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# Vitamin E Supplementation and Its Impact on Pulmonary Tuberculosis Treatment Outcomes: A Systematic Review

**Adhelia Zalsabilah Basir[1], Edward Pandu Wiriansya[2], Suciati Damopolii[3], Hasan[4], Indah Lestari Daeng Kanang[5]**

*[1]Students of the Medical Profession Study Program, Universitas Muslim Indonesia, Makassar, Indonesia.*
*[2]Departement of Pulmonology and Respiratory Medicine, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia.*
*[3]Department of Radiology, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia.*
*[4]Department of Internal Medicine, Faculty of Medicine, Universitas Muslim Indonesia, Makassar, Indonesia.*

**Corresponding Author: Edward Pandu Wiriansya*
*Email: edwardpandu.wiriansya@umi.ac.id*

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**Abstract**

*Pulmonary tuberculosis remains a global health problem, and antioxidant deficiencies such as vitamin E contribute to increased oxidative stress in patients. The aim of this study was to assess the effect of vitamin E supplementation on the effectiveness of pulmonary tuberculosis treatment through a systematic review based on PRISMA 2020 guidelines. This systematic review included clinical and observational studies investigating the relationship between vitamin E and pulmonary tuberculosis. Literature searches were conducted in PubMed and Google Scholar (2008–2021) using the keywords "Vitamin E," "Tuberculosis," and "Lung." Methodological quality was assessed using the JBI Checklist and Cochrane RoB2. The process was carried out at the Faculty of Medicine, Muslim University of Indonesia, Makassar, from March to August 2024. Secondary data from published studies were used; therefore, ethical approval was not required. Six studies met the inclusion criteria, consisting of two randomized controlled trials, two in vitro studies, one case–control study, and one cross-sectional study. The synthesis results showed that vitamin E supplementation consistently reduced oxidative stress, as indicated by a significant decrease in malondialdehyde (MDA) levels and an increase in enzyme activity. In addition, vitamin E improved inflammatory status through reduced C-reactive protein (CRP) levels and increased serum leptin, as well as enhanced cellular immune responses through elevated IL-2 and IFN-γ levels. Overall, vitamin E supplementation contributed to improved treatment effectiveness and quality of life in patients with pulmonary tuberculosis.Vitamin E supplementation has potential as an adjuvant therapy that enhances the effectiveness of pulmonary tuberculosis treatment through antioxidant and immunomodulatory mechanisms.*

## Introduction

Pulmonary tuberculosis (TB) remains a global health problem with high morbidity and mortality (Lienhardt et al., 2012; Navarro et al., 2022; Singh et al., 2023). Oxidative stress and

antioxidant deficiency, including vitamin E, are factors that influence the course of the disease, which can worsen patients' clinical conditions (Amaral et al., 2021; Fâcă et al., 2025). Vitamin E supplementation has the potential to enhance immune capacity, reduce oxidative stress, and support the recovery of TB patients (Reyes-Lazcano et al., 2023; Seyedrezazadeh et al., 2008; Shams et al., 2021).

Specifically, this study aims to determine whether vitamin E administration can improve pulmonary TB treatment outcomes, both in terms of improving clinical status and patient immune capacity (Wagnew et al., 2022; Cioboata et al., 2024; Maaz et al., 2024). Furthermore, this study also seeks to understand the mechanism of action of vitamin E in supporting TB therapy, including its role in reducing oxidative stress and enhancing the body's immune response (Hernandez et al., 2013; Moriguchi & Muraga, 2000; Thanoon & Solaiman, 2017). Pulmonary TB requires long-term treatment with standard anti-TB drugs, and antioxidant deficiency can delay recovery. Therefore, vitamin E supplementation is expected to reduce oxidative markers, improve the quality of life of TB patients, and provide clear scientific evidence for the potential of vitamin E as an adjunct therapy, while contributing to the literature on nutrition and immunology in TB (Aibana et al., 2017; Patti et al., 2021; Usman et al., 2023; Zhang et al., 2023).

