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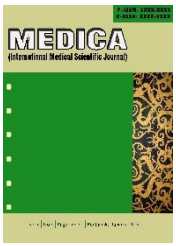

The Role of Vitamin D in TNF-α Levels in Pulmonary TB Patients

Sahidan[1]✉, Wiwit Sulistyasmi[1], Jon Farizal[1], Supri Hartini[2], Sri Ujiani[3]

[1] Department of Medical Laboratory Technology, Poltekkes Kemenkes Bengkulu, Bengkulu City, Bengkulu, Indonesia
[2] Department of Medical Laboratory Technology, Poltekkes Kemenkes Kalimantan Timur, Samarinda City, East Kalimantan, Indonesia
[3] Department of Medical Laboratory Technology, Poltekkes Kemenkes Tanjung Karang, Bandar Lampung, Lampung, Indonesia

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Abstract

Tuberculosis (TB) remains a major global health problem, with immune responses particularly tumor necrosis factor-alpha (TNF-α) playing a key role in disease progression. Vitamin D, synthesized through sunlight exposure, has been suggested to modulate immune responses; however, its effect on TNF-α in TB patients remains unclear. This study aimed to evaluate the effect of sunlight exposure on TNF-α levels in patients with pulmonary tuberculosis. A quasi-experimental pre–post study was conducted among 60 TB patients divided into control and intervention groups. TNF-α levels were measured before and after intervention and analyzed using appropriate statistical tests, including the Wilcoxon signed-rank test. The results showed a slight increase in mean TNF-α levels after sunlight exposure; however, the difference was not statistically significant ($p = 0.475$). Increased variability in TNF-α levels after the intervention suggests heterogeneous individual responses. These findings indicate that sunlight exposure may have a limited effect on TNF-α modulation in TB patients. Further studies with larger sample sizes and comprehensive biomarker assessments are needed to clarify the relationship between sunlight exposure, vitamin D, and immune responses in tuberculosis.

Corresponding Author:
✉ Sahidan
Department of Medical Laboratory Technology, Poltekkes Kemenkes Bengkulu, Bengkulu City, Bengkulu, Indonesia
Email: sahidan_labor@yahoo.com

1. INTRODUCTION

Tuberculosis (TB) remains a major global health problem and continues to be one of the leading causes of death from infectious diseases (World Health Organization, 2023). Effective control of TB transmission relies heavily on early and accurate diagnosis, particularly in resource-limited settings where sputum smear microscopy remains the primary diagnostic method (Sulistyasmi et al., 2021). Beyond diagnosis, host immune response plays a crucial role in determining disease progression and clinical outcomes, as the balance between protective and pathological immune mechanisms directly influences infection control and tissue damage (Vu et al., 2024; Yuk et al., 2024).

Following infection with Mycobacterium tuberculosis, the host immune system activates a complex inflammatory response, in which tumor necrosis factor-alpha (TNF-α) plays a central role. TNF-α is essential for macrophage activation and granuloma formation, which are critical for containing bacterial spread. However, TNF-α also acts as a double-edged sword: while adequate levels help control infection, excessive or dysregulated production may lead to tissue damage and worsening of disease pathology (Kireev et al., 2025).

In recent years, vitamin D has gained attention as an important immunomodulatory factor in tuberculosis. Vitamin D enhances innate immune responses through the induction of antimicrobial peptides and regulation of cytokine production, including TNF-α. It is suggested that vitamin D may influence inflammatory pathways and contribute to the balance between protective and pathological immune responses in TB (Martineau, 2026).

Vitamin D status is largely influenced by sunlight exposure, particularly ultraviolet B (UVB) radiation, which stimulates its synthesis in the skin. Therefore, environmental factors such as sunlight exposure may indirectly affect immune responses in TB patients by altering vitamin D levels. Several studies have explored the relationship between vitamin D and TNF-α; however, the findings remain inconsistent. Some studies suggest that vitamin D suppresses excessive inflammation, while others indicate a more complex modulatory role depending on the host condition and disease status (Zeng et al., 2026).

Despite these findings, the relationship between serum vitamin D levels and TNF-α concentrations in patients with pulmonary tuberculosis has not been clearly established, as previous studies have reported inconsistent and sometimes contradictory results (Santos-Mena et al., 2024; Papagni et al., 2022). However, most previous studies have focused on serum vitamin D levels rather than environmental exposure such as sunlight, and the effect of short-term sunlight exposure on TNF-α levels in TB patients remains unclear. Therefore, this study aims to evaluate the effect of sunlight exposure on TNF-α levels in patients with pulmonary tuberculosis.

2. METHOD

This study employed a quasi-experimental design with a control group and a pre–post approach to evaluate the effect of sunlight exposure on TNF-α levels in patients with pulmonary tuberculosis. The study was conducted from June to November 2024 in Bengkulu City, Indonesia, involving participants recruited from two primary healthcare centers, namely Puskesmas Betungan and Puskesmas Nusa Indah. A total of 60 pulmonary TB patients who met the inclusion criteria were enrolled using a consecutive sampling technique and then allocated into two groups, consisting of 30 participants in the control group and 30 participants in the intervention group. Inclusion criteria included confirmed pulmonary TB patients aged ≥18 years who were undergoing treatment. Exclusion criteria included patients with severe comorbidities, immunosuppressive conditions, or those receiving vitamin D supplementation.

