

## Original Research Article

# Thyroid profile in pulmonary tuberculosis patients: a prospective study in a tertiary medical college of southern Odisha

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## ABSTRACT

**Background:** Globally, an estimated 10.0 million (range, 9.0 to 11.1 million) people infected with tuberculosis (TB). Developing country like India accounts for one fourth of the global tuberculosis burden. TB is associated with diffuse functional impairment of most endocrine organs.

**Methods:** We conducted a study to evaluate the thyroid profile status in new sputum positive pulmonary tuberculosis patients, aged 12 years and above; attended and admitted to chest and TB, Medicine Department of SLN MCH, Koraput, Odisha from January 2019 to December 2019. Patients with H/o old pulmonary tuberculosis, patient with known neurological, hypothalamic-pituitary or thyroid disorders, kidney disease, malignancies and patients receiving medications known to interfere with thyroid hormone metabolism were excluded from the study. Statistical analysis was done by using SPSS version 21.0 software. Results were expressed in average±SD, frequencies and percentages. Continuous data were compared using Student's t-test. A p value <0.05 was considered as statistically significant and p value <0.001 was considered as statistically extremely significant.

**Results:** Mean age of the study group was 37.31±15.63 years. 54 patients (40.30%) were in 20 to 40 years of age group. We found, 48 (35.82%) pulmonary tuberculosis patients had sick euthyroid syndrome out of 134 pulmonary tuberculosis patients.

**Conclusions:** Sick euthyroid syndrome occurs commonly in pulmonary tuberculosis patients with increasing incidence with advanced age, and also seen in patients with advanced pulmonary tuberculosis patients; therefore, requires monitoring of thyroid function test for its timely initiation of therapy.

**Keywords:** Pulmonary tuberculosis, Thyroid profile, Sick-euthyroid, Hypothyroid, Hyperthyroid

## INTRODUCTION

Tuberculosis (TB) is a communicable disease that is a major cause of ill health, one of the top 10 causes of death worldwide and the leading cause of death from a single infectious agent (ranking above HIV or AIDS). Most people who develop TB (about 90%) are adults, the male: female ratio is 2:1, and case rates at national level vary from less than 50 to more than 5000 per 1 million populations per year. Globally, an estimated 1.7 billion

people are infected with *Mycobacterium tuberculosis* and are thus at risk of developing the disease.

It is caused by the bacillus *M. tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air; for example, by coughing. It typically affects the lungs (pulmonary TB) but can also affect other sites (extra pulmonary TB). About a quarter of the world's population is infected with *M. tuberculosis* and thus at risk of developing TB disease.<sup>1</sup> It is known by various

other names throughout the history like consumption, phthisis, scrofula, Pott's disease and white plague.

Globally, an estimated 10.0 million (range, 9.0 to 11.1 million) people infected with tuberculosis in 2018, a number that has been relatively stable in recent years.<sup>2</sup> The burden of disease varies enormously among countries, from fewer than five to more than 500 new cases per 100,000 population per year, with the global average being around 130.

TB affects people of both sexes in all age groups but the highest burden is in men (aged  $\geq 15$  years), who accounted for 57% of all TB cases in 2018. By comparison, women accounted for 32% and children (aged  $< 15$  years) for 11%. Among all TB cases, 8.6% were people living with HIV (PLHIV). Geographically, most TB cases in 2018 were in the WHO regions of South-East Asia (44%), Africa (24%) and the Western Pacific (18%), with smaller percentages in the Eastern Mediterranean (8%), the Americas (3%) and Europe (3%). Eight countries accounted for two thirds of the global total: India (27%), China (9%), Indonesia (8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). These and 22 other countries in WHO's list of 30 high TB burden countries accounted for 87% of the world's cases.<sup>3</sup>

Developing country like India accounts for one fourth of the global tuberculosis burden. It is estimated that tuberculosis kills more adults in India, more than any other infectious disease. According to the latest survey it is estimated that it kills 2 persons in every 5 minutes.<sup>4</sup>

