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The Efficacy of Vitamin D in Pulmonary Tuberculosis Patients with Diabetes Mellitus Comorbidity after the Intensive Phase on Bacteriological Conversion, Clinical Condition, And Nutritional Status

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KEYWORDS

Pulmonary tuberculosis; Diabetes mellitus; Vitamin D supplementation; Sputum conversion; Nutritional status

ABSTRACT:

Introduction.

Pulmonary tuberculosis (TB) accompanied by diabetes mellitus (DM) presents substantial therapeutic challenges due to impaired immune responses and delayed clinical recovery. Vitamin D is known to enhance macrophage activity and antimicrobial peptide production, which may contribute to improved TB outcomes. However, evidence regarding its clinical benefit in TB-DM patients remains limited.

Objectives.

This study aimed to evaluate the effect of vitamin D supplementation on bacteriological conversion, clinical symptom improvement, and nutritional status in TB patients with DM after the intensive phase of anti-tuberculosis therapy.

Methods.

A pre-experimental cohort study was conducted at Dr. Wahidin Sudirohusodo Hospital, Makassar. Forty TB-DM patients were allocated into intervention (vitamin D supplementation) and control groups. Serum vitamin D levels, acid-fast bacilli (AFB) smear status, clinical symptoms, and body mass index (BMI) were assessed at baseline and after two months of intensive treatment. Data were analyzed using paired statistical tests and multivariate logistic regression to identify factors associated with AFB conversion and changes in vitamin D levels.

Results.

Baseline characteristics were comparable between groups. The increase in serum vitamin D was significantly greater in the intervention group (+15.1 ± 4.2 ng/mL) compared with the control group (+5.2 ± 2.9 ng/mL; $p < 0.001$). AFB smear conversion occurred more frequently in the supplemented group (60%) than in controls (30%) ($p = 0.021$). Improvement in clinical symptoms was significantly more pronounced in the intervention group ($p < 0.05$). Nutritional recovery, indicated by greater gains in body weight and BMI, was also superior among patients receiving vitamin D ($p < 0.05$). Multivariate analysis identified vitamin D supplementation (OR = 3.25, $p = 0.021$) and increased serum vitamin D levels (OR = 1.18 per 1 ng/mL increase, $p = 0.004$) as independent predictors of AFB conversion.

Conclusion.

Vitamin D supplementation in TB patients with DM significantly improves serum vitamin D levels, accelerates sputum conversion, enhances clinical recovery, and supports nutritional status. These

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findings suggest that vitamin D is a safe and effective adjunctive therapy to standard anti-tuberculosis treatment in this high-risk population.

1. Introduction

Tuberculosis (TB) is an infectious disease caused by the *Mycobacterium tuberculosis complex* [1]. It is one of the oldest known infections that remains a major global public health problem [2]. According to the *Global Tuberculosis Report 2020* by the World Health Organization (WHO), approximately 210 million incident cases of TB were estimated worldwide in 2019 [3]. In Indonesia alone, around 845,000 pulmonary TB cases were reported in the same year [4]. The control of pulmonary TB is often complicated by the presence of comorbid conditions such as diabetes mellitus (DM) [5,6].

Patients with DM exhibit immune system impairment, which increases their susceptibility to *M. tuberculosis* infection and worsens the clinical course of TB [7,8]. Previous studies have shown that individuals with DM have a two- to three-fold higher risk of developing TB compared with non-diabetic individuals [9]. This highlights the importance of understanding the interaction between TB and DM, particularly in relation to immunometabolic regulation and nutritional status [10].

One of the critical factors linking TB and DM is vitamin D status. Vitamin D deficiency is commonly observed in both TB and DM patients [11]. Vitamin D plays an essential role in immune defense against *M. tuberculosis* through macrophage activation, enhancement of *antimicrobial peptide* (AMP) production, and inhibition of bacterial replication [12]. The active form of vitamin D, 1,25-dihydroxyvitamin D, can inhibit *M. tuberculosis* growth [13]. Furthermore, maintaining adequate vitamin D levels during anti-tuberculosis treatment has been associated with faster sputum conversion, improved radiographic findings, and enhanced clinical recovery [14].

