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Original Research Article

Association Between Vitamin D Status and Tuberculosis Outcomes: A Clinical Study

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Abstract:

Background: Tuberculosis (TB) remains the leading cause of infectious disease mortality worldwide, and vitamin D (Vit-D) has emerged as a potentially important modulator of host defense against TB infection.

Methods: This cross-sectional study was conducted over one year at a tertiary care hospital, enrolling 180 patients aged 18–60 years with confirmed pulmonary TB through simple random sampling. Serum 25(OH)D levels were measured using the Elecsys Vit-D3 assay and classified per Endocrine Society guidelines, with associations analyzed using SPSS version 20.

Results: The majority of patients (55.6%) were above 51 years, with a male preponderance (62.2%). Vitamin D deficiency was highly prevalent, affecting 75% of patients, while 19.4% had insufficient and only 5.6% had sufficient levels (mean 25(OH)D: 16.68 ng/mL). Deficiency was significantly associated with female gender (92.6% deficient, p=0.026) and bilateral lung involvement (p=0.002), while age (p=0.473) and area of residence (p=0.829) showed no significant association.

Conclusion: Vitamin D deficiency is highly prevalent among pulmonary TB patients, particularly among women and those with more extensive lung disease, supporting routine screening and supplementation as a potential therapeutic adjunct.

Keywords: Vitamin D Deficiency, Pulmonary Tuberculosis, 25-hydroxyvitamin D, Gender Disparity, Lung Involvement.

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Introduction

Tuberculosis (TB) has surpassed HIV/AIDS as the leading cause of death from infectious disease worldwide, with more than a quarter of the global population estimated to have been exposed to infection [1-3]. The burden falls disproportionately on Africa, the Western Pacific, and Southeast Asia, driven largely by poverty, HIV co-infection, and drug resistance, with developing nations accounting for nearly 95% of cases [4,5]. Although global incidence has declined by roughly 2% annually since 2003, progress toward the WHO's target of eliminating TB by 2030 has been undermined by the COVID-19 pandemic and the rising prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) strains, both of which continue to drive higher rates of morbidity and mortality [1,6].

This divergence is reflected starkly in treatment outcomes: drug-susceptible TB achieves cure rates exceeding 90% with adequate diagnostic and therapeutic infrastructure, whereas MDR-TB cure rates remain markedly lower, reaching at best 57% by recent WHO estimates [7]. Outcomes are further shaped by socioeconomic conditions, healthcare access, and medication adherence [7], underscoring the need to explore adjunctive treatment strategies that could improve outcomes across both drug-resistant and drug-susceptible disease.

Vitamin D (Vit-D) status has emerged as one such factor of interest [8-10]. Beyond its established role in bone metabolism, Vit-D is increasingly recognized as an important mediator of host defense against infection [11]—a relationship first observed in the 1930s, when cod liver oil was used therapeutically for TB, before being supplanted by antimicrobial chemotherapy in the 1950s [12]. More recent studies have linked low Vit-D levels to heightened susceptibility to infections such as septic shock, influenza, and other respiratory illnesses

[8,13,14]. Mechanistically, the active metabolite 1,25-dihydroxyvitamin D binds the vitamin D receptor (VDR) to activate antimicrobial pathways, including autophagy and intracellular killing of TB bacteria [15,16]. Severe or prolonged deficiency also disrupts calcium and phosphate homeostasis, predisposing patients to secondary hyperparathyroidism and consequent bone demineralization [17].

Despite this evidence, the specific role of Vit-D in pulmonary TB remains comparatively underexplored. The present cross-sectional study was therefore undertaken to determine the prevalence of Vit-D deficiency among patients with pulmonary tuberculosis and to examine its potential clinical significance in this population.

Materials and Methods

Study Duration: This cross-sectional study was conducted over one year at a tertiary care hospital. This duration was chosen to account for seasonal variation in vitamin D levels, given the well-documented influence of sunlight exposure on serum 25(OH)D concentrations across different times of the year.

Study Population: Participants were recruited from patients presenting to the outpatient and inpatient units of the general medicine and respiratory medicine departments.

Inclusion Criteria: Eligible participants were adults of either sex, aged 18 to 60 years, with a confirmed diagnosis of pulmonary tuberculosis.

