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# PREVALENCE OF LATENT TUBERCULOSIS INFECTION (LTBI) DETECTED BY IGRA AMONG THE HOUSEHOLD CONTACTS OF ACTIVE TUBERCULOSIS CASES IN TIRUVALLORE DISTRICT

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Abstract

BACKGROUND: Tuberculosis (TB) is a major public health problem and a leading cause of death worldwide. Latent tuberculosis infection (LTBI) is a condition of persistent immune response to infection by Mycobacterium tuberculosis. Household contacts of active TB cases need to be investigated for the presence of LTBI for detection and management.

OBJECTIVE : Detection of Latent TB Infection(LTBI) by Interferon Gamma Release Assay (IGRA) from close contacts of TB cases in Tiruvallur District.

METHODS : Blood samples of 1200 Household contacts of Pulmonary TB Patients from Tiruvallur District were collected and referred to State Public Health Laboratory for diagnosis of LTBI by Interferon Gamma Release Assay (IGRA).

RESULTS : Among the 1200 Household contacts of TB cases tested for IGRA, a total 520 (43%) were positive for LTBI and female was predominantly positive (62.3%) than male (37.7%). 59% of the LTBI was observed between 15-44 Age Group.

CONCLUSION : Early Diagnosis and treatment of Latent TB infection among the household contacts of TB patients are very important to reduce the TB disease burden in the community.

KEYWORDS : Tuberculosis, LTBI, Interferon Gamma.

## INTRODUCTION

Tuberculosis (TB) is a major public health problem and a leading cause of death worldwide. Over 10 million people are estimated to have developed TB in 2020; the majority were from high TB burden, resource-constrained, low and middle-income countries including India [1]. In 2014, the World Health Assembly adopted End TB Strategy which aims to eliminate the global TB epidemic by the year 2035 [2].

Latent tuberculosis infection (LTBI) is a condition of persistent immune response to infection by Mycobacterium tuberculosis (M.tb) in people without any evidence of active TB disease [3,4]. It is estimated that approximately 1.7 billion individuals were infected with LTBI in 2014, with a 5%–10% lifetime risk of developing active TB. Over 50% of the household contacts of pulmonary TB patients in resource constrained countries have LTBI [5,6].

Hence, WHO recommends that those with LTBI should be treated with tuberculosis preventive therapy (TPT) to realise the goals of the End TB Strategy [7]. Contact investigation is an essential component of the WHO's TB management protocol to detect those with LTBI among high-risk groups, and to initiate TPT [8]. WHO recommends the tuberculin skin test (TST) or interferon-gamma release assays (IGRA) to detect LTBI. TST is a reasonably low-cost tool; however, its production is limited. IGRA results in fewer false-positive results than with TST, but has higher cost and supply chain issues that challenge its routine induction in National TB programmes [8].

Both the tests are based on stimulating the cell-mediated immune response to detect whether it recognizes the antigens of Mtb. However, both TST and IGRA have reduced sensitivity in immunocompromised patients and cannot determine between active TB and LTBI.

The QuantiFERON®-TB Gold Plus (QFTPlus), a new version of IGRAs, have been recently evaluated in the field of latent TB diagnosis. The QFT-Plus exploit both CD4+ and CD8+ T cells immune response to Mtb, having an important clinical value in conditions of immune depression due to CD4 T-cell impairments as in HIV-infection. In addition, a number of studies suggest that the CD8+ response is present at the onset of the infection and RD1-specific CD8 T-cells

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are more frequently detected during active TB compared to LTBI and, within LTBI, in recent infection compared with remote infection. [9,10]

## OBJECTIVES

To detect Latent Tuberculosis infection (LTBI) among the household contacts of bacteriologically confirmed TB patients by Interferon Gamma Release Assay (IGRA) in Tiruvallur District and also to assess the age and sex wise preponderance of LTBI in the community.

## METHODOLOGY

**STUDY DESIGN :** Cross sectional study

**STUDY PLACE AND TIME :** Tiruvallur District during March to October 2022.

**STUDY POPULATION :** Household contacts of bacteriologically confirmed TB patients.

**INCLUSION CRITERIA :** Household contacts of active TB Patients.

**EXCLUSION CRITERIA :**

- Non contacts of Active TB patients.
- Children <5 years & HIV patients.