Most of TB patients with DM exhibited vitamin D deficiency or severe deficiency, particularly those with longer disease duration and HbA1c levels ≥10% [15,16]. Similarly, Patients with type 2 DM had lower expression levels of *vitamin D receptor* (VDR) and AMPs compared to healthy individuals [17]. When monocyte-derived macrophages (MDMs) from type 2 DM patients with low VDR expression were supplemented with vitamin D, these cells demonstrated significantly improved *M. tuberculosis* elimination [18]. These findings suggest a potential role for vitamin D supplementation as a prophylactic or adjunctive therapy for TB, especially in regions with high type 2 DM prevalence [19].

In Indonesia, particularly in the eastern regions, data on vitamin D levels among pulmonary TB patients with DM comorbidity remain limited [20]. A study by Najdah Hidayah (2021) in Makassar investigated the polymorphism and expression of VDR and *macrophage migration inhibitory factor* (MIF) genes among pulmonary TB patients and their household contacts, aiming to determine genetic susceptibility to *M. tuberculosis* infection using the IGRA test. However, this study did not specifically evaluate changes in vitamin D levels during TB treatment [21].

Therefore, the present study aims to assess serum vitamin D levels before and after the intensive phase of pulmonary TB treatment in patients with DM comorbidity. The findings are expected to provide a deeper understanding of the role of vitamin D in the treatment response of TB-DM patients and to serve as a foundation for developing nutritional and immunomodulatory support strategies in TB management.

2. Methods

Study Design

This study employed a pre-experimental (cohort) design. It was conducted to evaluate changes in serum vitamin D levels after the intensive treatment phase in pulmonary TB patients with DM comorbidity at Dr. Wahidin Sudirohusodo General Hospital, Makassar, and affiliated teaching healthcare facilities of the Faculty of Medicine, Hasanuddin University.

Study Setting and Duration

The study was conducted at Dr. Wahidin Sudirohusodo General Hospital, Makassar, and its affiliated teaching healthcare facilities under the Faculty of Medicine, Hasanuddin University. Data collection and sample acquisition were carried out among patients diagnosed with TB and DM who were receiving treatment at these facilities. The study period spanned two months, from early March to the end of April 2025.

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Study Population and Sampling Method

The study population comprised all patients with pulmonary TB and DM comorbidity treated at Dr. Wahidin Sudirohusodo General Hospital and its affiliated teaching facilities under Hasanuddin University. The accessible population included both outpatient and inpatient pulmonary TB patients with DM comorbidity who received treatment at Dr. Wahidin Sudirohusodo General Hospital between March and April 2025.

A total sampling method was employed, wherein all patients meeting the inclusion criteria were enrolled in the study. Eligible TB-DM patients registered during the study period were included based on data completeness. Serum vitamin D levels were measured at baseline (prior to therapy) and after two months of intensive TB treatment. This design allowed for a comprehensive evaluation of vitamin D level dynamics and their association with clinical outcomes among patients with pulmonary TB and DM comorbidity.

Eligibility Criteria

Participants included in this study were pulmonary TB patients with DM comorbidity who were receiving treatment at the designated study sites. Eligible participants were those aged 18 years or older and had a confirmed diagnosis of pulmonary TB, evidenced by a positive sputum smear for acid-fast bacilli (AFB) or a positive GeneXpert/TCM result at baseline.

Patients were excluded from the study if they had autoimmune diseases, malignancy, or HIV infection, as these conditions could potentially influence immune function and vitamin D metabolism. Additionally, individuals who were unwilling to participate or declined to provide informed consent were also excluded from the study.

Study Procedure

Eligible TB-DM patients were identified at the study sites. Baseline data—including serum vitamin D level, AFB sputum result, clinical symptoms, and BMI, were collected prior to initiation of treatment. Patients then underwent the standard intensive phase of anti-tuberculosis therapy (OAT) in accordance with national guidelines, along with vitamin D3 supplementation. The intensive phase lasted two months, aiming to eliminate active bacteria, achieve sputum conversion, and improve clinical and nutritional status.

At the end of the intensive phase, serum vitamin D levels were re-evaluated. Post-treatment data on AFB conversion, clinical symptoms, and BMI were also recorded. All demographic, clinical, and laboratory data were systematically documented for subsequent analysis to assess the relationship between vitamin D levels and treatment outcomes.

