

## Comparison of TSH Levels Pulmonary Tuberculosis Patients at The Phase 0 and 6 Months Treatment

Alamanda Nurul Qo'imah, Dita Pratiwi Kusuma Wardani\*, Tantri Analisisawati  
Sударsono, Arif Mulyanto

Faculty of Health Science, Muhammadiyah University of Purwokerto, Indonesia

\*Email: dita.tiwhie@gmail.com

### Article history

Posted, Apr 4<sup>th</sup>, 2022

Reviewed, Aug 11<sup>th</sup>, 2022

Received, Sept 28<sup>th</sup>, 2022

### ABSTRACT

*Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis. Pulmonary TB has become a health problem worldwide, including in Indonesia, because the sufferers' prevalence is increasing every year. The increase in TB drug resistance will pose a severe health threat. The continuous consumption of drugs in large quantities and high doses can affect the function of the thyroid gland. This study aimed to determine the levels of thyroid stimulating hormone (TSH) in pulmonary tuberculosis patients with treatment phases of 0 months and six months. This research is analytical observational research with a cross-sectional research design. The sampling method uses accidental sampling. A total of 42 respondents participated in this study to determine the levels of TSH in pulmonary TB. The results of the Mann-Whitney U test showed no difference in TSH levels in pulmonary TB patients with different treatment phases of 0 months and six months ( $p = 0.3$ ). There was no significant difference between TSH levels in pulmonary TB patients in the 0 and 6-month treatment phases.*

**Keywords:** *pulmonary tuberculosis; thyroid stimulating hormone TSH; Mycobacterium tuberculosis*

### ABSTRAK

Tuberkulosis (TB) merupakan penyakit menular yang disebabkan oleh *Mycobacterium tuberculosis*. TB paru menjadi permasalahan kesehatan di dunia termasuk Indonesia karena prevalensi jumlah penderita semakin meningkat setiap tahunnya. Peningkatan resistensi obat TB akan menimbulkan ancaman kesehatan yang serius di masa mendatang. Konsumsi obat secara terus menerus dalam jumlah banyak dan dosis tinggi dapat mempengaruhi fungsi kelenjar tiroid. Penelitian ini bertujuan untuk mengetahui kadar *thyroid stimulating hormone* (TSH) pada pasien tuberkulosis paru dengan fase pengobatan 0 bulan dan 6 bulan. Penelitian berjenis observasional analitik dengan rancangan penelitian *cross sectional*. Metode pengambilan sampel dilakukan dengan cara *accidental sampling*. Sebanyak 42 responden mengikuti penelitian ini untuk diketahui kadar TSH pada TB paru. Hasil uji Mann-Whitney U menunjukkan kadar TSH pada pasien TB paru dengan fase pengobatan 0 bulan dan 6 bulan

( $p=0,3$ ). Tidak terdapat perbedaan kadar TSH pasien TB paru pada fase pengobatan 0 dan 6 bulan.

**Kata Kunci:** *tuberkulosis paru; hormon TSH; Mycobacterium tuberculosis*

## INTRODUCTION

Pulmonary Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. These bacteria are acid-fast and can transmit diseases to the respiratory tract (Dasopang, Hasanah, and Nisak, 2019). Pulmonary TB is a health problem in the world, including in Indonesia, because the prevalence of sufferers is increasing every year (Biranu *et al.*, 2021). World Health Organization (2021) reports that the eight countries with the highest TB prevalence in the world are India, China, Indonesia, Philippines, Pakistan, Nigeria, Bangladesh, and South Africa. These eight countries, together with WHO, in the last 20 years have made efforts to reduce the prevalence of pulmonary TB.

Central Java in 2018 was the area with the third highest Tuberculosis in Indonesia, with cases of the disease estimated to have reached 38,270 people. The success rate of treatment in 2018 was 76.58%, a decrease from 2016 with a treatment success rate of 82.89% (Adyaningrum, Suryawati, and Budiyananti, 2019). The number that shows all newly discovered and recorded patients among 100,000 residents in a particular area is called the Case Notification Rate

(CNR). In 2017, the CNR in Banyumas in TB cases was 213.8 per 100,000 (Kemenkes RI, 2018).