It is well proved that, in a variety of nonthyroidal illnesses, alterations of circulating thyroid hormone concentrations occur.<sup>5,6</sup> The changes are characterized by reduction in serum total triiodothyronine (T3) as well as free T3 concentrations, serum total thyroxine (T4) concentrations may be reduced, elevated or normal; free T4 concentrations vary depending on assay methodology and are difficult to interpret.<sup>7</sup> Despite these changes, most patients remain clinically euthyroid and have a relatively normal basal serum thyroid-stimulating hormone (TSH) concentration with a normal or blunted response to thyrotropin-releasing hormone; hence the term euthyroid sick syndrome.<sup>5,6</sup>

TB is associated with diffuse functional impairment of most endocrine organs. The spectrum of TB associated endocrinopathies is extensive. The prevalence of TB involvement of thyroid gland ranges from 2 to 7%. The commonest manifestation of pulmonary tuberculosis involving thyroid gland was found to be sick euthyroid syndrome.<sup>8</sup> The exact mechanism responsible for the alteration is still unknown, though the following mechanisms were suggested; like decreased T4 to T3 conversion, decreased TSH production.<sup>9,10</sup> A minority of patients with TB presents with clinically overt symptoms;

hence, the need among clinicians to possess a high index of suspicion for early diagnosis and initiation of appropriate treatment. There were many studies done in MDR TB cases to know the incidence of drug induced hypothyroidism.<sup>11</sup> Thyroid function test is mandatory test before the initiation of MDR TB drugs, but no such protocol is made in new smear positive pulmonary tuberculosis patients.

Objective of the study is to find out the prevalence of thyroid dysfunction among the newly diagnosed sputum positive tuberculosis patients before initiation of anti-tubercular drugs.

## METHODS

It is a prospective cohort study conducted after getting the ethical committee clearance from the institute. The patients attended and admitted to chest and TB, Medicine Department of SLN medical college and Hospital, Koraput, Odisha from January 2019 to December 2019 with pulmonary tuberculosis were included in the study. PTB was diagnosed as per the institutional protocol, i.e. on clinical presentation of the patient, microscopic examination suggestive of acid-fast bacilli (AFB) and sputum cartridge based nucleic acid amplification test (CBNAAT).

### Inclusion criteria

Adult patients aged 12 years and above diagnosed with active pulmonary tuberculosis were taken into the study.

### Exclusion criteria

Patients with less than 12 years, H/o old pulmonary tuberculosis, patient with known neurological, hypothalamic-pituitary or thyroid disorders, kidney disease, malignancies, patients receiving medications known to interfere with thyroid hormone metabolism (such as iodide, beta-blockers, lithium, phenytoin, corticosteroids, dopamine and dobutamine) were excluded.

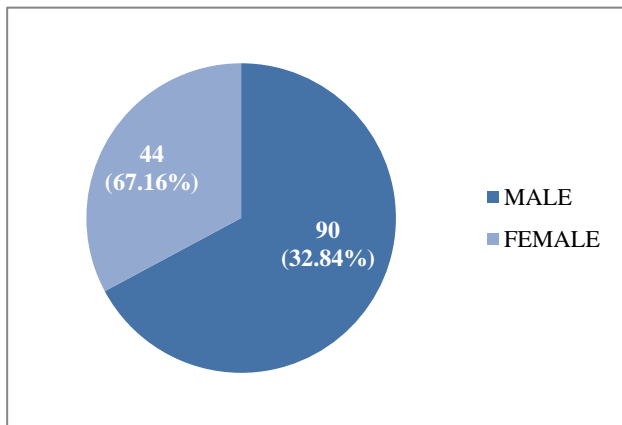
Demographic characteristics and laboratory data of the patients were recorded and analyzed. The microbiological tests were done in the RNTCP lab of our hospital. Thyroid profile was done in all the patients. Based on thyroid dysfunction, patients were classified as Overt hypothyroidism (high TSH (more than 5.5  $\mu$ IU/l) with low T4 and T3), subclinical hypothyroidism (high TSH (more than 5.5  $\mu$ IU/l) and normal T4 and T3), Overt hyperthyroidism (low TSH (less than 0.35  $\mu$ IU/l) with high T4 and/or T3), subclinical hyperthyroidism (low TSH (less than 0.35  $\mu$ IU/l) and normal T4 and T3), euthyroid (normal TSH, T3 and T4), and sick euthyroid (low T3 with normal TSH and T4 or low T4 and T3 with normal TSH).<sup>12</sup> Thyroid profile of 65 healthy persons was taken as control in our study.

