Prevalence of vitamin- D deficiency in newly diagnosed Pulmonary Tuberculosis cases in South India- A tertiary care hospital based cross sectional study

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ABSTRACT

Background

Tuberculosis remains a significant global health concern, with a disproportionate burden in developing countries. Vitamin D plays a crucial role in the immune system's response to Mycobacterium tuberculosis, the causative agent of tuberculosis. Vitamin D is known to be involved in the activation of immune cells, such as macrophages, that are responsible for the phagocytosis and destruction of the tuberculosis pathogen.

Methodology

This cross-sectional study conducted at a tertiary care hospital in south India, to assess the association between vitamin D and Pulmonary tuberculosis. We included 100 newly diagnosed Pulmonary tuberculosis cases meeting the inclusion and exclusion criteria. Their vitamin D levels were assessed before starting them on ATT (anti – tubercular treatment) according to NTEP (National tuberculosis elimination programme). Also, its association with severity of diseases – assessed with sputum smear severity and chest x-ray involvement.

Results

We found that 72% (72 out of 100) of the patients were deficient (<20 ng/mL), 20% (20 out of 100) were insufficient (21–29 ng/mL), and 8% (8 out of 100) had sufficient levels (≥30 ng/mL), showed the high prevalence of vitamin D deficiency, emphasizing the need for screening and possible supplementation. It also shows significant association between vitamin D deficiency and sputum smear severity (p value <0.001).

Conclusion

We suggest conducting more studies in the south Indian population and to include screening of vitamin D levels in the NTEP programme.

Keywords: Pulmonary Tuberculosis, Vitamin D, macrophages, sputum smear positivity, immunity.

INTRODUCTION

Tuberculosis (TB) still poses a major public health challenge worldwide, with a particular burden on vulnerable groups in low- and middle-income countries. (1) Vitamin D deficiency is one of several risk factors that has gained attention in recent months because of its role in immune function. Vitamin D is critical to the activation of the immune response to Mycobacterium tuberculosis, the bacterium that causes TB. Lack of this micronutrient can weaken the body's ability to respond effectively, thereby increasing the risk of infections and modulating disease progression. (2)

Calcitriol's classical role is maintaining calcium and phosphate homeostasis for bone mineralization. It enhances intestinal calcium absorption, promotes renal calcium reabsorption, and mobilizes calcium from bone via osteoclast activation (8). However, its non-skeletal functions are equally vital. Calcitriol modulates immunity by upregulating antimicrobial peptides (e.g., cathelicidin and β-defensin), enhancing macrophage phagocytosis, and regulating T-cell responses (9). These actions bridge innate and adaptive immunity, positioning vitamin D as a key player in infection defence.

Malnutrition, a prevalent global issue, has been closely linked to an increased risk of tuberculosis. Nutrient deficiencies, particularly in vitamins A, D, and E, as well as minerals such as iron and zinc, can impair the immune system's ability to effectively combat M. tuberculosis, leading to a higher likelihood of disease progression. (6 – 7). Malnutrition, a common condition among tuberculosis patients, can lead to decreased dietary intake and absorption of vitamin D. Additionally, the inflammatory response associated with tuberculosis may result in increased vitamin D utilization, further exacerbating the deficiency. (4)

Socioeconomic factors, such as poverty, poor living conditions, and limited access to healthcare, can also hinder the ability of individuals to maintain adequate vitamin D levels. These social determinants of health can unevenly affect vulnerable populations, such as immigrants and individuals living in underserved communities, who often have a higher burden of tuberculosis. (3)

In regions like Kerala, India, despite abundant sunlight, vitamin D deficiency is prevalent. This paradox is attributed to factors such as indoor lifestyles, cultural clothing practices, and dietary habits that limit vitamin D synthesis and intake. Studies have indicated that individuals with active TB often exhibit lower vitamin D levels compared to healthy controls, suggesting a potential link between deficiency and increased disease risk.