Pulmonary TB can be treated and cured through regular treatment procedures. The treatment procedures consists of two stages: an intensive stage in the first two months and an advanced stage in the next 4-6 months (Fitriani *et al.* 2020). Judging from the high cases of pulmonary TB and the high risk of transmission, the government issued a policy to control pulmonary TB through the procurement of Anti Tuberculosis Drugs (ATD), with the Directly Observed Treatment Shortcourse (DOTS) strategy aimed to reducing the spread of pulmonary TB disease (Kemenkes RI, 2018). Pulmonary TB patients are recommended to take ATD routinely and regularly. Success in treating pulmonary TB must be accompanied by patient compliance in undergoing a series of treatments. The impact of consuming ATD is the emergence of side effects, so it is necessary to monitor the side effects of the treatment being undertaken by the patient (Dasopang, Hasanah, and Nisak, 2019).

The increase in pulmonary TB drug resistance will pose a severe public health threat in the future. Consumption of drugs continuously in large quantities and in high doses can affect the function of the thyroid gland (Andries *et al.* 2013). The Thyroid Stimulating Hormone (TSH) levels change after taking ATD is a sign of disruption of the balance of thyroid gland function. The normal value of the TSH hormone in adults ranges from 0.4 to 4.5 mIU/L (Ige *et al.* 2016).

TSH is a hormone in the form of a glycoprotein secreted by the anterior pituitary and stimulates the thyroid gland. The function of TSH levels in pulmonary TB patients is to diagnose hypothyroidism (Suparyatmo *et al.*, 2014). The thyroid gland plays a vital role in maintaining the stability of the body's metabolism, with the principle of secreting thyroxine (T4) and triiodothyronine (T3) under the influence of the TSH hormone. Drugs consumed by patients with pulmonary TB can cause hypothyroidism by inhibiting thyroid hormone synthesis by inhibiting the mechanism of iodine action (Matveyeva *et al.* 2017).

There was no significant difference in TSH levels in pulmonary TB patients before and after treatment (Hamza & Sabee, 2016).

There was an increase in TSH levels during the treatment process and at the end of treatment in most pulmonary TB patients (Varghese, Menon, and Green, 2018). This study aims to determine the levels of TSH in pulmonary TB patients with treatment phases of 0 months and six months.

## **METHOD**

This research used a cross-sectional research design, and it was conducted in December 2021-January 2022 at Balai Kesehatan Paru Masyarakat (BKPM) Purwokerto after obtaining ethical approval from KEPK FK Unsoed No. 200/KEPK/IX/2021. Sampling was carried out at BKPM Purwokerto, while the specimen was examined at the Laboratory of Haematology, Medical Laboratory Technology Department, Muhammadiyah University Purwokerto.

Forty-two patients with pulmonary TB were included in this study using the accidental sampling technique. The subjects included in this research are: willing to sign in the informed consent, aged 20-70 years, registered as pulmonary TB patients at BKPM Purwokerto with treatment phases of 0 months and six months; not suffering from HIV, hypertension, or diabetes mellitus based on anamnesis and laboratory examination

results.

The excluded subjects have the following characteristics: the sufferer of autoimmune disorders, metabolic syndrome, hematological disorders, thyroid disorders, heart disease, urinary disorders, and liver disorders based on anamnesis and laboratory results; extrapulmonary TB patients, MDR (Multi Drugs Resistant) tuberculosis, and XDR (Extensively Drugs Resistant) Tuberculosis; pulmonary tuberculosis patients who are taking allergy medicine as an alternative to fixed-dose combination anti-tuberculosis drugs (OAT-KDT) category 1; lysis/lipemic serum specimens: and subject who does not attend during research.

### **Materials**

Syringe (BD 3 ml), tourniquet, gloves, mask, plaster, alcohol cotton, dry cotton, centrifuge, micropipette, tip, tube rack, serum cup (Eppendorf), plastic bag, Easy Reader, and the patient's venous blood sample.

### **Procedure for venous blood drawn**

The specimen was taken from venous blood. The patient was asked to sit by straightening the arm and clenching the fist, placing a tourniquet  $\pm 10$  cm above the elbow crease, selecting the median cubital vein by palpation, disinfecting it with 70%

alcohol, stabbing the vein with a syringe tilted  $\pm 15^\circ$  with the syringe needle facing up, then withdraw the syringe until the blood sample volume is considered sufficient (Kemenkes RI, 2013).

### **The Thyroid Stimulating Hormone Test (AIM, 2019)**

The TSH levels examination in this study was using a rapid quantitative (quantitative immunochromatographic) method. The respondent's blood sample was centrifuged to obtain serum and placed into a serum cup. The required 25  $\mu\text{L}$  serum sample was dropped into the TSH Rapid Test well, then 150  $\mu\text{L}$  of diluent was added. The results were read at 15 minutes using Easy Reader with normal values for adults  $< 5$  mIU/L. The data were analyzed by Mann-Whitney U Test using Jeffery's Amazing Statistics Program (JASP) ver. 16.

