participants: Female participants accounted for 51.5% (136 in number) of the study group. The average age of HHCs was 34.55 ± 16.45 years, with an average BMI of 22.29 ± 4.16 kg/m². Tobacco use was reported by 73 (27.7%) participants, while 39 (14.8%) of them reported alcohol use. A total of 30 participants (11.4%) had diabetes mellitus (DM), and 27 participants (10.3%) had Hypertension (HTN) [Table/Fig-2].

Characteristics	n (%)
Age	
Mean age±SD (years)	34.55±16.45
Gender	
Female	136 (51.5)
Male	128 (48.5)
BMI category	
Underweight	43 (16.3)
Normal	169 (64.0)
Overweight	35 (13.3)
Obesity	17 (6.4)
Tobacco use	
Yes	73 (27.7)
No	191 (72.3)
Alcohol use	
Yes	39 (14.8)
No	225 (85.2)
Diabetes mellitus	
Present	30 (11.4)
Absent	234 (88.6)
Hypertension (HTN)	
Present	27 (10.3)
Absent	237 (89.7)

[Table/Fig-2]: Sociodemographic and clinical characteristics of Household Contacts (HHC).
SD: Standard deviation; BMI: Body mass index

Detection of LTBI and active TB among HHCs: Out of 264 HHCs, 43 individuals (16.3%) tested positive on the TST and were classified as having LTBI. Furthermore, two individuals (0.8%) were diagnosed with active pulmonary TB through a positive sputum Acid-Fast Bacillus (AFB) smear. The remaining 219 (82.95%) had no evidence of TB infection or disease at the time of evaluation.

Among the various demographic and clinical parameters analysed, LTBI was significantly more common in female contacts (67.4 vs. 48.4%, p=0.022) and those with diabetes mellitus (20.9 vs. 9.6%, p=0.032) [Table/Fig-3]. After adjusting for potential confounders, female gender (adjusted OR: 2.08; 95% CI: 0.88-4.87; p=0.039) had an independently elevated risk of LTBI relative to males. Diabetes mellitus (adjusted OR: 2.10; 95% CI: 0.65-6.76; p=0.041) also emerged as a significant predictor of LTBI. However, no significant associations were observed with other variables including age, BMI, tobacco or alcohol use, and HTN, in the multivariable logistic regression model [Table/Fig-4].

Characteristics	LTBI (N=43) n (%)	Normal (N=219) n (%)	p-value
Age			
Mean age \pm SD (Years)	36.70 \pm 13.70	34.16 \pm 16.98	0.357
Gender			
Female	29 (67.4)	106 (48.4)	0.022
Male	14 (32.6)	113 (51.6)	
BMI category			
Underweight	5 (11.6)	37 (16.9)	0.655
Normal	31 (72.1)	137 (62.6)	
Overweight	5 (11.6)	30 (13.7)	
Obesity	2 (4.7)	15 (6.8)	
Tobacco use			
Yes	11 (25.6)	62 (28.3)	0.497
No	32 (74.4)	157 (71.7)	
Alcohol use			
Yes	7 (16.3)	32 (14.6)	0.558
No	36 (83.7)	187 (85.4)	
Diabetes mellitus			
Present	9 (20.9)	21 (9.6)	0.032
Absent	34 (79.1)	198 (90.4)	
Hypertension			
Present	5 (11.6)	22 (10.0)	0.755
Absent	38 (88.4)	197 (90.0)	
Willingness for TPT			
Yes	41 (95.3)	172 (78.5)	0.010
No	2 (4.7)	47 (21.5)	
TPT initiated			
Yes	41 (100.0)	166 (96.5)	0.004
No	0 (0.0)	6 (2.8)	
TPT status			
Completed	16 (39.0)	61 (36.8)	0.787
Discontinued	25 (61.0)	88 (53.0)	
On treatment	0 (0.0)	17 (10.2)	

[Table/Fig-3]: Comparison of demographics and clinical characteristics between contacts with and without Latent Tuberculosis Infection (LTBI).