**SAMPLE COLLECTION:**

- Blood samples (5 mL) were collected in Lithium Heparin blood collection tube.
- 1 ml of blood is drawn from the sample and transferred to each of the QFT-Gold Plus tubes and gently shaken well. Incubated for 16-24 hrs followed by centrifugation to separate the plasma.

**SAMPLE SIZE :**

- Total Number of TB Cases enumerated in Tiruvallur District was 829.
- Samples for IGRA from Close Contacts 1200.

## IMMUNE ASSAYS

The Interferon-Gamma (IFN-γ) Release Assays (IGRAs) provide an alternative to the century-old tuberculin skin test (TST) for diagnosing latent tuberculosis infection (LTBI). The QuantiFERON®-TB Gold(QFT) assay, is an enzyme-linked immunosorbent assay (ELISA) that measures the amount of IFN-γ produced by T-cells stimulated by Mycobacterium tuberculosis-specific antigens namely Early Secreted Antigenic Target 6 (ESAT-6), Culture Filtrate Protein 10 (CFP-10) and TB 7.7. Many studies in adults have shown IGRAs to be more specific than the TST for detecting LTBI and at least as sensitive as the TST for detecting tuberculosis (TB) disease.

## RESULTS

A total of 1200 household contacts of Active TB Patients in Tiruvallur District were subjected to IGRA using QuantiFERON®-TB Gold (QFT) Assay, out of which 520 household contacts (43%) were detected with LTBI (Fig-1).

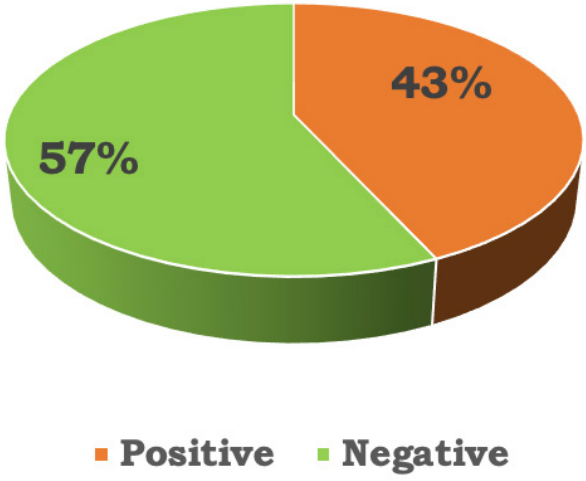


*Figure 1 : Prevalence of LTBI among Household contacts*

Out of the 1200 samples tested, only 22 samples (2%) became indeterminate.

Among the 520 LTBI cases detected in Tiruvallur District, there is a clear preponderance of infection in Female (62.3%) than Male (37.7%) (Fig-2).

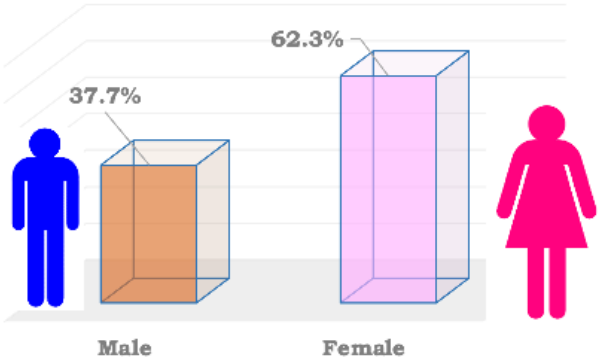


*Figure 2 : Sex wise distribution of LTBI among household contacts*

Among the LTBI positive household contacts detected in Tiruvallur District, age wise distribution of cases is shown in Fig-3. In children between 5-14 years age group (13%) and in elderly persons above 55 Years of age (12%), the LTBI prevalence was found to be less when compared to the other age groups. The age group between 15-44 years has almost 59% of the total of LTBI cases detected in this study.