The independent variable in this study was sunlight exposure, while the dependent variable was TNF-α level. Potential confounding variables, including age, sex, nutritional status (body mass index), and treatment status, were also recorded and considered in the analysis.

At baseline, blood samples were collected from all participants to measure TNF-α levels. The intervention group was exposed to sunlight for approximately 15 minutes per day between 09:00 and 10:00 AM for a period of four weeks, while the control group did not receive structured sunlight exposure during the same period. At the end of the intervention, blood samples were collected again from all participants to assess changes in TNF-α levels.

TNF-α levels were measured using the Quantikine™ HS ELISA Human TNF-α Immunoassay according to the manufacturer's protocol. Data analysis was performed using both parametric and non-parametric statistical tests, depending on data distribution. Paired t-test was used to compare TNF-α levels before and after intervention within groups, and independent t-test was used to compare differences between groups. For non-normally distributed data, Wilcoxon signed-rank test and Mann–Whitney test were applied. Statistical significance was set at $p < 0.05$.

This study was approved by the Health Research Ethics Committee of Poltekkes Kemenkes Bengkulu (No. KEPK.BKL/616/07/2424), and written informed consent was obtained from all participants prior to data collection.

3. RESULTS AND DISCUSSION

Table 1. Characteristics of Study Participants.

Characteristic	**n**	**%**
Sex		
Male	17	56.67
Female	13	43.33
Age (years)		
18–60	25	83.33
>60	5	16.67
Occupation		
Housewife (IRT)	8	26.67
Entrepreneur	8	26.67
Farmer	7	23.33
Laborer	2	6.67
Civil Servant (PNS)	3	10.00
Unemployed	2	6.67
BMI (kg/m²)		
Underweight (<18.5)	13	43.33
Normal (18.5–24.9)	11	36.67
Pre-obese (25.0–29.9)	3	10.00
Obese (≥30.0)	3	10.00
Blood Pressure (mmHg)		
Normal (<120/<80)	8	26.67
Prehypertension (120–139/80–89)	17	56.67
Stage I–II (≥140/≥90)	5	16.67

The characteristics of tuberculosis patients are presented in Table 1. Most participants were male (56.67%) and aged 18–60 years (83.33%). The most common occupations were

housewives and entrepreneurs (26.67% each). In terms of nutritional status, the majority of participants were underweight (43.33%), followed by normal BMI (36.67%). Based on blood pressure classification, most participants were categorized as prehypertensive (56.67%).

Table 2. Distribution and Comparison of TNF-α Levels Before and After Sunlight Exposure.

Variable	Mean ± SD (pg/mL)	Median (IQR) (pg/mL)	Min–Max	Normality (Shapiro-Wilk p)	Z	p-value
TNF-α Before	2.27 ± 0.55	2.29 (IQR: 0.85)	1.25–3.28	0.704	-0.714	0.475
TNF-α After	2.33 ± 1.17	2.17 (IQR: 0.80)	1.25–7.95	0.000*		

The distribution of TNF-α levels before and after the intervention is presented in Table 2. Prior to the intervention, the mean TNF-α level was 2.27 ± 0.55 pg/mL with a median of 2.29 pg/mL (IQR: 0.85). After the intervention, the mean TNF-α level slightly increased to 2.33 ± 1.17 pg/mL, with a median of 2.17 pg/mL (IQR: 0.80). The range of values was wider after the intervention compared to baseline.

Normality testing using the Shapiro-Wilk test indicated that TNF-α levels before the intervention were normally distributed ($p = 0.704$), whereas post-intervention data were not normally distributed ($p < 0.001$). Therefore, a non-parametric Wilcoxon signed-rank test was applied.

The results of the Wilcoxon test showed that there was no statistically significant difference in TNF-α levels before and after the intervention ($Z = -0.714$, $p = 0.475$). Although a slight increase in the mean TNF-α level was observed, the magnitude of change was minimal and not statistically significant. The increase in standard deviation following the intervention suggests greater variability in individual responses, indicating that the effect of sunlight exposure on TNF-α levels was not consistent across participants.

This study evaluated the effect of sunlight exposure on TNF-α levels in patients with pulmonary tuberculosis. The findings showed a slight increase in mean TNF-α levels after the intervention; however, the difference was not statistically significant ($Z = -0.714$, $p = 0.475$). These results suggest that short-term sunlight exposure may have limited clinical relevance for systemic TNF-α levels in TB patients. The observed changes may reflect natural biological variability rather than a direct effect of the intervention, indicating that although a biological effect may exist, the magnitude of change is too small to be clinically meaningful under the current intervention conditions.

The characteristics of participants (Table 1) indicate that most patients were within the productive age group and had underweight nutritional status. This finding is consistent with the epidemiology of tuberculosis, where malnutrition and impaired immune status are known to influence host immune responses, including cytokine production such as TNF-α. Malnutrition has been associated with reduced immune competence and altered inflammatory responses, which may affect the consistency of intervention outcomes (Asad et al., 2020; Bhargava et al., 2014).

