Section: Pulmonary Medicine

Original Research Article

EVALUATION OF THYROID PROFILE IN PATIENTS WITH PULMONARY TUBERCULOSIS: A PROSPECTIVE OBSERVATIONAL STUDY

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Received : 07/02/2025
Received in revised form : 24/03/2025
Accepted : 13/04/2025

Keywords:
Pulmonary Tuberculosis, Thyroid Function, Sick Euthyroid Syndrome, Subclinical Hypothyroidism.

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DOI: 10.47009/jamp.2025.7.2.169

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2025; 7 (2); 834-838

Abstract

Background: Pulmonary tuberculosis (PTB), a chronic infectious disease, is known to cause systemic inflammation that may affect endocrine function, particularly the hypothalamic-pituitary-thyroid (HPT) axis. Thyroid dysfunction in tuberculosis patients is often under-recognized despite its potential clinical implications. This study aimed to evaluate alterations in thyroid hormone levels during and after anti-tubercular therapy (ATT) in patients with newly diagnosed PTB. **Materials and Methods:** A prospective observational cohort study was conducted on 100 newly diagnosed CBNAAT-positive, rifampicin-sensitive PTB patients aged 18–65 years at a tertiary care center over 13 months. Thyroid function tests (T3, T4, TSH) were performed at four time points: baseline (pre-ATT), after 2 months (end of intensive phase), at 6 months (completion of ATT), and 6–8 weeks post-treatment. Patients were categorized based on thyroid status using standard reference ranges. **Result:** At baseline, 70% of patients showed thyroid dysfunction, predominantly sick euthyroid syndrome (42%) and subclinical hypothyroidism (21%). Over the course of ATT, T3 and T4 levels improved significantly ($p < 0.001$), while TSH remained within the normal range ($p = 0.08$). By 6–8 weeks post-treatment, 85% of patients returned to a euthyroid state, indicating reversible thyroid dysfunction associated with TB. **Conclusion:** Thyroid function is commonly altered in pulmonary tuberculosis patients, likely due to chronic systemic inflammation. Monitoring thyroid hormones during ATT can guide timely interventions and improve patient outcomes.

INTRODUCTION

Tuberculosis (TB) is a chronic infectious disease caused by Mycobacterium tuberculosis, primarily affecting the lungs, and continues to pose a significant global health challenge. According to the Global Tuberculosis Report 2022, the estimated global incidence of TB was between 9.9 and 11 million cases, with India accounting for approximately 2.10 million new cases in 2021. Within India, Telangana reported 62,342 active TB cases in the same year, underscoring the regional burden of the disease.

While pulmonary tuberculosis (PTB) is classically a respiratory illness, its systemic manifestations are increasingly being recognized. Chronic infections such as TB are known to interfere with the hypothalamic-pituitary-thyroid (HPT) axis, leading to disruptions in endocrine function—particularly involving the thyroid gland.[1,2] The thyroid plays a vital role in regulating cellular metabolism, thermogenesis, growth, and immune responses through the secretion of triiodothyronine (T3) and thyroxine (T4), both controlled by thyroid-stimulating hormone (TSH).

Systemic inflammation and immune dysregulation associated with active TB may impair peripheral metabolism, hormone binding, and receptor sensitivity of thyroid hormones. This can result in non-thyroidal illness syndrome (NTIS), also referred to as sick euthyroid syndrome, or subclinical hypothyroidism.[3,4] Cheng et al. (2022) further highlighted a bidirectional relationship between TB and hypothyroidism, suggesting mutual influence and potential clinical implications.[4] Moreover, MDR-TB patients on second-line drugs have shown higher risks of hypothyroidism, especially due to adverse drug reactions.[5,7]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Recent evidence also links low serum free T3 levels with increased mortality in severe PTB cases, underlining the prognostic value of thyroid hormone evaluation.[6] Despite these insights, thyroid dysfunction in TB patients remains under-evaluated in clinical practice, and there is a need to better understand its course and reversibility during anti-tubercular therapy.

This study was designed to evaluate the changes in thyroid function in patients with pulmonary tuberculosis throughout the course of anti-tubercular therapy, with the goal of identifying reversible endocrine alterations and informing clinical management strategies.

MATERIALS AND METHODS

Study Design and Setting: This was a prospective observational cohort study conducted in the Department of Respiratory Medicine, Government General Hospital, Siddipet, a tertiary care center in Telangana, India.

Study Period: The study was carried out over a 13-month period, from May 2023 to May 2024.

Study Population: The study included 100 patients diagnosed with pulmonary tuberculosis using CBNAAT (Cartridge-Based Nucleic Acid Amplification Test). All participants were rifampicin-sensitive, aged between 18 and 65 years, and of both sexes.