SD: Standard deviation; BMI: Body mass index; TPT: Tuberculosis preventive treatment

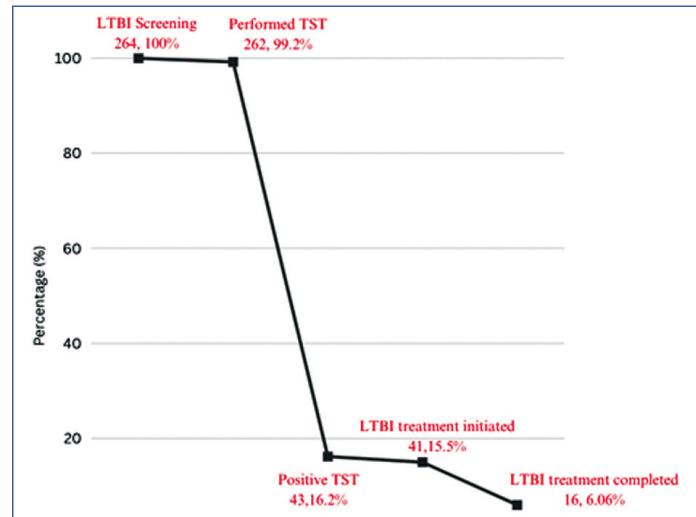
Among LTBI-positive contacts, 41 (95.3%) were willing to initiate TPT, and all initiated treatment. In the LTBI-negative group, 172 (78.5%) were willing, with treatment being initiated in 166 (96.5%) individuals. However, TPT completion rates remained low, with 61 (39.0%) LTBI-positive and 61 (36.8%) LTBI-negative contacts

Characteristics	Univariate	Analysis	Multivariate	Analysis
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Age (In years)	1.00 (0.97, 1.03)	0.357	0.99 (0.97, 1.02)	0.871
Gender				
Female	1.48 (0.20, 3.12)	0.022	2.08 (0.88, 4.87)	0.039
Male	1.00		1.00	
BMI category				
Normal	1.00		1.00	
Underweight	1.44 (0.35, 5.90)	0.482	0.69 (0.16, 2.84)	0.613
Overweight	0.78 (0.12, 5.03)	0.927	1.26 (0.19, 8.09)	0.801
Obesity	1.61 (0.55, 4.66)	0.253	0.61 (0.21, 1.79)	0.376
Tobacco use				
Yes	1.75 (0.62, 4.93)	0.497	0.56 (0.20, 1.59)	0.284
No	1.00		1.00	
Alcohol use				
Yes	0.73 (0.21, 2.54)	0.558	1.36 (0.39, 4.71)	0.628
No	1.00		1.00	
Diabetes mellitus				
Present	1.47 (0.14, 4.52)	0.032	2.10 (0.65, 6.76)	0.041
Absent	1.00		1.00	
Hypertension				
Present	0.94 (0.29, 3.06)	0.755	1.05 (0.32, 3.43)	0.925
Absent	1.00		1.00	

[Table/Fig-4]: Logistic regression analysis of factors associated with LTBI among Household Contacts (HHC).

BMI: Body mass index; OR: Odds ratio; CI: Confidence interval; aOR: adjusted odds ratio

completing the treatment [Table/Fig-5]. Discontinuation was common in both groups [Table/Fig-3].



[Table/Fig-5]: Cascade of LTBI screening and treatment among Household Contacts (HHC).

Among those unwilling to initiate TPT, the main reason was lack of awareness or misconceptions about the necessity of TPT in healthy states, observed in 46 (93.9%) HHCs. The fear of side-effects emerged as a barrier to initiating TPT in two individuals (4.1%) as they perceived that the risks of TPT may outweigh the benefits. One individual (2.0%) had previously completed full course of treatment.

DISCUSSION

Out of the 264 HHCs enrolled, 62 (23.5%) patients were within the age group of 26-35 years, 58(22.0%) and 45(17.0%) patients, in the age groups of 16-25 years and 36-45 years respectively. The average age of the study group being 34.55 \pm 16.45 years. In the current study, it was found that the gender inclination was towards females with 51.5% of HHCs (136 in number) and were independently

associated with the development of LTBI, which corroborates the results of the study carried out in Sao Paulo, Brazil by Wysocki AD et al., which also consisted majorly of female population (50.7%) [18]. Studies from South Indian states by Munisankar S et al., and Krishnamoorthy Y et al., also showed female preponderance [10,19]. This may be attributed to the fact that female patients had prolonged domestic exposure and increased transmission risk. However, this contrasts with findings from a study by Nair D et al., where male gender was associated with a higher LTBI risk [20]. No significant association was observed between LTBI and age, nutritional status, or substance use ($p>0.05$).

Among the HHCs tested for LTBI, positive reaction was observed in 43 HHCs. The current study revealed that among HHCs with pulmonary TB, the prevalence of latent TB was 16.3%. As far as the latent TB burden is considered, globally, nearly one-fourth of the world's population is estimated to have latent TB [21]. In India, the National TB prevalence Survey 2019-21 documented the prevalence of TB as 21.7% in the age group ≥ 15 years [22]. Compared to the 38% pooled LTBI prevalence reported by Chauhan A et al., in their systematic review and meta-analysis [23]. However, this study identified a comparatively lower rate. Given that these lower numbers only reflect statistics from a limited geographic area and do not reflect the prevalence of a nation, they must be evaluated with caution.