Exclusion Criteria: Patients were excluded if they had category II or multidrug-resistant TB (MDR-TB), or if they presented with secondary immunodeficiency arising from conditions such as HIV infection, organ transplantation, malignancy, or corticosteroid use. Additional exclusions included hepatitis B or C seropositivity, extrapulmonary TB, and cases requiring surgical management. Individuals undergoing cytotoxic therapy currently or within the preceding three months, pregnant or lactating women, and those with seizure disorders, symptomatic cardiac disease, impaired renal or hepatic function, hematological abnormalities, or serious concurrent illness were also excluded, as were patients unlikely to adhere to the treatment protocol or those with a history of substance abuse.

Sample Size Determination: Sample size was calculated using the standard formula, based on parameters reported by Talat et al. [18]—a confidence coefficient (z) of 1.96, an expected prevalence (p) of 76%, and a margin of error (d) of 7%—yielding a minimum requirement of approximately 143 patients. To account for anticipated dropouts and loss to follow-up, and given the extended one-year recruitment window, the sample size was increased to 180, a target considered readily achievable given the high patient volume typically seen at Indian tertiary care centers managing TB.

Ethical Approval and Informed Consent: Approval for the study was granted by the Gujarat Adani Institute of Medical Sciences Institutional Ethics Committee (Letter No.-GAIMS/IEC/APPROVAL/2024/94, Dated-12/07/2024), and informed consent was obtained from patients' next of kin prior to enrollment.

Data Collection: Participants were enrolled through simple random sampling. A structured proforma was used to document sociodemographic characteristics, medical and pharmacological history, and relevant laboratory findings. Tuberculosis diagnosis was established based on sputum smear positivity for acid-fast bacilli, culture confirmation of Mycobacterium tuberculosis, positive TB PCR results, or histopathological evidence of persistent caseating granulomatous inflammation.

Laboratory Measurements: Venous blood samples were obtained for complete blood count, serum 25(OH)D, albumin, and calcium estimation, alongside renal function tests (serum creatinine and urea) and liver function parameters (ALP and ALT). Serum 25(OH)D concentrations were quantified using the Elecsys Vit-D3 assay.

Vitamin D Status Definition: Vitamin D status was classified in accordance with Endocrine Society clinical practice guidelines [19]. Serum 25(OH)D concentrations of ≥30 ng/mL were classified as normal, 21–29 ng/mL as insufficient, and ≤20 ng/mL as deficient.

Statistical Analysis: Data were analyzed using SPSS version 20. Descriptive statistics were used to summarize continuous and categorical variables, and a p-value of <0.05 was considered statistically significant.

Results

In this study, the majority (55.6%) of the patients were above 51 years of age, followed by the 31–40 year age group (17.8%), the 41–50 year age group (13.9%), and those aged 30 years or younger (12.8%). A male preponderance was observed, with men comprising 62.2% of the cohort compared to 37.8% women (Table 1).

Table 1: Age and Gender Distribution of the Study Population (N=180)

Age Group	Number (%)
≤30 years	23 (12.8%)
31–40 years	32 (17.8%)
41–50 years	25 (!3.9%)
>51 years	100 (55.6%)
Male	112 (62.2%)
Female	68 (37.8%)

Vitamin D deficiency was observed across all age groups, with no statistically significant association between age and Vit-D status (p=0.473), suggesting that deficiency was fairly uniformly distributed regardless of patient age. In contrast, gender showed a statistically significant association with Vit-D status (p=0.026), with a notably higher proportion of female patients (92.6%) classified as deficient compared to male patients (64.3%), indicating that women in this cohort were disproportionately affected by low Vit-D levels (Table 2).