The lack of a statistically significant change in TNF-α levels (Table 2) may be explained by the complex immunological role of TNF-α in tuberculosis. TNF-α plays a critical role in granuloma formation and containment of Mycobacterium tuberculosis, and its expression is tightly regulated through multiple immune pathways. Therefore, short-term environmental interventions such as sunlight exposure may not be sufficient to disrupt or significantly alter this regulatory balance (Silva et al., 2018; Fallahi-sichani et al., 2010).

Although sunlight exposure is known to stimulate vitamin D synthesis, its downstream immunomodulatory effects on TNF-α remain inconsistent. Recent evidence suggests that vitamin D can reduce pro-inflammatory cytokines; however, its effectiveness is influenced by baseline vitamin D status, genetic variability, and disease severity. The absence of direct measurement of serum vitamin D levels in this study limits the ability to confirm this mechanistic pathway. The lack of significant findings may be attributed to insufficient exposure intensity and the absence of baseline vitamin D assessment, both of which are important determinants of individual immune responses. These findings indicate that the proposed immunomodulatory pathway linking sunlight exposure, vitamin D, and TNF-α regulation may not be sufficiently activated under short-term exposure conditions, particularly in the absence of controlled vitamin D status (Grant et al., 2020; Lin et al., 2021).

The minimal difference observed in TNF-α levels (2.27 vs 2.33 pg/mL) indicates a small effect size that is unlikely to be clinically significant, reinforcing the limited clinical relevance of the observed change. The absence of direct measurement of serum vitamin D levels also limits the ability to confirm the proposed mechanism linking sunlight exposure to immune modulation. Previous studies have reported that short-term interventions often fail to produce meaningful changes in inflammatory biomarkers in TB patients, suggesting that cytokine modulation may require longer duration or more intensive interventions (Martineau, 2026).

Furthermore, the increase in standard deviation after the intervention indicates substantial inter-individual variability. This heterogeneity suggests that immune responses to sunlight exposure are not uniform and are influenced by host-related factors such as age, nutritional status, comorbidities, and environmental exposure, as reflected in Table 1 (Aranow & Md, 2011; Calder et al., 2020).

Another important factor is the duration and intensity of sunlight exposure. In this study, participants were exposed to sunlight for approximately 15 minutes daily over four weeks, which may not be sufficient to significantly increase vitamin D levels or produce measurable effects on immune regulation. Longer duration or vitamin D supplementation may be required to achieve significant immunological outcomes (Grant et al., 2020; Raymond-lezman & Riskin, 2023).

In addition, the high proportion of underweight participants may have contributed to the findings. Malnutrition is strongly associated with impaired immune responses and altered cytokine production, which may mask or attenuate the effects of interventions such as sunlight exposure. This highlights the importance of considering nutritional status when interpreting immunological outcomes in TB patients (Farid et al., 2025; Sinha et al., 2019).

Importantly, the non-significant findings in this study should not be interpreted as the absence of effect, but rather as a reflection of the complexity of immune regulation in tuberculosis. TNF-α is part of a highly dynamic cytokine network, and its modulation may require multifactorial approaches rather than a single environmental intervention (Liu et al., 2025; Nogueira et al., 2022; Torrelles & Sclesinger, 2018).

This study has several limitations that should be considered when interpreting the findings. The relatively small sample size may limit the statistical power to detect small differences. In addition, the short duration of the intervention may not have been sufficient to induce measurable biological changes, particularly in immunological parameters such as TNF-α. The absence of direct measurement of serum vitamin D levels also limits the ability to confirm the proposed mechanism linking sunlight exposure to immune modulation. Additionally, the absence of baseline vitamin D status may have introduced unmeasured variability, limiting the ability to interpret individual responsiveness to sunlight

exposure. Furthermore, potential confounding factors such as nutritional status, comorbidities, and treatment adherence may have influenced TNF-α levels, although these conditions reflect real-world clinical settings in TB patients (Mi et al., 2021; Rajamanickam et al., 2025).

Despite these limitations, this study provides important preliminary insights into the response of TNF-α to sunlight exposure in patients with pulmonary tuberculosis. The findings highlight the need for further research with larger sample sizes, longer intervention periods, and more comprehensive measurement of biological markers, including vitamin D levels, to better understand the relationship between environmental exposure and immune response in TB. Future studies should incorporate direct measurement of serum vitamin D levels and control for nutritional and clinical factors to better elucidate the immunomodulatory effects of sunlight exposure in tuberculosis patients.

4. CONCLUSION

This study found that sunlight exposure resulted in only a slight, non-significant increase in TNF-α levels in patients with pulmonary tuberculosis. These findings suggest that sunlight exposure may have a limited impact on immune modulation. Most participants had underweight nutritional status and varying clinical conditions, which may have influenced the results. Given the study limitations, including small sample size, short intervention duration, and the absence of serum vitamin D measurement, the findings should be interpreted with caution. Therefore, further research with more robust study designs is needed to clarify the role of sunlight exposure and vitamin D in immune responses among TB patients.

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