In the present study, active TB was identified in 2 (0.8%) HHCs. This observed rate falls below the previously reported data from Chandigarh (3.03%) and Chennai (1.33%) in India, as well as in Central Ethiopia (1.44%) and Kenya, where a notably high prevalence of 3.5% was observed [24-27]. However, other studies from South India and Ghana reported much lower prevalence rates of 0.65% and 0.4%, respectively [19,28]. The wide variation in prevalence rates across studies may be attributed to differences in the sample sizes of contacts screened. Additionally, screening methodologies varied; for instance, studies conducted in Chennai [25] and Central Ethiopia [26] employed GeneXpert for diagnosis, while study in Kenya [27] also utilised sputum cultures for contact screening.

DM emerged as a significant predictor of LTBI in the study population (adjusted OR=2.10), underscoring its role as an important co-morbid condition influencing TB risk. This is biologically plausible, as the immunosuppressive effects of hyperglycaemia on both innate and adaptive responses have been implicated in greater susceptibility to latent infection and its clinical progression. A meta-analysis by Jeon CY and Murray MB demonstrated that individuals with DM had a threefold heightened risk of acquiring LTBI and progressing to active disease [29]. Supporting evidence from Djibougou DA et al., also showed a significant correlation with a prevalence of 11.88% [30]. In contrast, Krishnamoorthy Y et al., reported no significant association despite a high diabetes prevalence (63%) [19]. Nonetheless, the current findings reinforce the need for routine LTBI screening among individuals with diabetes, particularly in high TB burden settings, to facilitate early intervention and reduce progression to active disease.

Encouragingly, 95.3% of LTBI-positive contacts were willing to initiate TPT, and 100% of them successfully initiated therapy, compared to 96.5% among LTBI-negative but willing contacts. This reflects high acceptance of TPT when latent infection is confirmed, emphasising the importance of clear diagnosis and patient education in increasing adherence. However, treatment completion rates remained suboptimal (39%). The treatment completion rate observed in the present study aligns with that reported in a cross-sectional Indian study by Kumar A et al., (22%) [31]. However, markedly higher completion rates were reported by Shah D et al., and Mahajan P et al., highlighting the variability in outcomes likely influenced by differences in programmatic support, patient education, and follow-up strategies [32,33].

In the present study, of the eligible HHCs, 49 (18.7%) individuals were unwilling to initiate TPT. The predominant reason for refusal,

cited by 93.9% of them, was a lack of awareness regarding TPT and misconceptions about its necessity in asymptomatic individuals. Fear of drug-related adverse effects was identified in 2 (4.1%) individuals, who believed that the risks might outweigh the benefits of preventive therapy. The findings of the study are comparable to those described by Sharma N et al., (Delhi) [34], who noted that absence of clinical symptoms (33.1%), a sense of being in good health (42.9%), and fear of side-effects (27.5%) were the major deterrents to TPT initiation. Ren J et al., in a study based in Delhi, likewise found that 57.8% of participants doubted the efficacy of TPT, while 32.7% expressed concern about potential side effects [35]. These results underscore the critical need for targeted education and counselling to improve awareness and dispel misconceptions surrounding TPT.

Limitation(s)

The study was hospital-based and included contacts of index cases attending inpatient or outpatient departments, therefore, may not be representative of the general population. Secondly, the study evaluated a limited range of variables. Important determinants that could impact LTBI treatment initiation and completion- such as socioeconomic conditions and educational attainment- have not been assessed. A broader analysis of these modifiable determinants is crucial for designing targeted interventions to enhance treatment uptake and adherence among high-risk groups. Additionally, more specific diagnostic methods for LTBI, such as the IGRA and Cy-TB, was not utilised in this study, which may have affected the accuracy of prevalence estimates.

CONCLUSION(S)

The present study provides important insights into the prevalence of LTBI and treatment uptake and completion among HHCs. Prevalence of LTBI among HHCs in this study was 16.3%. The observation of an increased LTBI prevalence among female and diabetics recently exposed to infectious TB in their households underscores the need for targeted interventions to address the needs of this group. Additionally, the low rates of LTBI treatment completion emphasise the urgency of identifying the reasons for these barriers and developing effective strategies to overcome them through targeted education, patient counselling, and robust health system support. These efforts are essential to interrupt transmission, reduce disease progression, and achieve national TB elimination goals. Future research should investigate strategies to address barriers to LTBI treatment initiation and completion.

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