**Statistical analysis**

All the data were fed on excel spreadsheet and statistical analyses were made using SPSS version 21.0 software. Results were expressed in average±SD, frequencies and percentages. Continuous data were compared using Student’s t-test. A p<0.05 was considered as statistically significant and p<0.001 was considered as statistically extremely significant for all tests conducted.

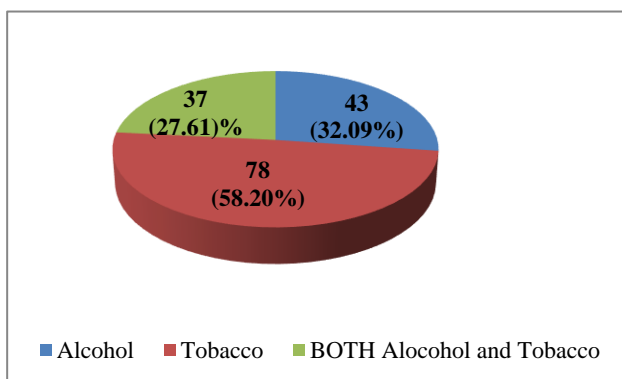
**RESULTS**

During the study period we included 134 smear positive pulmonary tuberculosis patients in our study that fulfills inclusion and exclusion criteria. In our study group, we found 56 (41.79%) patients who are sputum smear negative and CBNAAT positive. Three (2.24%) patients were PLHA.



**Figure 1: Sex distribution.**

Figure 1 shows the sex distribution of pulmonary tuberculosis patients among the study group. The M:F ratio was 2.04:1.



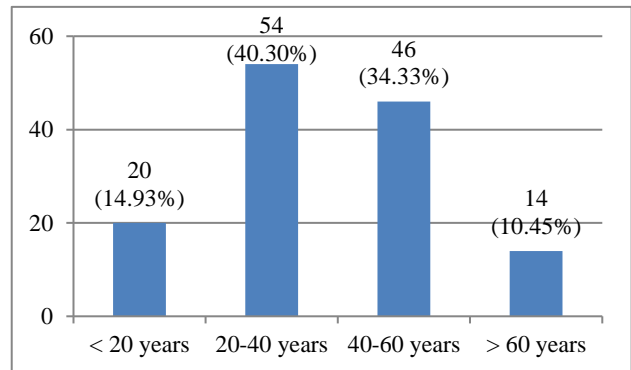
**Figure 2: Substance addiction of pulmonary tuberculosis patients.**

In our study group, Figure 2 shows 43 (32.09%) patients were addicted to alcohol, 78 (58.20%) patients were addicted to tobacco and 37 (27.61%) patients were addicted to both alcohol and tobacco.

**Table 1: Mean age of patients in the study group.**

Gender	Mean±SD
Male	40.32±15.09
Female	31.14±15.05
Total	37.31±15.63

Table 1 show mean age of the study group was 37.31±15.63 years. Mean age of male patients was 40.32±15.09 years; mean age of female patients was 31.14±15.05 years. In our study, the youngest patient was 12 years old and oldest was 80 years old.



**Figure 3: Number of patients as per age group.**

Figure 3 show number of pulmonary tuberculosis patients in different age group. Highest number of patients 54 (40.30%) was in 20 to 40 years of age group followed by 46 (34.33%) in 40 to 60 years age group.