The link between vitamin D status and TB points out the need for comprehensive approaches in disease management. Addressing vitamin D deficiency through nutritional interventions and public health strategies could enhance immune responses and improve treatment outcomes for TB patients. (5) Further research is essential to establish definitive correlations and inform policy decisions aimed at integrating vitamin D assessment and supplementation into TB control programs.

METHODOLOGY

This prospective cross-sectional study was conducted at a tertiary care hospital in South India to investigate vitamin D level among patients newly diagnosed with Pulmonary Tuberculosis (TB).

A total of 100 participants were included based on inclusion and exclusion criteria. Eligible individuals were aged 18 years or older, with newly diagnosed cases of Pulmonary TB confirmed through clinical evaluation, sputum smear positivity, and chest radiographic findings. Written informed consent was obtained from all participants prior to enrolment.

Exclusion criteria included individuals with HIV infection, malignancy, ongoing chemotherapy, or chronic liver or renal disease. Pregnant and lactating women were excluded, as were patients who were receiving vitamin D or calcium supplementation, anticonvulsants, diuretics, or other medications known to interfere with vitamin D metabolism.

All participants underwent a detailed clinical history and physical examination. Prior to the initiation of anti-tubercular therapy (ATT), serum 25-hydroxyvitamin D [25(OH)D] levels were measured. Blood samples (0.5 mL) were collected in green or yellow top tubes. Samples were allowed to clot and then centrifuged within two hours to separate serum or plasma. The samples were stable for analysis when maintained at room temperature for up to 8

hours, refrigerated for up to 4 days, or frozen for a maximum of 24 weeks. Severity of Pulmonary Tuberculosis was measured using sputum smear positivity and radiological severity using the Timika scoring system. Sputum smear positivity was graded using the standard scoring criteria (Table 1 – Grading of sputum smear positivity). Radiological severity of Pulmonary TB was assessed using the Timika scoring system, which evaluates two components: the extent of parenchymal involvement and the presence of cavitation. The lungs were divided into six anatomical zones (upper, middle, and lower zones on both sides), and the percentage of involvement in each zone was visually estimated. The total affected area across all six zones was summed and divided by 600, yielding a score from 0 to 100. An additional 40 points were assigned if cavitation was present, with the maximum total score being 140.

Table 1 - Grading of sputum smear positivity

Examination	Result	Grading	No. of fields should be examined
>10 AFB per oil immersion field	+ve	3+	20
1-10 AFB per oil immersion field	+ve	2+	50
10-99 AFB per oil immersion field	+ve	1+	100
1-9 AFB per oil immersion field	Scanty	Record exact number seen	100

Vitamin D status was classified in accordance with the Endocrine Society Clinical Practice Guidelines: levels ≤20 ng/mL were considered deficient, 21–29 ng/mL as insufficient, and ≥30 ng/mL as optimal.Data were recorded in a structured proforma and entered into Microsoft Excel. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as means with standard deviations, while categorical variables were summarized as frequencies and percentages. The chi-square test was used to assess associations between vitamin D status and clinical parameters.This study was approved by the Institutional Ethics Committee of Jubilee Mission Medical College and Research Institute, Thrissur (IEC Study Ref. No. 50/23/IEC/JMMC&RI), and was conducted in accordance with the ethical standards of the Declaration of Helsinki.