Inclusion Criteria

- Newly diagnosed pulmonary tuberculosis patients.
- CBNAAT positive for *Mycobacterium tuberculosis*.
- Rifampicin-sensitive cases.
- Age group 18–65 years.
- Patients willing to give written informed consent.

Exclusion Criteria

- CBNAAT-negative patients.
- Patients with past history of pulmonary/extrapulmonary TB.
- Drug-resistant TB cases.
- Patients with known thyroid, hypothalamic, or pituitary disorders.
- HIV-positive individuals.
- Patients on medications known to affect thyroid function (e.g., beta-blockers, phenytoin).
- Individuals with liver or renal comorbidities.
- Patients unwilling to participate.

Data Collection Tools and Investigations

The following investigations were performed:

Thyroid Function Tests (T3, T4, TSH) using electrochemiluminescence method.

Liver Function Tests (LFTs) and **Renal Function Tests (RFTs)** to rule out hepatic and renal comorbidities.

CBNAAT, **sputum microscopy**, and **chest X-ray** for TB diagnosis and monitoring.

Timing of Thyroid Function Tests

Thyroid function was evaluated at four time points:

Baseline – at the time of TB diagnosis (before ATT initiation).

After 2 months – completion of the intensive phase of ATT.

After 6 months – upon completion of the full ATT course.

6–8 weeks post-treatment – to assess hormonal recovery.

Treatment Protocol

Patients were initiated on standard weight-based anti-tubercular therapy as per National Tuberculosis Elimination Programme (NTEP) guidelines.

Data Management and Statistical Analysis

All data were recorded in predesigned proformas and entered into Microsoft Excel 2016. Statistical analysis was performed using SPSS version 27. Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent sample t-test. Categorical data were analyzed using the Chi-square test. A p-value < 0.05 was considered statistically significant.

Ethical Considerations: The study was conducted after obtaining ethical clearance from the Institutional Ethics Committee of Government Medical College, Siddipet. Informed written consent was obtained from all participants prior to their inclusion in the study.

RESULTS

Baseline Characteristics: A total of 100 patients with newly diagnosed, CBNAAT-positive pulmonary tuberculosis were enrolled in the study. The mean age of participants was 42.8 ± 11.3 years, with a predominance of male patients (65%) compared to females (35%). All patients were rifampicin-sensitive [Table 1].

Baseline Thyroid Profile: At baseline, prior to the initiation of anti-tubercular therapy (ATT), thyroid function tests revealed a mean T3 level of 0.76 ± 0.15 ng/ml, which was below the standard reference range of 0.8–2.0 ng/ml. Mean T4 levels were 4.1 ± 0.9 µg/dl, close to the lower limit of the reference range, and the TSH levels remained within normal limits at 3.2 ± 1.4 µIU/ml [Table 2]. Based on thyroid hormone levels, 42% of patients were classified with sick euthyroid syndrome, 21% with subclinical hypothyroidism, 7% with primary hypothyroidism, and only 30% were euthyroid at baseline [Table 3].

Post-Intensive Phase Assessment (After 2 Months of ATT): After the completion of the intensive phase of ATT (2 months), a gradual improvement in thyroid function was observed. T3 levels rose to 0.89 ± 0.18 ng/ml, and T4 levels increased to 4.7 ± 1.2 µg/dl, while TSH levels decreased to 2.8 ± 1.3 µIU/ml [Table 4]. The proportion of patients categorized as euthyroid increased to 45%, while those with sick euthyroid syndrome declined to 25% [Table 5].

Post-Treatment Completion (After 6 Months of ATT): By the end of the 6-month ATT course, further normalization of thyroid function was

ISSN (O): 2687-5365; ISSN (P): 2753-6556

evident. Mean T3 and T4 levels increased to 1.02 ± 0.22 ng/ml and 5.5 ± 1.4 µg/dl, respectively. TSH levels continued to remain within the normal range at 2.1 ± 1.0 µIU/ml [Table 6]. Euthyroid status was observed in 70% of patients, with significant reductions in sick euthyroid syndrome (15%), subclinical hypothyroidism (12%), and primary hypothyroidism (3%) [Table 7].

Follow-Up After Treatment Completion (6–8 Weeks Post-ATT): Six to eight weeks following treatment completion, the majority of participants demonstrated normalized thyroid profiles. Mean T3 and T4 levels were 1.12 ± 0.20 ng/ml and 6.3 ± 1.5 µg/dl, respectively, with TSH levels stabilizing at 1.8 ± 0.9 µIU/ml [Table 8]. At this point, 85% of the patients had a euthyroid status, and the occurrence of thyroid dysfunction was minimal [Table 9].