Table 2: Relationship Between Age, Gender, and Vitamin D Status

Parameter	Total	Deficient	Insufficient	Sufficient	p-value
Age Group					
≤30	23	13	10	0	0.473
31–40	32	22	7	3	
41–50	25	23	2	0	
>51	100	77	16	7	
Gender					
Male	112	72	30	10	0.026
Female	68	63	5	0	
Total	**180**	**135**	**35**	**10**	

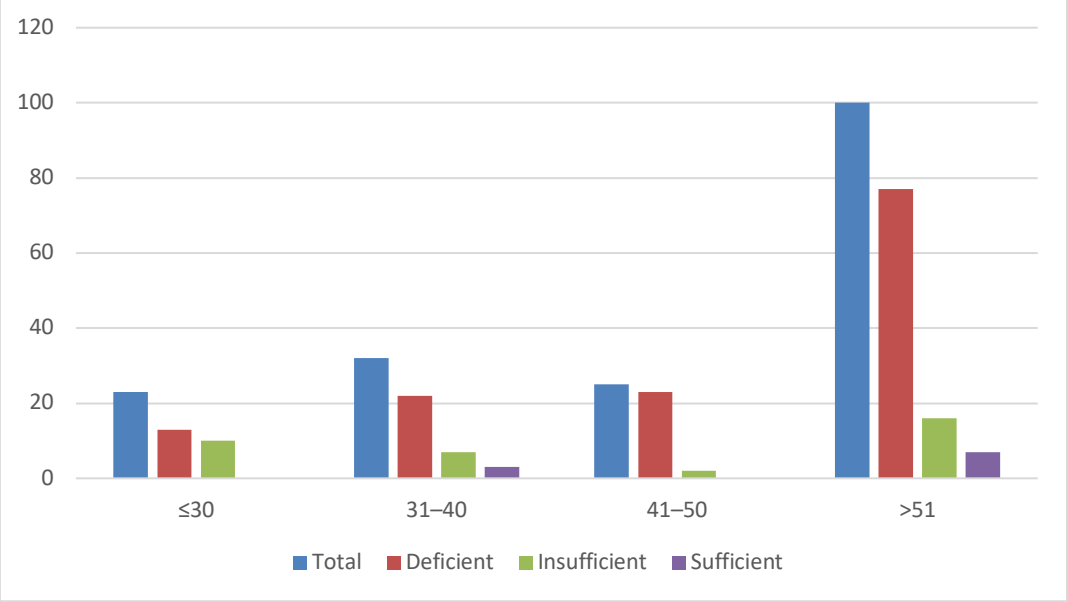

Figure 1: Distribution of Vitamin D Status Across Age Groups.

A statistically significant association was noted between the site of lung involvement and Vit-D status (p=0.002): all patients classified as having insufficient or sufficient Vit-D levels presented with unilateral disease, whereas bilateral lung involvement was seen exclusively among patients with Vit-D deficiency, pointing to a possible link between more severe or extensive disease and lower Vit-D levels. Area of residence, however, showed no significant association with Vit-D status (p=0.829), indicating that deficiency was similarly prevalent among both rural and urban patients in this cohort (Table 3).

Table 3: Association of Vitamin D Status with Site of Lung Lesion and Area of Residence

Parameter	Deficient	Insufficient	Sufficient	p-value
Lesion Site				
Unilateral (UL)	80 (59.3%)	35 (100%)	10 (100%)	0.002
Bilateral (BIL)	55 (40.7%)	0 (0%)	0 (0%)	
Residence				
Rural	72 (53.3%)	18 (51.4%)	8 (80%)	0.829
Urban	63 (46.7%)	17 (48.6%)	2 (20%)	