RESULTS
The age analysis indicates a mean age of 54.40 years, with both the median and mode at 55 years, a range spanning from 18 to 87 years, and an interquartile range (IQR) of 18.5 years. Majority fall under the age group of 50 – 70 years, with the majority showing vitamin D deficiency. Among the gender distribution 72 male and 28 females, no particular gender association has been noted with vitamin D deficiency. (Figure 1 – association of BMI and vitamin D levels).
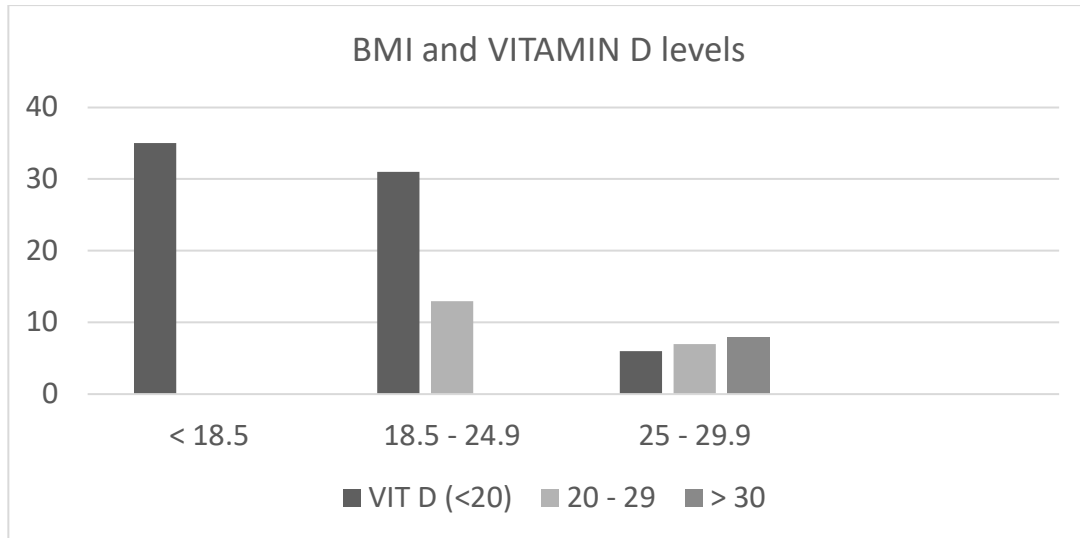
Figure 1 – Association of BMI and vitamin D levels

Vitamin D Deficiency (< 20 ng/mL) is highly prevalent (72 individuals), indicating a major public health concern. Insufficiency (21-29 ng/mL) affects 20 individuals, suggesting a need for increased Vitamin D intake. Sufficiency (≥ 30 ng/mL) is found in only 8 individuals, indicating that most of the population has inadequate levels. (Table 2 – association of vitamin D levels and sputum smear severity).

Table 2 - Association of vitamin D levels and sputum smear positivity

AFB Results	<20	21 − 29	>30	Total
1+	14	0	0	14
2+	31	0	0	31
3+	27	14	0	41
Scanty	0	6	8	14
Total	72	20	8	100

The p-value (0.0001) confirms a highly significant association between AFB Results and Vitamin D Levels, suggesting that Vitamin D deficiency is more prevalent in higher AFB positivity groups. Out of 72 cases - 33 cases had a Timika scoring between (0-40), 27 had a scoring between (41 – 80) and 12 showed (>

80). Severity of chest x-ray involvement did not show a statistically significant association with vitamin D levels, with (p value 0.054). (Table 3 – association of vitamin D levels and chest x- ray involvement) Although regarding cavitary lesions, 31 cases showed cavity formation.

Table 3 - Association between chest x-ray involvement and vitamin D levels

CXR SCORING (TIMIKA SCORING)	VIT D (<20)	VIT D (20 – 29)	VIT D (> 30)	
0 - 40	33	15	7	55
41 - 80	27	3	1	31
>80	12	2		14
TOTAL	72	20	8	100

Presence of cavity in chest x-ray had a direct association with severity of disease because majority of them showed 3+ sputum smear positivity. And a large proportion of cases (28 cases

out of 31) had vitamin D deficiency. (Figure 2 – association of cavitary lesions in chest x-ray and vitamin D levels)