**Table 2: Prevalence of anemia among pulmonary tuberculosis patients.**

Types of anemia	Male (n=90)		Female (n=44)	
	N	%	N	%
Mild (11-12.9 g/dl in males) and (11-11.9 g/dl in females)	2	2.22	1	2.27
Moderate (8-10.9 g/dl)	14	15.56	11	25.00
Severe (<8 g/dl)	3	3.33	1	2.27
Total	19	21.11	13	29.55

Table 2 show prevalence of anemia among pulmonary tuberculosis patients. We found anemia in 32 (23.88%) patients in our study group. Among them, 25 (78.12%) patients had moderate anemia. Nineteen (21.11%) male patients and thirteen (29.55%) female patients had anemia in our study group.

We found, 48 (35.82%) pulmonary tuberculosis patients had sick euthyroid syndrome out of 134 pulmonary tuberculosis patients. Table 3 shows sick euthyroid patients in different age group, we found the percentage of pulmonary tuberculosis patients having sick euthyroid syndrome was increasing with advanced age.

**Table 3: Sick euthyroid patients in different age group.**

Age (years)	Sick euthyroid patients in corresponding age group	%
<20	3	15.00
20-40	12	22.22
40-60	23	50.00
>60	10	71.42
<b>Total</b>	<b>48</b>	

Table 4 show type of thyroid dysfunction in study group comparing with control. We found, 78 (58.21%) pulmonary tuberculosis patients were having euthyroid status, 56 (58.21%) persons among the control group had euthyroid status; which is statistically extremely significant ( $p < 0.0001$ ). It was observed in our study that, 48 (35.82%) pulmonary tuberculosis patients were having sick euthyroid status, only one (1.53%) person among the control group had sick euthyroid status; which is statistically extremely significant ( $p < 0.0001$ ).

**Table 4: Type of thyroid dysfunction in study group comparing control.**

Types of thyroid dysfunction	Study group (n=134)		Control (n=65)		P value
	N	f	N	f	
<b>Euthyroid</b>	78	58.21%	56	86.15%	0.0001
<b>Sick euthyroid</b>	48	35.82%	1	1.53%	0.0001
<b>Subclinical hypothyroid</b>	0	0%	2	3.08%	0.1056
<b>Subclinical hyperthyroid</b>	3	2.24%	2	3.08%	0.6624
<b>Overt hypothyroid</b>	3	2.24%	2	3.08%	0.6624
<b>Overt hyperthyroid</b>	2	1.49%	2	3.08%	0.5980
<b>Total</b>	134	100.00%	65	100.00%	

**Table 5: Thyroid profile comparison between male vs. female.**

Thyroid profile	Male (n=90)	Female (n=44)	P value
<b>T3 (ng/ml)</b>	0.69±0.36	0.74±0.34	0.4435
<b>T4 (µg/dl)</b>	10.35±3.23	10.88±2.78	0.3529
<b>TSH (µIU/l)</b>	2.16±2.49	2.17±1.69	0.9809

**Table 6: Thyroid profile comparison between study group vs. control.**

Thyroid profile	Study group (n=134)	Control (n=65)	P value
<b>T3 (ng/ml)</b>	0.71±0.35	1.08±0.29	0.0001
<b>T4 (µg/dl)</b>	10.52±3.09	10.16±2.44	0.4117
<b>TSH (µIU/l)</b>	2.16±2.25	5.93±20.50	0.0001

**Table 7: Thyroid profile comparison between smear positive vs. smear negative, CBNAAT positive patients.**

Thyroid profile	Smear positive (n=78)	Smear negative, CBNAAT positive (n=56)	P value
<b>T3 (ng/ml)</b>	0.71±0.36	0.70±0.33	0.8699
<b>T4 (µg/dl)</b>	10.55±3.09	10.49±3.10	0.9121
<b>TSH (µIU/l)</b>	1.82±1.12	2.64±3.18	0.0372

Table 5 show thyroid profile comparison in mean±S.D. between male vs. female, which was not statistically significant.

Table 6 shows thyroid profile comparison in mean±S.D. between study group vs. control. Serum T3 level in study group was 0.71±0.35 ng/ml and in control group was 1.08±0.29 ng/ml; which is statistically extremely significant ( $p < 0.0001$ ). Also, serum TSH level in study group was 2.16±2.25 µIU/l and in control group was 5.93±20.50 µIU/l; which is statistically extremely significant ( $p < 0.0001$ ).