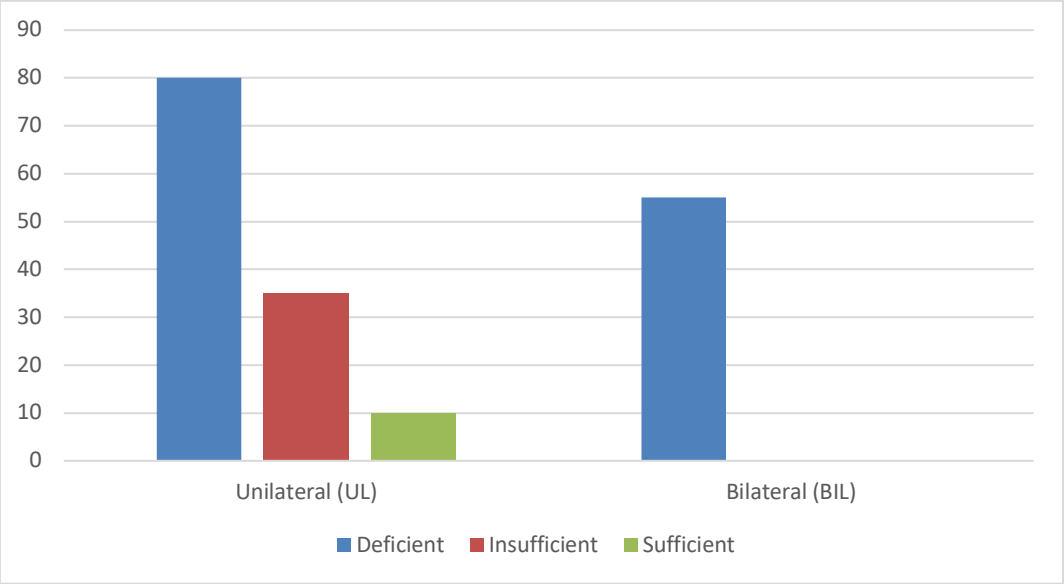

Figure 2: Distribution of Vitamin D Status by Site of Lung Lesion.

Discussion

This study evaluated Vit-D status among 180 pulmonary TB patients, examining its relationship with demographic and clinical parameters. Patients above 51 years constituted the largest proportion of the cohort, consistent with the recognized vulnerability of older individuals to TB. Overall, a substantial burden of Vit-D deficiency was observed, with 75% of patients classified as deficient, 19.4% as insufficient, and only 5.6% as sufficient, and the mean serum 25(OH)D level in the population was 16.68 ng/mL. Although deficiency was most frequent in the >51 age group, the association between age and Vit-D status did not reach statistical significance (p=0.473), a finding broadly in line with prior literature suggesting only a modest age-related effect on Vit-D status [20].

A significant gender disparity emerged, with 92.6% of women found to be Vit-D deficient compared to 64.3% of men (p=0.026). This pattern mirrors findings from other studies reporting a higher prevalence of hypovitaminosis D among women, particularly younger women [21]. Contributing factors identified in the literature include reduced sun exposure due to covering practices, inadequate dietary Vit-D intake, urban residence, parity, elevated BMI, and lower educational attainment, whereas seasonal variation and overall sun exposure have not consistently emerged as significant predictors [22].

A notable association was also observed between the extent of lung involvement and Vit-D status, with deficiency significantly more common among patients with bilateral disease compared to those with unilateral lesions (p=0.002). This aligns with evidence linking Vit-D deficiency to poorer respiratory outcomes, including increased respiratory mortality risk reported in longitudinal studies of older adults with impaired lung function [23]. However, the precise mechanisms underlying this association remain unclear and warrant further investigation. In contrast, no significant relationship was found between Vit-D status and area of residence, with deficiency similarly prevalent among rural (53.3%) and urban (46.7%) patients (p=0.829), a finding consistent with reports of high Vit-D deficiency across both rural and urban populations [19].

Taken together, these findings reinforce existing evidence supporting a high prevalence of Vit-D deficiency among patients with pulmonary tuberculosis and its potential relevance to disease severity. Given the reported benefits of Vit-D supplementation in TB management, including favorable outcomes observed in pediatric TB patients [24], routine assessment and correction of Vit-D status may represent a valuable adjunct to

standard TB therapy. Further clinical research is needed to establish the optimal timing, dosage, and role of Vit-D supplementation in improving treatment response and overall outcomes in this patient population.

Conclusion

This study highlights a high prevalence of vitamin D deficiency among patients with pulmonary tuberculosis, with three-fourths of the study population found to be deficient and a mean serum 25(OH)D level well below the sufficiency threshold. Female patients and those with more extensive bilateral lung involvement were significantly more likely to be Vit-D deficient, suggesting that Vit-D status may be linked to both patient demographics and disease severity, while age and area of residence showed no significant association. These findings underscore the potential value of incorporating routine Vit-D screening into the clinical evaluation of pulmonary TB patients, particularly among women and those with more extensive disease. Given the vitamin's established role in immune-mediated antimycobacterial defense, correction of deficiency through supplementation may serve as a useful adjunct to standard anti-tubercular therapy, though larger prospective studies are warranted to establish its impact on treatment outcomes and to define optimal dosing strategies in this population.

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