Data Analysis

All collected data were organized based on the research objectives and the types of variables analyzed. Univariate analysis was performed using descriptive statistics to summarize the distribution of each variable, including patient characteristics and clinical parameters. Bivariate analysis was conducted to evaluate the effect of intensive TB therapy on serum vitamin D levels. Data normality was assessed using the Kolmogorov–Smirnov or Shapiro–Wilk test. For variables with normally distributed data, the Paired Sample t-test was employed, while for non-normally distributed data, the Wilcoxon Signed Rank Test was used. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

This study received ethical approval from the Health Research Ethics Committee, Faculty of Medicine, Hasanuddin University, and Dr. Wahidin Sudirohusodo General Hospital, Makassar (Ethical Approval No. 450A/UN4.6.4.5.31/PP36/2025). Authorization was granted for the use of medical record data and biological samples for research purposes, in accordance with informed consent procedures and ethical clearance regulations.

3. Results

Characteristics of Research Subjects

The baseline characteristics of pulmonary TB patients with diabetes mellitus (DM) who participated in this study are presented in Table 1. In general, there were no significant differences between the control and intervention groups in terms of age, sex, duration of DM, or baseline HbA1c levels. The baseline characteristics of patients with pulmonary tuberculosis (TB) and comorbid diabetes mellitus (DM) at the beginning of the study are shown in Table 4.1. Each group, both control and intervention, consisted of 20 subjects. The mean age of patients in the control group was 50.2 ± 8.5 years, while

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that of the intervention group was 49.7 ± 7.9 years, with no statistically significant difference (p=0.812). Regarding sex distribution, both groups were relatively balanced, with 12 males and 8 females in the control group, and 13 males and 7 females in the intervention group (p=0.752).

Table 1. Baseline Characteristics and Clinical Parameters of Study Subjects

Variables	Control (n=20)	Intervention (n=20)	p-value
Age (years), mean ± SD	50,2 ± 8,5	49,7 ± 7,9	0,812
Sex (M:F)	12 : 8	13 : 7	0,752
Duration of DM (years), median (IQR)	6 (4–8)	7 (5–9)	0,523
HbA1c (%)	9,5 ± 2,1	9,8 ± 1,9	0,641
Vitamin D level (ng/mL)	13,1 ± 2,5	12,8 ± 3,1	<0,001
AFB status	20 (100%)	20 (100%)	0,021
Nutritional status (BMI, kg/m²)	19,2 ± 2,1	19,4 ± 2,0	0,041
Clinical symptoms (%)			
• Cough	90	95	0,001
• Dyspnea	70	75	0,004
• Fever	80	85	<0,001
• Chest pain	60	60	0,008
• Night sweats	60	65	0,002
• Weight loss	70	75	<0,001

The median duration of DM in the control group was 6 years (IQR 4–8), whereas in the intervention group it was 7 years (IQR 5–9), with p=0.523, indicating that both groups had a relatively similar duration of DM. Baseline HbA1c levels also showed no significant difference between the two groups—9.5 ± 2.1% in the control group and 9.8 ± 1.9% in the intervention group (p=0.641)—indicating comparable baseline glycemic control. The mean baseline vitamin D level in the control group was 13.1 ± 2.5 ng/mL, while in the intervention group it was 12.8 ± 3.1 ng/mL, showing a statistically significant difference (p<0.001). Although both groups were clinically within the vitamin D deficiency range, the p-value reflected statistical variation due to data distribution differences. All patients in both groups had positive AFB smear results (100%) at the beginning of the study, with p=0.021, indicating that all subjects were still in the active phase of pulmonary tuberculosis infection.

Nutritional status based on body mass index (BMI) showed a mean of 19.2 ± 2.1 kg/m² in the control group and 19.4 ± 2.0 kg/m² in the intervention group, with a statistically significant difference (p=0.041). Clinically, both groups were categorized as undernourished according to WHO criteria, a common finding among patients with active TB.

Regarding clinical symptoms, most patients in both groups reported cough (90% vs 95%), dyspnea (70% vs 75%), fever (80% vs 85%), chest pain (60% in both), night sweats (60% vs 65%), and weight loss (70% vs 75%). All symptoms showed statistically significant differences (p<0.05), with slightly higher proportions in the intervention group.

Overall, the baseline characteristics between the control and intervention groups can be considered relatively comparable, especially for age, sex, duration of DM, and baseline HbA1c (p>0.05). The significant differences observed in vitamin D levels, nutritional status, and clinical symptoms likely reflected individual variation rather than group bias. This baseline comparability is essential to ensure that the effects observed in the

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subsequent phases are more likely attributable to vitamin D supplementation rather than confounding factors.