Vitamin E supplementation has been shown to play a crucial role not only in mitigating oxidative stress but also in regulating cellular immune responses during tuberculosis infection (Gaglani et al., 2023; Muhammad et al., 2022; Sahoo et al., 2024). Experimental studies demonstrate that vitamin E modulates nuclear factor kappa B (NF-κB) signaling pathways, thereby reducing the overproduction of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, which are typically elevated in pulmonary tuberculosis (Shastri et al., 2018; Xie et al., 2025). By stabilizing cell membranes and maintaining redox homeostasis, vitamin E preserves the functional integrity of macrophages and T lymphocytes that are essential for mycobacterial clearance (Maggini et al., 2018). Furthermore, combined supplementation of vitamin E with selenium has been shown to enhance antioxidant enzyme activities such as glutathione peroxidase (GPx) and catalase leading to a significant decrease in oxidative damage in TB patients (Pourmoradian et al., 2014; Vilchèze et al., 2025). These mechanisms highlight the multifaceted role of vitamin E as both an antioxidant and an immunomodulator in pulmonary tuberculosis management (Mitroi et al., 2025).

Nutritional factors are increasingly recognized as determinants of treatment success in tuberculosis. Patients suffering from micronutrient deficiencies, particularly vitamins A, C, D, and E, exhibit delayed sputum conversion and impaired immune recovery (Tafere et al., 2020; Kumar et al., 2024; Fâcă et al., 2025). Clinical trials have shown that adjunctive antioxidant supplementation can improve treatment outcomes, enhance weight gain, and reduce relapse risk among TB patients receiving standard therapy (Bhaskaram, 2002; Visser et al., 2011). Moreover, observational studies in low- and middle-income countries have revealed that individuals with higher dietary intake of vitamin E and zinc display improved immune markers and lower rates of infection (Gebremariam et al., 2010; Wintergerst et al., 2007). Collectively, these findings suggest that addressing micronutrient deficiencies especially vitamin E deficiency through targeted supplementation could strengthen host defenses, enhance antioxidant capacity, and promote faster clinical recovery in pulmonary tuberculosis.

## Methods

This study is a PRISMA 2020–based systematic review aimed at evaluating the effects of vitamin E supplementation on treatment outcomes in patients with pulmonary tuberculosis. The review included randomized controlled trials, in vitro studies, case–control studies, and cross-sectional studies to provide comprehensive evidence. The analyzed population consisted of patients with active pulmonary TB from multiple countries, ranging from young adults to

the elderly, and including both sexes. Inclusion criteria included studies examining the effects of vitamin E on pulmonary TB patients, while exclusion criteria included non-clinical studies, case reports, and literature reviews.

The study employed the PICOS framework (Population, Intervention, Comparison, Outcome, Study Design) to define the research question and systematically establish inclusion and exclusion criteria. Population included patients with active pulmonary TB; Intervention was vitamin E supplementation; Comparison included patients receiving standard antituberculosis therapy without vitamin E; Outcomes included oxidative stress markers (MDA), inflammatory markers (CRP), immune responses (IL-2, IFN-γ), treatment effectiveness, and quality of life; Study Design included randomized controlled trials, in vitro studies, case–control studies, and cross-sectional studies. Literature searches were conducted in PubMed and Google Scholar (2008–2021) using keywords "Vitamin E," "Tuberculosis," and "Lung," at the Faculty of Medicine, Muslim University of Indonesia, Makassar, from March to August 2024.

Data were extracted on study design, population characteristics, interventions, outcomes, and relevant biochemical and immunological parameters. Methodological quality was assessed using the JBI Critical Appraisal Checklist for observational studies and the Cochrane RoB 2 tool for randomized trials. Analysis was narrative due to heterogeneity in study designs, with attention to reported confounding factors. To ensure data quality, extraction was performed by trained researchers and independently verified, with integrity maintained through standardized extraction forms and cross-checks. Limitations include a small number of eligible studies, heterogeneity in study designs, and potential publication bias, which may affect the generalizability of the findings.