## **RESULTS AND DISCUSSION**

The predominant of pulmonary TB patients was 25 (59.5%) male. The median age was 44.00 (20-70) years. The treatment phase of respondents 0 months was 21 (50%) with a median TSH level of 2.219 (2-5.7) mIU/L and six months was 21 (50%) with a median TSH level of 2.019 (2-2.4) mIU/L. The details of the characteristics of the subject are described in Table 1.

Table1. Characteristic Subjects

Characteristic	Frequency (n)	Percentage (%)	Median (min-max)
<b>Gender</b>			
Male	25	59.5	
Female	17	40.5	
<b>Age (year)</b>			44.00 (20-70)
<b>The treatment phase</b>			
0 months	21	50	
six months	21	50	

Male patients are more dominant than women because men have a relatively low concern about health care compared to women and easier to contact with Tuberculosis risk factors (Hutama, 2019). Hadifah *et al.* (2019) reported that the failure of treatment for pulmonary TB patients due to irregular treatment also causes a high number of male pulmonary TB patients. The dominance of male patients in pulmonary TB is also caused by

higher alcohol consumption and smoking history. Absor *et al.* (2020) also reported that three factors influence adherence to ATD consumption. First, there are predisposing factors consisting of gender, age, education level, and occupation. Second, there is a driving factor, consisting of side effects of OAT consumption, and the third is a reinforcing factor, in the form of support from family and health workers.

Table 2. TSH levels in Pulmonary TB Patients against treatment phases, gender, and age

Parameter	Median (min-max) TSH Levels	p
<b>The treatment phases</b>		
0 months (n= 21)	2.219 (2.0-5.7)	0.3
6 months (n=21)	2.019 (2.0-2.4)	
<b>Gender</b>		
Male (n= 25)	2.200 (2.0-5.7)	0.087
Female (n= 17)	2.000 (2.0-2.0)	
<b>Age</b>		
< 50 tahun (n = 31)	2.000 (2.0-2.3)	0.233
>50 tahun (n= 11)	2.000 (2.0-5.7)	

Based on Table 2 represented the TSH level in the 0-month treatment phase was 2,219 (2-5.7) mIU/L. TSH levels in the 6-month treatment phase were 2,019 (2-2.4) mIU/L.

There was no difference in TSH levels between the 0-month and 6-month treatment phases ( $p = 0.3$ ). These results are similar to Hamza and Sabee (2016), who

also reported no difference in TSH levels in female TB patients before treatment, two months after treatment, and six months after treatment. In contrast with Varghese, Menon, and Green (2018) study reported that there were differences in TSH levels before treatment, three months after treatment, and six months after treatment ( $p < 0.001$ ).

The TSH level in men is 2,200 (2.0-5.7) mIU/L while in women it is 2,000 (2.0-2.0) mIU/L. There was no difference in TSH levels between male and female TB patients ( $p = 0.087$ ). Dash, Behera, and Sen (2020) also reported that there was no difference in TSH levels between male and female pulmonary TB patients in Odisha, India ( $p = 0.98$ ). The TSH level in TB patients aged  $<50$  years is 2,000 (2.0-2.3) mIU/L while those  $>50$  years is 2,000 (2.0-5.7) mIU/L. There was no difference in TSH levels between TB patients aged  $<50$  years and  $>50$  years ( $p = 0.233$ ). Kurniawan and Arif (2018) state that the factors that influence the measurement of TSH levels include discrepancies between a person's clinical signs and TSH levels, people with an acute illness, old age, and consumption of drugs. The presence of the Rheumatoid Factor can cause a false positive TSH

result.

TSH levels in patients with pulmonary TB are still within a normal value, and this can be due to a decrease in the dose of drugs consumed in the advanced stage of treatment until the completion of the treatment stage, which is only consumed three times a week. This case is different from the initial stage of treatment, which must take OAT every day for two months. Reducing the dose can reduce the side effects of ATD so that TSH levels in patients with dominant pulmonary TB are still within normal levels (Mustafa dan Sugireng, 2019).