Statistical Analysis: A statistically significant improvement was observed in serum T3 and T4 levels over the four time points assessed ($p < 0.001$ for both), while the change in TSH levels was not statistically significant ($p = 0.08$) (Table 10). These findings indicate that pulmonary tuberculosis, a chronic systemic infection, is associated with transient thyroid dysfunction, which tends to normalize with effective anti-tubercular treatment.

Table 1: Demographic Profile of Study Participants (N = 100).

Parameter	Value
Mean Age (years)	42.8 ± 11.3
Gender Distribution	
– Males (%)	65%
– Females (%)	35%
CBNAAT Positive	100%
Rifampicin Sensitivity	100%

Table 2: Thyroid Function Test at Baseline (Before ATT Initiation)

Parameter	Mean ± SD	Reference Range	Interpretation
T3 (ng/ml)	0.76 ± 0.15	0.8 – 2.0 ng/ml	Below Normal
T4 (µg/dl)	4.1 ± 0.9	4.5 – 9.8 µg/dl	Low Normal
TSH (µIU/ml)	3.2 ± 1.4	0.4 – 5.5 µIU/ml	Normal

Table 3: Thyroid Status Classification at Baseline

Thyroid Status	Number of Patients	Percentage (%)
Euthyroid	30	30%
Sick Euthyroid Syndrome	42	42%
Subclinical Hypothyroidism	21	21%
Primary Hypothyroidism	7	7%

Table 4: Thyroid Function Test After 2 Months of ATT (End of Intensive Phase)

Parameter	Mean ± SD	Interpretation
T3 (ng/ml)	0.89 ± 0.18	Improving
T4 (µg/dl)	4.7 ± 1.2	Slight Improvement
TSH (µIU/ml)	2.8 ± 1.3	Normal

Table 5: Thyroid Status Classification After 2 Months

Thyroid Status	Number of Patients	Percentage (%)
Euthyroid	45	45%
Sick Euthyroid Syndrome	25	25%
Subclinical Hypothyroidism	21	21%
Primary Hypothyroidism	9	9%

Table 6: Thyroid Function Test After 6 Months (End of ATT Treatment)

Parameter	Mean ± SD	Interpretation
T3 (ng/ml)	1.02 ± 0.22	Near Normal
T4 (µg/dl)	5.5 ± 1.4	Improving
TSH (µIU/ml)	2.1 ± 1.0	Normal

Table 7: Thyroid Status Classification After 6 Months

Thyroid Status	Number of Patients	Percentage (%)
Euthyroid	70	70%
Sick Euthyroid Syndrome	15	15%
Subclinical Hypothyroidism	12	12%
Primary Hypothyroidism	3	3%

Table 8: Thyroid Function Test After 6–8 Weeks of Treatment Completion

Parameter	Mean ± SD	Interpretation
T3 (ng/ml)	1.12 ± 0.20	Normal
T4 (µg/dl)	6.3 ± 1.5	Normal

ISSN (O): 2687-5365; ISSN (P): 2753-6556

TSH (µIU/ml)	1.8 ± 0.9	Normal

Table 9: Final Thyroid Status After 6–8 Weeks of Treatment Completion

Thyroid Status	Number of Patients	Percentage (%)
Euthyroid	85	85%
Sick Euthyroid Syndrome	5	5%
Subclinical Hypothyroidism	8	8%
Primary Hypothyroidism	2	2%

Table 10: Statistical Significance of Changes in Thyroid Profile Over Time

Parameter	p-value	Interpretation
T3	< 0.001	Statistically significant improvement
T4	< 0.001	Statistically significant improvement
TSH	0.08	Not statistically significant