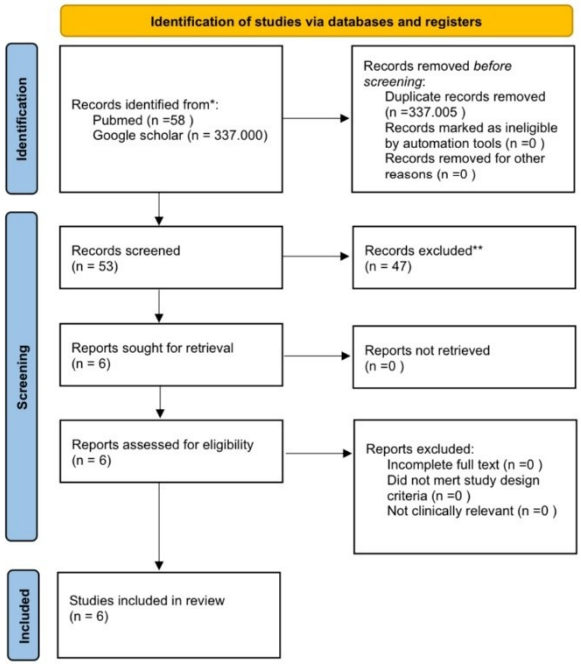


*Figure 1. Implementation of Theory*

Figure 1 shows that the initial search in Google Scholar and PubMed using the predetermined keywords yielded 337,058 articles. A total of 337,005 articles were excluded because they were outside the year range of 2008–2021. In the end, 53 articles remained. After applying the inclusion and exclusion criteria, 6 articles were obtained that specifically discussed the role of vitamin E in patients with pulmonary tuberculosis.

## Result and Discussion

This research is a systematic review with a PRISMA 2020–based design, conducted at the Faculty of Medicine, Muslim University of Indonesia, Makassar, from March to August 2024. A total of six studies met the inclusion criteria, consisting of two randomized controlled trials, two in vitro studies, one case–control study, and one cross-sectional study. The inclusion criteria covered studies examining the effects of vitamin E supplementation on patients with active pulmonary tuberculosis, while non-clinical studies, case reports, and literature reviews were excluded. The reviewed population involved pulmonary TB patients from various countries with diverse demographic characteristics, including young to elderly adults of both sexes. In the clinical trials, participants were randomly assigned to an intervention group receiving vitamin E supplementation and a control group receiving only standard antituberculosis therapy.

### Descriptive Statistics

This systematic review analyzed six scientific articles investigating the effect of vitamin E supplementation on the treatment outcomes of patients with pulmonary tuberculosis. The selected studies were published between 2008 and 2021 and originated from several countries, including Iran, Iraq, Nigeria, Mexico, and Indonesia. Among these, two were randomized controlled trials (RCTs), one was a nested case–control study, one was cross-sectional, and two were in vitro experimental studies. The total number of human participants across all studies was approximately 380, consisting of individuals diagnosed with active pulmonary tuberculosis, multidrug-resistant tuberculosis (MDR-TB), and household contacts of TB patients. In most interventional studies, vitamin E was administered at a dosage of 400 IU per day alongside standard anti-tuberculosis therapy for a duration of six to eight weeks. The main variables assessed included oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and total antioxidant capacity (TAC); inflammatory biomarkers including C-reactive protein (CRP) and leptin; immunological parameters such as interleukin-2 (IL-2), interferon-gamma (IFN-γ), and lymphocyte proliferation; and clinical outcomes such as quality of life and rate of recovery. Overall, all six studies demonstrated good methodological quality, with Joanna Briggs Institute (JBI) appraisal scores exceeding 75%.

### Primary Outcome Measures

The primary outcome of this systematic review was to determine the impact of vitamin E supplementation on the effectiveness of pulmonary tuberculosis treatment through changes in biological and clinical parameters. Pooled findings indicated that vitamin E supplementation significantly reduced oxidative stress markers, particularly MDA, while enhancing antioxidant enzyme activities such as SOD and GPx, as well as improving total antioxidant capacity (TAC). In addition to its antioxidative effect, vitamin E also improved the immunological status of TB patients by increasing the levels of IL-2 and IFN-γ, both of which play essential roles in macrophage activation and T-lymphocyte proliferation. Furthermore, vitamin E supplementation led to a reduction in systemic inflammation markers, including CRP and leptin. Clinically, patients who received vitamin E supplementation demonstrated faster recovery, reduced systemic symptoms, and improved quality of life compared to those who did not receive supplementation. These findings confirm that vitamin E serves as an effective adjuvant therapy in pulmonary tuberculosis through both antioxidant and immunomodulatory mechanisms.