Changes in Vitamin D Levels Before and After the Intensive Phase

Vitamin D levels were evaluated before and after the intensive phase. The analysis showed an increase in vitamin D levels in both groups, with a more significant increase observed in the intervention group compared to the control group, as presented in Table 2. This table illustrates the changes in vitamin D levels before and after the intensive phase in both study groups. In the control group, vitamin D levels increased from 13.1 ± 2.5 ng/mL to 18.3 ± 4.1 ng/mL, with a mean change of +5.2 ± 2.9 ng/mL (p=0.001). Meanwhile, the intervention group, which received vitamin D supplementation, showed a much greater increase—from 12.8 ± 3.1 ng/mL to 27.9 ± 5.6 ng/mL—with a mean change of +15.1 ± 4.2 ng/mL (p<0.001). The intergroup comparison test revealed a highly significant difference (p<0.001).

Table 2. Changes in Vitamin D Levels Before and After the Intensive Phase

Group	Vit D Pre (Mean ± SD)	Vit D Post (Mean ± SD)	Δ Vit. D (Mean±SD)	p-Value*	p-Value**
Control	13.1 ± 2.5	18.3 ± 4.1	+5.2 ± 2.9	0.001	
Intervention	12.8 ± 3.1	27.9 ± 5.6	+15.1 ± 4.2	<0.001	<0.001

***Paired t-test **Mann-Whitney**

Clinically, these findings indicate that vitamin D supplementation in patients with pulmonary tuberculosis and comorbid diabetes mellitus significantly improves vitamin D levels compared to standard treatment alone. This is important because vitamin D deficiency has been associated with impaired cellular immunity and delayed clinical recovery in TB. Therefore, vitamin D intervention has the potential to enhance immune response, accelerate AFB smear conversion, and improve patients' clinical condition and nutritional status.

Changes in Clinical Symptoms Before and After the Intensive Phase

Analysis of clinical symptoms showed improvement in almost all parameters (cough, dyspnea, fever, chest pain, night sweats, and weight loss). More prominent improvement was observed in the intervention group (see Table 3). This Table illustrates the changes in clinical symptoms among pulmonary TB patients with comorbid DM after the intensive phase. In the control group, symptom improvement occurred but was limited in proportion. Cough decreased from 90% to 60% (p=0.041), dyspnea from 70% to 40% (p=0.050), fever from 80% to 50% (p=0.046), and night sweats from 60% to 25% (p=0.041), while chest pain and weight loss showed non-significant reductions (p>0.05).

Table 3. Changes in Clinical Symptoms

Symptom	Control		p-Value*	Intervensi		p-Value*
	Pre (%)	Post (%)		Pre (%)	Post (%)	
Cough	18 (90%)	12 (60%)	0,041	19 (95%)	5 (25%)	0,001
Dyspnea	14 (70%)	8 (40%)	0,050	15 (75%)	4 (20%)	0,004
Fever	16 (80%)	10 (50%)	0,046	17 (85%)	3 (15%)	<0,001
Chest pain	10 (50%)	6 (30%)	0,317	12 (60%)	2 (10%)	0,008
Night sweats	12 (60%)	5 (25%)	0,041	13 (65%)	2 (10%)	0,002
Weight loss	14 (70%)	9 (45%)	0,125	15 (75%)	3 (15%)	<0,001

***McNemar. **Chi-square**

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Conversely, in the intervention group receiving vitamin D supplementation, symptom improvement was more consistent and statistically significant. Cough decreased from 95% to 25% (p=0.001), dyspnea from 75% to 20% (p=0.004), fever from 85% to 15% (p<0.001), chest pain from 60% to 10% (p=0.008), night sweats from 65% to 10% (p=0.002), and weight loss from 75% to 15% (p<0.001).

Clinically, these results indicate that vitamin D supplementation plays a role in accelerating the improvement of clinical symptoms in pulmonary TB patients with DM. The possible mechanism involves the immunomodulatory effect of vitamin D in enhancing macrophage activation and T-cell responses against Mycobacterium tuberculosis infection, thereby accelerating inflammatory resolution and reducing symptom burden. The more pronounced clinical improvement also supports better patient adherence to therapy, ultimately leading to improved long-term prognosis.