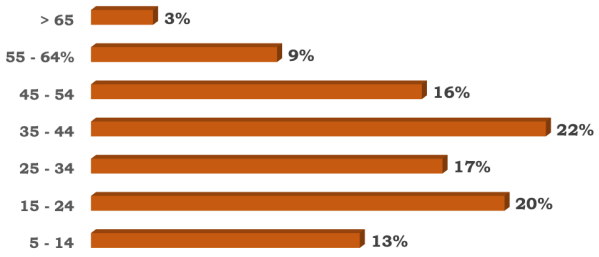


*Figure 3 : Age wise distribution of LTBI among household contacts*

## DISCUSSION

The global prevalence of LTBI is estimated to be nearly 33%. [12] In India, there are no estimates regarding the prevalence of LTBI in the general population; however, the WHO data indicate that roughly 3.5 lakh children below the age of 5 years were eligible for LTBI treatment [13]. Although most of the infected persons do not manifest the disease. They are at high risk of developing active infection and hence represent a reservoir of bacteria. The lifetime risk of reactivation of TB is estimated to be around 5-10% [14]. The risk is much higher in those with HIV, with a 10% annual risk of activation, and in young children. If untreated, 40% of the LTBI children under 1 year of age develop active disease, whereas it is 24% in children of 1-10 years and 16% in those between 11 and 15 years. [15,16]

It has been proposed that the infected persons accumulate in the pool of LTBI from which individuals having latent TB exit with active TB. To control the active infection, reducing the magnitude of the pool of latent infection is required [17]. Hence, screening and treatment of LTBI should be an important part of global TB control activities if we want to achieve End TB strategy [18]. WHO recommends systematic screening, identification and treatment of LTBI especially in groups at high risk for developing active TB like people living with HIV, child contacts of pulmonary TB cases, patients with silicosis and other forms of immunosuppression. [19] After ruling out active TB cases by a symptom screen, individuals should be tested for LTBI by either interferon-gamma release assays (IGRA) or tuberculin skin test (TST). Hence, detection of LTBI is of paramount importance in the course of achieving elimination of TB by 2025 in India.

Both TST and IGRA, the two currently available tests for diagnosis of LTBI, work on the principle of cell-mediated immunity. The TST detects M.tb sensitization via a delayed-type hypersensitivity response to M.tb antigens from purified protein derivatives(PPD) while IGRAs measure interferon-gamma (IFN-γ) release in response to specific M.tb antigens. Limitations of TST is cross-reaction with environmental non-tuberculous mycobacteria and the BCG vaccine. IGRA claims to overcome these limitations and be more specific than TST.

This study has a sizable population of household contacts of active tuberculosis patients screened for the presence of LTBI by IGRA and the results reveals the prevalence of 43% of LTBI in Tiruvallur District. WHO estimates that approximately 40% of the Indians are infected with Mycobacterium tuberculosis, the vast majority of who have LTBI. Similar study conducted in Chennai, the LTBI prevalence was 74% detected by either a positive TST or positive QFT-GIT. [11]

More men than women develop and die of tuberculosis (TB) but fewer data exist on sex differences in Latent TB infection (LTBI). Compared to numerous reports on active TB, disparities between sexes in LTBI are less frequently analyzed and have inconsistent findings. Male sex has been identified as an independent risk factor associated with LTBI in some studies. [20-22]

Limited evidence is available in Tamil Nadu to indicate the proportion of LTBI between males and females. In our study, the proportion of LTBI was significantly higher in females than in males (62.3% Vs 37.7%) similar to the one reported from Brazil. [23] Behavioural factors that affect sex differences in active TB disease may play a role in LTBI. Women spend more time performing indoor household tasks which could affect exposure dynamics for domestic close contacts.

Limited studies are available to report the age-specific prevalence of LTBI among household contacts, including adolescents and young adults exposed to an active index case in a TB endemic setting. In the present study, we have shown an increased prevalence of LTBI between 15-44 years (59%). South African investigators also found an increasing prevalence of LTBI among a younger age group [24,25,26].

## CONCLUSION

Our study showed a high prevalence of LTBI (43%) among household contacts of pulmonary TB patients in a high burden setting in Tiruvallur district. It also revealed an interesting finding on the higher prevalence of LTBI in females than males, suggesting the need to confirm the pattern in other districts of Tamil Nadu. Higher prevalence LTBI observed in young adult is also is a cause of concern and need to be counter checked with other districts of Tamil Nadu.

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