### Secondary Outcome Measures

The secondary outcomes evaluated across the included studies comprised the effects of vitamin E on quality of life, plasma vitamin E levels, and specific immune responses at the cellular level. The cross-sectional study conducted in Indonesia reported that MDR-TB patients with

higher intake of vitamin E and dietary fat achieved better quality-of-life scores than those with lower intake. The nested case–control study in Nigeria revealed that individuals with lower plasma vitamin E concentrations were significantly more likely to develop active tuberculosis when living in close contact with TB patients, indicating a protective role of vitamin E against disease progression. Meanwhile, in vitro research by Hernández and colleagues demonstrated that exogenous vitamin E supplementation enhanced immune cell proliferation and the secretion of IL-2 and IFN-γ in cultured lymphocytes from TB patients, suggesting improved adaptive immune function. In parallel, interventional studies from Iran and Iraq reported that vitamin E, alone or in combination with selenium, reduced CRP levels and restored oxidative balance. These secondary findings strengthen the primary outcomes by showing that vitamin E not only mitigates oxidative stress but also enhances immune defense, improves clinical well-being, and lowers the risk of tuberculosis progression.

**Subgroup Analysis**

Subgroup analysis was performed to compare outcomes across different study designs and population characteristics. In the RCT subgroup from Iran and Iraq, vitamin E supplementation at 400 IU/day during standard TB therapy produced significant reductions in MDA and CRP levels, along with notable increases in GPx activity and overall oxidative balance. In the cross-sectional subgroup conducted in Indonesia among MDR-TB patients, higher vitamin E intake was positively associated with improved quality-of-life scores, particularly in physical and psychological domains. In the Nigerian case–control subgroup, low plasma vitamin E levels were identified as a significant risk factor for developing active TB among household contacts of infected patients. Furthermore, the in vitro subgroup from Mexico demonstrated that exogenous vitamin E enhanced T-lymphocyte proliferation and increased secretion of the protective cytokines IL-2 and IFN-γ. Collectively, these findings indicate a consistent beneficial effect of vitamin E across all subgroups clinical, observational, and experimental showing its role in reducing oxidative stress, enhancing immune function, and improving the overall clinical condition of pulmonary tuberculosis patients.

Table 1. Characteristics of Studies Included in the Systematic Review

| No | Author (Year) | Country / Sample Size | Study Design | Intervention (Vitamin E) | Outcome / Main Findings | Conclusion |
|---|---|---|---|---|---|---|
| **1** | (Seyedrezazadeh et al., 2008) | Iran / 35 pulmonary TB patients | Double-blind trial (RCT) | Supplementation with vitamin E and selenium during TB therapy | Reduced oxidative stress and increased antioxidant status | Vitamin E and selenium help restore oxidative balance during TB treatment |
| **2** | (Aibana et al., 2017) | Nigeria / 180 household contacts of TB patient | Nested case–control | Plasma vitamin E levels measured without direct intervention | Low vitamin E levels associated with increased risk of active TB | Vitamin E and selenium help restore oxidative balance during TB treatment |

| | | | | | | |
|---|---|---|---|---|---|---|
| **3** | (Thanoon & Solaiman, 2017) | Iraq / 66 pulmonary TB patients | Double-blind trial (RCT) | Vitamin E 400 IU/day during TB treatment | Decreased CRP levels and increased serum leptin | Low vitamin E status is a risk factor for TB |
| **4** | (Hernandez et al., 2013) | Mexico / 7 TB patients | Experimental in vitro | Exogenous vitamin E on peripheral blood mononuclear cells of TB patients | Enhanced immune cell proliferation and cytokine production | Vitamin E strengthens cellular immune response to TB antigens |
| **5** | (Ortiz - Martínez et al., 2013) | Mexico / 7 active TB patients + 6 healthy controls | Experimental in vitro | Exogenous vitamin E on cultured immune cells | Increased IL-2 and IFN-γ production | Vitamin E plays a role in activating cellular immunity in TB patients |
| **6** | (Fitri et al., 2021) | Indonesia / 92 MDR-TB patients | Cross-sectional | Daily vitamin E intake measured via FFQ | Higher fat and vitamin E intake correlated with better quality of life | Vitamin E intake influences quality of life in MDR-TB patients |

**Interpretation of Key Findings**

This systematic review found that vitamin E supplementation consistently reduces oxidative stress markers and improves immune function in patients with pulmonary tuberculosis. The most frequently observed effects included decreased levels of malondialdehyde (MDA) and C-reactive protein (CRP), along with increased activity of antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase (GPx). In addition, several studies reported improved production of key cytokines like interferon-gamma (IFN-γ) and interleukin-2 (IL-2), suggesting that vitamin E enhances both antioxidant and immunomodulatory pathways. Collectively, these results support the potential role of vitamin E as an adjuvant therapy that strengthens host defenses and accelerates recovery in tuberculosis patients.