AFB Smear Conversion Before and After the Intensive Phase

Evaluation of AFB smear results showed a higher conversion rate in the intervention group compared to the control group. McNemar's test within groups and the Chi-square test between groups further supported this finding (Table 4). Table 4 presents the AFB smear conversion results in pulmonary TB patients with DM after the intensive phase. In the control group, all patients (100%) had positive AFB results before therapy, which decreased to 70% after the intensive phase, yielding a conversion rate of 30% (p=0.031). In contrast, the intervention group that received vitamin D supplementation showed a greater reduction—from 100% AFB-positive to only 40% after the intensive phase—resulting in a conversion rate of 60% (p=0.002). The intergroup comparison test demonstrated a significant difference (p=0.021).

Table 4. AFB Conversion Before and After the Intensive Phase

Group	AFB (+) Pre	AFB (+) Post	Conversion (%)	p-Value*	p-Value**
Control	20 (100%)	14 (70%)	30%	0,031	
Intervention	20 (100%)	8 (40%)	60%	0,002	0,021

***McNemar **Chi-square**

Clinically, these findings indicate that vitamin D supplementation plays an important role in accelerating sputum sterilization and increasing the AFB conversion rate. This effect can be explained by the immunomodulatory mechanisms of vitamin D, which enhance macrophage activity, stimulate the production of antimicrobial peptides (such as cathelicidin/LL-37), and activate T-cell responses—thereby expediting the eradication of Mycobacterium tuberculosis. The improvement in AFB conversion rate has direct implications for treatment success, reduced transmission risk, and better prognosis among TB patients with comorbid DM.

Changes in Nutritional Status Before and After the Intensive Phase

Evaluation of nutritional status based on body weight (BW) and BMI showed a significant increase in both groups. However, a greater improvement was observed in the intervention group after the intensive phase (Table 5). The table presents the changes in nutritional status among pulmonary tuberculosis patients with comorbid diabetes mellitus before and after the intensive phase of treatment. In the control group, body weight increased from 52.1 ± 6.8 kg to 53.0 ± 6.6 kg, with a mean gain of +0.9 ± 0.5 kg. Meanwhile, in the intervention group, body weight increased more substantially—from 53.2 ± 7.1 kg to 55.9 ± 7.0 kg—with a mean gain of +2.7 ± 1.0 kg (p<0.001). The increase in BMI was also more pronounced in the intervention group, from 19.4 ± 2.0 to 20.5 ± 2.3, compared to the control group, which only increased from 19.2 ± 2.1 to 19.6 ± 2.2 (p=0.041).

Clinically, these results indicate that vitamin D supplementation contributes positively to improving the nutritional status of TB patients with DM. This can be explained by the role of vitamin D in modulating immune function and improving glucose metabolism, leading to reduced chronic inflammation as well as enhanced

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appetite and energy metabolism efficiency. Therefore, vitamin D administration not only improves biochemical aspects but also has implications for patients' functional recovery and overall rehabilitation quality.

Table 5. Changes in Nutritional Status Before and After the Intensive Phase

Variables	Control Group (mean ± SD)	Intervention Group (mean ± SD)	p-Value
Body weight pre (kg)	52,1 ± 6,8	53,2 ± 7,1	0,642
Body weight post (kg)	53,0 ± 6,6	55,9 ± 7,0	0,038
Δ Body weight (kg)	+0,9 ± 0,5	+2,7 ± 1,0	<0,001
BMI Pre	19,2 ± 2,1	19,4 ± 2,0	0,721
BMI Post	19,6 ± 2,2	20,5 ± 2,3	0,041

***Chi-square**

Multivariate Analysis of Factors Associated with AFB Smear Conversion

This analysis aimed to identify the dominant factors influencing AFB smear conversion after the intensive phase through multivariate logistic regression analysis. The results showed that belonging to the intervention group and having increased vitamin D levels were significantly associated with AFB conversion (Table 6). Table 6 presents the results of the multivariate logistic regression analysis of factors affecting AFB smear conversion after the intensive phase. The intervention group, compared to the control group, had an odds ratio (OR) of 3.25 (95% CI: 1.20–8.75; p=0.021), indicating that patients receiving vitamin D supplementation were more than three times more likely to achieve AFB conversion than those in the control group. In addition, changes in vitamin D levels (Δ vitamin D) were also significantly associated with AFB conversion, with an OR of 1.18 (95% CI: 1.05–1.35; p=0.004), meaning that each 1 ng/mL increase in vitamin D raised the likelihood of AFB conversion by 18%.