It is necessary to measure the levels of T3 and T4 as a supporting examination of the TSH hormone in pulmonary TB patients. Devalraju *et al.* (2021) reported that the levels of T3 and T4 decreased after three years of ATD administration. The decrease in T4 levels occurred since the start of pulmonary TB activation and after three years of OAT administration. T3 and T4 hormones act as markers of resistance to *M. tuberculosis* infection. The lack of production of thyroid hormones triiodothyronine (T3) and thyroxine (T4) can cause thyroid gland dysfunction

(hypothyroidism) due to a lack of iodine so that the thyroid gland cannot meet sufficient TSH in the body. Iodine is a major component of the formation of thyroid hormones. Iodine deficiency for a long time can cause disorders due to iodine deficiency (IDA), such as inhibition of growth and development (cretinism), brain damage, hypothyroidism, goiter, and impaired mental function. Hypothyroidism can result in decreased fat, protein, and carbohydrate metabolism in the body (Adnan, 2021). Side effects of taking OAT can cause hypothyroidism in patients with pulmonary TB. Drastic weight loss can also lead to hypothyroidism due to low serum iodine concentrations (Biranu *et al.* 2021).

Adnan (2021) states that there are four types of causes of hypothyroidism, including primary hypothyroidism (it is caused by the influence of drug consumption, lack of iodine intake, and thyroidectomy), secondary hypothyroidism (it is caused by a problem with the pituitary gland in the brain), tertiary hypothyroidism (it is caused by a disturbance in the hypothalamus that affects TRH secretion), and peripheral hypothyroidism (it is caused by peripheral resistance to thyroid hormone invasion). Dash, Behera, and Sen (2020) study reported that the levels of T3 and T4

hormones in pulmonary TB patients before and after treatment showed a significant decrease in levels. It is necessary to examine the hormones T3 and T4 in TB patients before and after treatment. Meanwhile, TSH levels in pulmonary TB patients are within the normal levels. It could be due to pulmonary TB disease and ATD consumption did not affect the hypothalamus gland and Thyrotropin Releasing Hormone (TRH) in the pituitary gland. This fact is in line with conducted research because there are no differences in TSH levels in patients with pulmonary TB with different phases of treatment.

The limitation of this study is uses quantitative immunochromatographic methods with Easy reader, while Hamza and Sabee (2016) study uses the ELISA method, which has a higher sensitivity.

## **CONCLUSION**

There was no difference in TSH levels in pulmonary TB patients based on treatment phases of 0 and 6 months. For monitoring, TSH levels in pulmonary TB patients should be checked before and after treatment. There has not been an assessment between the hormones T3, T4, and TSH in pulmonary TB patients, so further research is needed.

## ACKNOWLEDGEMENT

The researchers would like to express gratitude to the Higher Education Research and Development Council of Muhammadiyah Central Leadership through the Muhammadiyah Research Grant Batch V in 2021 Number: 0842.255/PD/I.3/C/2021 for funding this research through the Basic Research scheme. Also, high appreciate to LPPM Muhammadiyah University of Purwokerto, Medical Laboratory Technology department, and BKPM Purwokerto for facilitating this research.

## REFERENCES

- Absor, S. *et al.* (2020) 'Hubungan Tingkat Pendidikan Dengan Kepatuhan Berobat Penderita Tb Paru Di Wilayah Kabupaten Lamongan Pada Januari 2016 – Desember 2018', *Medica Arteriana (Med-Art)*, 2(2), p. 80. doi: 10.26714/medart.2.2.2020.80-87.
- Adnan, M. (2021) 'ASUHAN GIZI PADA HIPOTIROID Nutritional Care On Hypothyroid Miftahul Adnan Universitas Muhammadiyah Semarang', 9(1), pp. 19–24.
- Adyaningrum, N., Suryawati, C. and Budiyanti, R. T. (2019) 'Analisis Pengawasan Menelan Obat Pasien Tuberkulosis (TB) Dalam Program Penanggulangan TB di Puskesmas Sempor II Kabupaten Kebumen', *Jurnal Kesehatan Masyarakat (e-Journal)*, 7(4), pp. 542–555.
- AIM (2019) *AIM TSH Q Rapid Test*. Jakarta: PT. Akurat Intan Madya.
- Andries, A. *et al.* (2013). 'High Rate of Hypothyroidism in Multidrug-Resistant Tuberculosis Patients Co-Infected with HIV in Mumbai, India', *PLoS ONE*, 8(10), pp. 1–7. DOI: 10.1371/journal.pone.0078313.
- Biranu, E. *et al.* (2021). 'Thyroid profile and factors associated with hypothyroidism among multidrug-resistant tuberculosis patients attending saint peter's specialized hospital Addis Ababa, Ethiopia', *Infection and Drug Resistance*, 14(June), pp. 2675–2684. doi: 10.2147/IDR.S310404.
- Dash, M., Behera, B. P. and Sen, R. K. (2020). 'Thyroid profile in pulmonary tuberculosis patients: a prospective study in a tertiary medical college of southern Odisha', *International Journal of Clinical Trials*, 7(2), p. 66. doi: 10.18203/2349-3259.ijct20200538.
- Dasopang, E. S., Hasanah, F. and Nisak, C. (2019) 'Analisis Deskriptif Efek Samping Penggunaan Obat Anti Tuberculosis Pada Pasien TBC di RSUD Dr. Pirngadi Medan', *Jurnal Penelitian Farmasi & Herbal*, 2(1), pp. 44–49. doi: 10.36656/jpvh.v2i1.180.
- Devalraju, K. P. *et al.* (2021). 'Reduced thyroxine production in young household contacts of tuberculosis patients increases active tuberculosis disease risk', *JCI Insight*, 6(13), pp. 1–17. DOI: 10.1172/jci.insight.148271.
- Fitriani, N. E., Sinaga, T. and Syahrani, A. (2020) 'Hubungan Antara Pengetahuan, Motivasi Pasien dan Dukungan Keluarga Terhadap