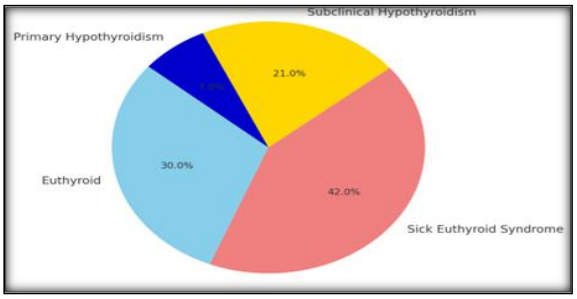

Figure 1: Thyrois Status Classification at Baseline

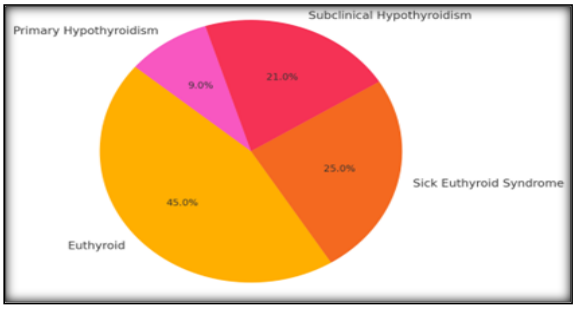

Figure 2: Thyrois Status Classification After 2 months of ATT

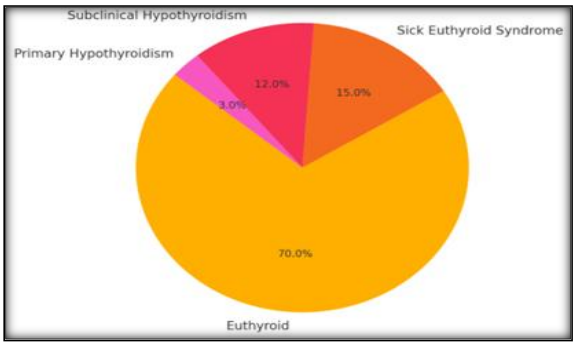

Figure 3: Thyrois Status Classification After 6 months of ATT

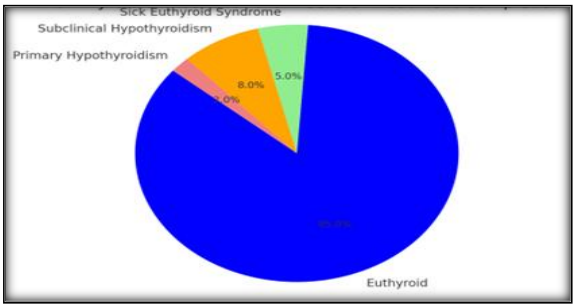

Figure 4: Final Thyrois Status After 6 to 8 weeks of Treatment Completion

DISCUSSION

This prospective observational study investigated the impact of pulmonary tuberculosis (PTB) and anti-tubercular therapy (ATT) on thyroid function. The findings revealed a high prevalence of thyroid dysfunction at the time of TB diagnosis, predominantly sick euthyroid syndrome (42%) and subclinical hypothyroidism (21%), which progressively normalized with treatment. These results underscore the dynamic, reversible nature of thyroid alterations associated with chronic infections like PTB.

At baseline, the pattern of low T3 and T4 levels with normal TSH is consistent with non-thyroidal illness syndrome (NTIS) or sick euthyroid syndrome, a phenomenon observed in patients with chronic systemic illnesses such as TB and trauma, where the body's adaptation to illness alters thyroid hormone metabolism without intrinsic thyroid gland disease.[8,14] Previous studies, including those by Hill et al. and Khan et al., have similarly reported transient thyroid hormone suppression in TB patients.[8]

The observed improvement in thyroid hormone levels (T3 and T4) during the intensive phase of ATT and further normalization by the end of the treatment align with findings from Kim et al. (2017), who showed recovery of thyroid function upon resolution of systemic inflammatory triggers and stabilization of HPT axis activity.[13] Moreover, our results are reinforced by Ige et al. (2016), who reported variable thyroid hormone patterns in TB patients, particularly those with multidrug-resistant strains and HIV co-infection.[12]

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Notably, rifampicin, a key component of ATT, is known to influence thyroid hormone metabolism by inducing hepatic enzymes, potentially lowering serum thyroid hormone levels, especially in patients on levothyroxine therapy.[13] Although none of our patients were on thyroid medications, this interaction highlights the importance of interpreting TFTs cautiously during ATT.

Interestingly, there are rare reports of direct thyroid involvement in miliary TB, causing more overt dysfunction, as documented in a recent case by Nagashima et al. (2024), where thyroid pathology co-occurred with hematologic complications during TB treatment.[9] Although not observed in our cohort, such possibilities warrant clinical vigilance.

Our study's findings align with broader literature suggesting that TB-related thyroid dysfunction is typically functional and reversible, resolving with successful infection control.[10,11] This was evident in our cohort, where 85% of patients achieved euthyroid status by 6–8 weeks post-ATT.

Overall, these results highlight the importance of routine thyroid function monitoring in PTB patients, particularly during early treatment when thyroid derangements are most pronounced. It also underscores the need to differentiate between transient illness-induced dysfunction and true primary thyroid disease to prevent unwarranted thyroid hormone replacement therapy, which may be unnecessary and potentially harmful.[10]

CONCLUSION

This study demonstrates that thyroid dysfunction, particularly sick euthyroid syndrome and subclinical hypothyroidism, is commonly observed in patients with pulmonary tuberculosis at the time of diagnosis. These alterations are likely due to the systemic inflammatory response and impaired hypothalamic-pituitary-thyroid axis regulation associated with chronic infection. However, significant improvement in thyroid hormone levels was observed with the progression of anti-tubercular therapy, and most patients returned to a euthyroid state by the end of treatment. Regular monitoring of thyroid function in TB patients is essential to differentiate transient dysfunction from primary thyroid disorders and to guide appropriate clinical management without unnecessary hormone replacement.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556