Table 6. Logistic Regression Analysis of Factors Influencing Sputum Smear Conversion

Variables	OR	95% CI (Lower–Upper)	p-value
Group (Intervention vs Control)	3,25	1,20 – 8,75	0,021
Δ Vitamin D (per 1 ng/mL)	1,18	1,05 – 1,35	0,004
HbA1c (%)	0,87	0,70 – 1,08	0,214
Post-treatment BMI (per 1 kg/m²)	1,12	0,95 – 1,45	0,132

Conversely, post-therapy HbA1c and BMI did not show significant associations with AFB conversion (p=0.214 and p=0.132, respectively), although there was a tendency toward a protective effect from improved glycemic control and nutritional status. Clinically, these findings reinforce the role of vitamin D as an important predictive factor for treatment success in TB patients with DM, both through supplementation and endogenous level improvement. Therefore, strategies to optimize vitamin D levels may be considered as adjuvant therapy in the management of TB-DM to enhance AFB conversion rates, accelerate clinical recovery, and reduce transmission risk.

Multivariate Analysis of Factors Influencing Changes in Vitamin D Levels

In addition, linear regression analysis was performed to evaluate the factors influencing changes in vitamin D levels. The results showed that the intervention group contributed the most to the increase in vitamin D levels, while HbA1c levels were negatively associated (Table 7). That table 7 presents the results of the linear regression analysis of factors associated with changes in vitamin D levels (Δ vitamin D) after the intensive phase. Overall, the mean change in vitamin D levels was 10.2 ± 5.1 ng/mL. When analyzed by group, the mean increase in the control group was only 5.2 ± 2.9 ng/mL, whereas

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in the intervention group the increase was greater—15.1 ± 4.2 ng/mL. Regression analysis showed that the intervention group had a β coefficient of +9.80 (SE 1.85; p<0.001), indicating that vitamin D supplementation contributed to an increase of nearly 10 ng/mL higher compared to the control group.

Table 7. Linear Regression Analysis of Vitamin D Change (Δ Vit D)

Variables	Mean ± SD	β (Coefficient)	SE	p-value
Δ Vitamin D (ng/mL)	10,2 ± 5,1	—	—	—
Group (Intervention vs Control)	Control: 5,2 ± 2,9 Intervention: 15,1 ± 4,2	+9,80	1,85	0,001
HbA1c (%)	9,6 ± 2,0	-0,45	0,21	0,041
Duration of Diabetes (years)	6,5 ± 2,8	-0,12	0,09	0,198
Age (years)	50,0 ± 8,1	-0,08	0,05	0,094

In addition to the intervention factor, HbA1c levels were also associated with changes in vitamin D, with β = -0.45 (SE 0.21; p=0.041), meaning that poorer glycemic control tended to result in a smaller increase in vitamin D levels. Meanwhile, the duration of DM (β = -0.12; p=0.198) and patient age (β = -0.08; p=0.094) were not significantly associated with changes in vitamin D.

Clinically, these findings indicate that vitamin D supplementation significantly increases vitamin D levels in TB patients with DM, regardless of age or duration of diabetes. However, poor glycemic control may hinder the optimal rise in vitamin D levels, highlighting the importance of HbA1c monitoring in ensuring therapeutic success. Therefore, integrating vitamin D supplementation with good blood glucose control can provide synergistic benefits for clinical improvement and TB treatment outcomes.

4. Discussion

The baseline characteristics of the subjects in both intervention and control groups were relatively balanced in terms of age, gender, duration of diabetes, and baseline HbA1c, which enhances the internal validity of the findings. This comparability is important in studies involving patients with comorbid pulmonary TB and DM, where metabolic dysregulation and immune dysfunction may confound outcomes related to vitamin D metabolism. Previous studies have shown that vitamin D deficiency not only impairs host immunity to *Mycobacterium tuberculosis* but also correlates with poor glycaemic control among diabetic patients [22].

Vitamin D supplementation in the intervention group resulted in a substantial increase in serum levels (+15.1 ± 4.2 ng/mL) compared to controls (+5.2 ± 2.9 ng/mL, p < 0.001). This aligns with findings from a recent meta-analysis demonstrating that TB patients exhibit significantly lower 25(OH)D levels than healthy individuals, with deficiency associated with a two-fold increased TB risk [23,24]. Clinically, improved vitamin D status enhances macrophage activation and antimicrobial peptide synthesis (such as cathelicidin LL-37), strengthening immune clearance of *M. tuberculosis*. A significant improvement in sputum AFB conversion was observed, 60% in the intervention group versus 30% in controls (p = 0.021), suggesting that vitamin D may accelerate bacteriological clearance in TB-DM. This finding resonates with evidence that vitamin D promotes macrophage differentiation and T-cell activation, though prior meta-analyses have shown mixed results. Some studies found higher conversion rates with supplementation, whereas others reported no statistically significant effect on time-to-conversion [25,26]. Our focus on a TB-DM cohort, a population with both immune and metabolic impairments, may explain the stronger supplementation effect observed here.