Table 7 show thyroid profile comparison between smear positive, CBNAAT positive vs. smear negative, CBNAAT positive pulmonary tuberculosis patients; the serum TSH level between the two groups is significant ( $p < 0.05$ ).

It was observed that, 78 (58.21%) pulmonary tuberculosis patients who were smear positive and CBNAAT positive in our study; out of which 30 (38.46%) patients had sick euthyroid syndrome; 56 (41.79%) pulmonary tuberculosis patients who were smear negative and CBNAAT positive in our study; out of which 30 (38.46%) patients had sick

euthyroid syndrome in our study, with p value of 0.4715, which is not significant statistically.

## DISCUSSION

During the study period we included 134 smear positive pulmonary tuberculosis patients in our study that fulfills inclusion and exclusion criteria out of which 90 (67.16%) patients were male and 44 (32.84%) patients were female with M:F ratio was 2.04:1. In our study group, 43 (32.09%) patients were addicted to alcohol, 78 (58.20%) patients were addicted to tobacco and 37 (27.61%) patients were addicted to both alcohol and tobacco. 65% of the patients were found to be male in Thomas et al study.<sup>13</sup> Thomas et al found 28% of their study group was smokers.

Mean age of the study group was  $37.31 \pm 15.63$  years with youngest being 12 years old and being 80 years old.

Highest number of patients 54 (40.30%) was in 20 to 40 years of age group followed by 46 (34.33%) in 40 to 60 years age group in our study population. Maximum number of patients belonged to the age group between 40 to 50 years with a mean age of  $49 \pm 16$  years in Varghese et al study.<sup>14</sup>

We observed anemia in 32 (23.88%) patients in our study group. Among them, 25 (78.12%) patients had moderate anemia. Lee et al study found anemia in 31.9% of tuberculosis patients at the time of diagnosis.<sup>15</sup>

Sick euthyroid syndrome is the most frequently encountered biochemical abnormality. In our study, we found that, 48 (35.82%) pulmonary tuberculosis patients had sick euthyroid syndrome out of 134 pulmonary tuberculosis patients. Kaplan et al in a cross-sectional study done in South Africa reported a prevalence of sick euthyroid syndrome of 42% among 40 patients with active TB.<sup>16</sup> In another cross-sectional study of 50 hospitalized patients with active tuberculosis in South Africa, 46 (92%) patients were found to have sick euthyroid syndrome.<sup>17</sup> We found the percentage of pulmonary tuberculosis patients having sick euthyroid syndrome was increasing with advanced age.

In our study, we observed 78 (58.21%) pulmonary tuberculosis patients were having euthyroid status, 56 (58.21%) persons among the control group had euthyroid status; which is statistically extremely significant ( $p < 0.0001$ ). It was observed in our study that, 48 (35.82%) pulmonary tuberculosis patients were having sick euthyroid status, only one (1.53%) person among the control group had sick euthyroid status; which is statistically extremely significant ( $p < 0.0001$ ).

Serum T3 level in study group was  $0.71 \pm 0.35$  ng/ml and in control group was  $1.08 \pm 0.29$  ng/ml; which is statistically extremely significant ( $p < 0.0001$ ). Also, serum TSH level in study group was  $2.16 \pm 2.25$   $\mu$ IU/l and

in control group was  $5.93 \pm 20.50$   $\mu$ IU/l; which is statistically extremely significant ( $p < 0.0001$ ).

With thyroid profile comparison between smear positive, CBNAAT positive vs. smear negative, CBNAAT positive pulmonary tuberculosis patients; we found in our study, the serum TSH level between the two groups is significant ( $p < 0.05$ ).

## CONCLUSION

This study shows that euthyroid sick syndrome occurs commonly in pulmonary tuberculosis patients with increasing incidence with advanced age, and also seen in patients with advanced pulmonary tuberculosis patients and therefore requires monitoring of thyroid function test for its timely initiation of therapy. Authors recommend thyroid function test to be done in all cases of pulmonary tuberculosis before initiating treatment with ATT.

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