**Comparison with Previous Studies**

The findings of this review are consistent with previous research demonstrating the protective effects of antioxidants in tuberculosis management. Seyedrezazadeh et al. (2008) and Thanoon (2013) similarly observed improvements in oxidative balance following vitamin E supplementation. Furthermore, studies by Hernández et al. (2013) and Moriguchi & Muraga (2000) reported enhanced immune responses and T-lymphocyte proliferation, supporting the current evidence that vitamin E plays a regulatory role in immune modulation. However, while earlier studies often focused on single biochemical parameters, this review integrates results from both clinical and experimental data, providing a broader understanding of vitamin E's influence on oxidative stress and immune biomarkers (Hernandez et al., 2013; Moriguchi & Muraga, 2000).

### Implications for Public Health

From a public health perspective, these findings highlight the importance of addressing micronutrient deficiencies particularly vitamin E deficiency among populations at high risk of tuberculosis. Integrating vitamin E–rich dietary sources or supplementation programs into TB control strategies could improve treatment response, enhance quality of life, and potentially reduce disease recurrence. Public health policies emphasizing nutritional assessment and antioxidant support may therefore complement conventional pharmacological treatment, especially in resource-limited settings where malnutrition and TB commonly coexist.

### Limitations and Cautions

This review has several limitations. The number of eligible studies was relatively small, and there was considerable heterogeneity in vitamin E dosage, intervention duration, and study design. Some included studies had limited sample sizes or lacked blinding procedures, potentially introducing bias. Additionally, most data were derived from short-term interventions, making it difficult to assess long-term clinical outcomes. Therefore, while the evidence supports the beneficial effects of vitamin E, the results should be interpreted with caution, and further large-scale randomized controlled trials are needed to confirm these findings.

### Recommendations for Future Research

Future studies should focus on standardized dosage regimens of vitamin E supplementation, longer follow-up periods, and larger, multi-center randomized controlled trials. Research should also explore the synergistic effects of vitamin E with other antioxidants such as selenium, zinc, and vitamin C in improving tuberculosis outcomes. Furthermore, mechanistic studies at the molecular level are recommended to clarify how vitamin E influences macrophage activation, cytokine regulation, and bacterial clearance. Integrating nutritional biomarkers into tuberculosis monitoring systems may also provide valuable insights into how antioxidant therapy can be optimized for individual patient care.

## Conclusion

This study describes the role of antioxidant deficiency, particularly vitamin E, in exacerbating oxidative stress and immune responses in patients with pulmonary tuberculosis, as well as providing valuable insights into the potential of vitamin E supplementation as an adjuvant therapy to enhance the effectiveness of antituberculosis treatment. A comprehensive analysis of findings from various studies indicates that vitamin E contributes to the reduction of oxidative stress, improvement of inflammatory status, and enhancement of cellular immune responses, thereby enriching global understanding of the relationship between micronutrient status and chronic infections.

In general, classical recommendations such as those used in the United States and supported by recent research (Marini et al., 2023) establish the requirement for vitamin E at 15 mg of α-tocopherol per day for healthy adults. However, this value may vary depending on individual conditions, dietary patterns, and overall health status. Based on these findings, vitamin E is considered not only essential for its antioxidant function but also plays an important role in maintaining immune health and preventing chronic diseases. Therefore, meeting vitamin E requirements through a balanced diet or supplementation when necessary constitutes an essential part of global public health strategies.

These findings have important implications for clinical practice and health policy, highlighting the need to consider micronutrient-based nutritional support as an integral part of tuberculosis management. Further large-scale research with multinational randomized clinical trial designs is recommended to determine the optimal dosage, duration, and safety of long-term supplementation.

For educational institutions, the results of this study can serve as a learning resource and scientific reference in the development of medical nutrition and infectious disease sciences. For healthcare providers particularly tuberculosis care facilities such as community health centers and hospitals these findings are expected to encourage improved nutritional education for TB patients and healthcare workers. Meanwhile, future researchers are encouraged to develop further studies with broader and more measurable methodologies to strengthen scientific evidence and support public health improvement efforts at both national and international levels.

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