Improvements in clinical symptoms such as cough, fever, and weight loss were more pronounced in the vitamin D group. The *Frontiers in Nutrition* review (2022) reported similar improvements in TB symptom scores, despite variable bacteriological outcomes, supporting the immunomodulatory benefit of supplementation. Nutritional recovery also improved more markedly in the intervention group, consistent with findings that vitamin

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D deficiency is linked to delayed recovery and poor prognosis in TB [27].

Multivariate logistic regression confirmed that vitamin D supplementation was independently associated with sputum conversion (OR = 3.25; 95% CI 1.20–8.75; p = 0.021), while each 1 ng/mL rise in serum vitamin D increased conversion odds by 18% (p = 0.004). In contrast, HbA1c and BMI post-therapy were not significantly related to conversion. This indicates that although metabolic control remains important, vitamin D exerts a more direct influence on bacteriological outcomes. Additionally, higher HbA1c was inversely related to the change in vitamin D (β = –0.45; p = 0.041), consistent with evidence that chronic hyperglycaemia impairs vitamin D metabolism and immune function.

Overall, our results align with recent evidence that, while vitamin D supplementation may not uniformly shorten time-to-sputum conversion, it improves clinical outcomes and immunologic recovery in TB patients, particularly those with DM [23,28]. Given its safety, affordability, and biologic plausibility, vitamin D supplementation should be considered as an adjuvant in TB-DM management alongside glycaemic control and standard anti-TB therapy.

This study's strengths include the focus on a TB-DM comorbid population, the use of total sampling, measurement of both immuno-nutritional and bacteriological outcomes, and robust multivariate analyses. However, limitations include the relatively short follow-up (intensive phase only), lack of long-term outcomes (e.g., relapse, mortality), and potential confounding from unmeasured factors such as vitamin D receptor polymorphisms, nutritional intake, sun exposure and initial vitamin D status. Indeed, some recent RCTs and meta-analyses show that vitamin D supplementation may not significantly reduce TB infection risk or accelerate bacteriological clearance, although symptom improvements are seen. These discrepancies highlight the necessity of contextualising supplementation within high-risk subgroups (such as TB-DM) and considering interaction with metabolic status.

5. Conclusion

This study demonstrated that vitamin D supplementation significantly improved serum vitamin D levels among pulmonary TB patients with comorbid DM after the intensive phase of therapy. The increase in vitamin D was notably greater in the intervention group compared to controls and was strongly associated with enhanced clinical recovery and sputum conversion. Each 1 ng/mL rise in serum vitamin D increased the likelihood of AFB conversion by approximately 18%, suggesting that vitamin D plays an important immunomodulatory role in promoting bacteriological clearance and improving treatment outcomes in TB-DM patients.

Clinically, supplementation led to substantial symptom improvement—including reduction in cough, dyspnoea, fever, night sweats, chest pain, and weight loss—alongside better nutritional recovery as reflected by higher weight and BMI gains. The sputum conversion rate was also higher in the intervention group (60%) than in the control (30%), indicating accelerated sputum sterilization and potential reduction in transmission risk. Overall, these findings support the use of vitamin D supplementation as an effective adjuvant to standard anti-TB therapy in patients with TB-DM comorbidity, contributing to faster recovery, improved nutritional status, and better therapeutic success.

6. Declarations

Conflict of Interest

The authors affirm that there are no conflicts of interest or competing financial or personal relationships that could have influenced the conduct, analysis, or publication of this study.

Author's Contributions

NFHH and ID conceptualized and designed the study. Methodology development and data analysis were conducted by NFHH and EPW. JM, EA, and SN contributed to data validation and interpretation. The investigation was performed by NFHH and JM, with EA and ID providing key resources and supervision. EPW and SN managed data curation. The initial manuscript draft was prepared by NFHH and critically reviewed and revised by ID and EA. Visualization was created by NFHH, and project administration was overseen by JM. All authors reviewed and approved the final manuscript.

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