- Kepatuhan Minum Obat Anti Tuberkulosis (OAT) Pada Penderita Penyakit TB Paru BTA (+) di Puskesmas Pasundan Kota Samarinda', *KESMAS UWIGAMA: Jurnal Kesehatan Masyarakat*, 5(2), p. 124. doi: 10.24903/kujkm.v5i2.838.
- Hadifah, Z., Subronto, Y. W. and Ikhsan, M. R. (2019) 'Faktor Risiko Gagal Konversi BTA pada Pasien Tuberkulosis Paru Fase Intensif di Kota Yogyakarta', *Buletin Penelitian Kesehatan*, 47(2), pp. 83–88. doi: 10.22435/bpk.v47i2.1002.
- Hamza, D. H. and Sabee, K. M. (2016). 'The Effect of pulmonary tuberculosis and short course treatment on some hormones of patients women', *Muthanna Medical Journal*, 3(2), pp. 139–146.
- Hutama, R. K. (2019) 'Gambaran Perilaku Penderita Tb Paru Dalam Pencegahan Penularan Tb Paru Di Kabupaten Klaten', *Jurnal Kesehatan Masyarakat (e-Journal)*, 7(1), pp. 491–500.
- Ige, O. M. *et al.* (2016). 'Thyroid function in multidrug-resistant tuberculosis patients with or without human immunodeficiency virus (HIV) infection before commencement of MDR-TB drug regimen', *African Health Sciences*, 16(2), pp. 596–602. DOI: 10.4314/ahs.v16i2.30.
- Kemendes RI (2013) *Cara Penyelenggaraan Laboratorium Klinik yang Baik*. Indonesia: Kementerian Kesehatan Republik Indonesia.
- Kemendes RI (2018) *Tuberkulosis (TB)*. 2018th edn, *Tuberkulosis*. 2018th edn. Jakarta Selatan: PUSAT DATA DAN INFORMASI KEMENTERIAN KESEHATAN RI.
- Kurniawan, L. B. and Arif, M. (2018) 'DIAGNOSIS TIROID (Diagnosis of Thyroid)', *Indonesian Journal of Clinical Pathology and Medical Laboratory*, 21(3), p. 304. doi: 10.24293/ijcpml.v21i3.1285.
- Matveyeva, S. L., Shevchenko, O. S. and Pogorelova, O. O. (2017). 'The function of the thyroid gland in patients with multi-drug resistant tuberculosis', *Antimicrobial Resistance and Infection Control*, 6(1), pp. 4–6. DOI: 10.1186/s13756-017-0238-4.
- Mustifa and Sugireng (2019) 'Fungsi ginjal penderita tuberkulosis paru (TB Paru) setelah penggunaan obat anti tuberkulosis kategori 1 (OAT Kat. 1) Di Puskesmas Katobu Kabupaten Muna', *Jurnal MediLab Mandala Waluya kendari*, 3(1), pp. 5–48.
- Suparyatmo *et al.* (2014) 'Kadar TSH di Multi Drug Resistance Tuberculosis Terkait Etionamid', *Indonesian Journal of Clinical Pathology and Medical Laboratory*, 20(3), pp. 238–241. Available at: <http://journal.unair.ac.id/download-fullpapers-IJCPML-12-3-08.pdf>.
- Varghese, V., Menon, K. S. and Green, S. R. (2018). 'Effect of anti-tuberculosis treatment on thyroid profile in newly detected smear-positive pulmonary tuberculosis cases', *Int J Adv Med*, 5(3), pp. 688–693. DOI: 10.5005/jp-journals-10085-7166.
- World Health Organization (2021) *Global Tuberculosis Report 2021*, World Health Organization. Geneva.