CAVITY

■ < 20   ■ 20 - 29   ■ > 30   ■
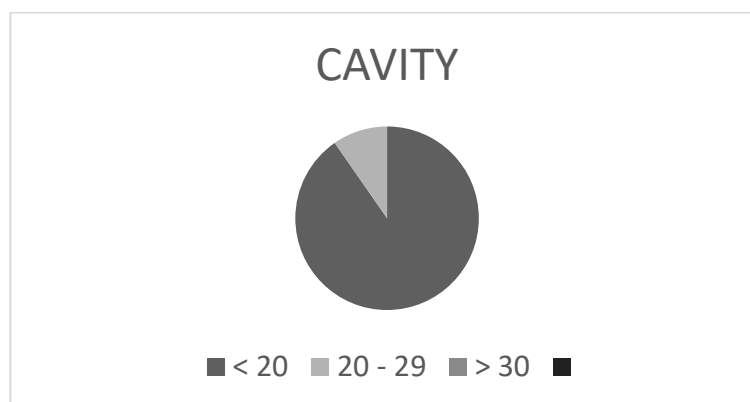
Figure 2 – Association of cavitary lesions in chest x-ray and vitamin D levels

DISCUSSION

Vitamin D, a fat-soluble vitamin essential for calcium regulation, bone health, and immune function, has gained attention for its potential role in infectious diseases, particularly tuberculosis (TB). TB remains a global health concern, with approximately 10 million new cases annually. Increasing evidence links Vitamin D deficiency to susceptibility and severity of TB, due to its immunomodulatory functions, especially in enhancing macrophage activity and antimicrobial peptide production. Among 100 newly diagnosed Pulmonary TB patients, we observed a notably high prevalence of Vitamin D deficiency—72% were deficient (<20 ng/mL), 20% insufficient (21–29 ng/mL), and only 8% sufficient (≥30 ng/mL). These findings align with global trends, such as the 96% deficiency reported by Iftikhar et al. (Pakistan) (11), 83.3% by Hashemi et al. (Iran) (12), and 86.7% by Koo et al. (South Korea) (13). The variability in reported prevalence may relate to differences in diagnostic cut-offs, geographic and genetic factors, and levels of sun exposure. The mean age of patients was 54.4 years, with the majority aged 50–70, indicating middle-aged adults bear a significant burden. Gender distribution (72 males, 28 females) did not show a significant correlation with Vitamin D levels. Importantly, all 35 underweight patients (BMI <18.5) were Vitamin D deficient, supporting prior evidence that undernutrition exacerbates TB susceptibility and poor outcomes. Notably, even among patients with normal BMI (18.5–24.9), 31 were deficient and 13 insufficient, indicating Vitamin D deficiency is not limited to undernourished patients. This reinforces the need for routine Vitamin D screening and supplementation across all TB patients. Sputum AFB smear grading revealed: A majority (72%) had moderate to high bacillary load, and Vitamin D deficiency was significantly associated with more severe smear positivity—specifically, among the 72 deficient patients, 31 had 2+ and 27 had 3+ results ($p < 0.001$), marking a strong link between deficiency and disease severity.

Chest X-rays were assessed using the Timika score:

- Among the 72 deficient patients:
  - 33 had scores 0–40
  - 27 had scores 41–80
  - 12 had scores >80

Although the association between Vitamin D levels and Timika scores did not reach statistical significance ($p = 0.054$), the trend suggests more severe radiological involvement with deficiency. Cavitary lesions were seen in 31 patients, of whom 28 (90%) were Vitamin D deficient, we concluded that there is a potential relationship between cavity formation and both bacillary load and Vitamin D deficiency. Pleural effusion was rare (3%) and showed no direct association with vitamin D deficiency. Comparable studies, such as Chitanika et al, reported higher Timika scores in Vitamin D deficient TB patients, supporting our findings. (14) Similarly, Chakraborthy et al (15) and Jaimni et al (16) also noted associations between cavitary disease and both high mycobacterial load and low Vitamin D levels.

The role of Vitamin D in TB may be both causal and consequential. On one hand, low Vitamin D impairs cathelicidin-mediated destruction of *M. tuberculosis* in macrophages. On the other, TB infection may itself deplete Vitamin D, via increased conversion to its active form in inflamed tissues. Koo et al (13) reported increases in Vitamin D levels post-treatment, supporting the depletion hypothesis. Genetic factors may further influence susceptibility. VDR (Vitamin D Receptor) polymorphisms, as noted by Rathored et al (17) and Joshi et al (18), were linked to both Vitamin D deficiency and poorer TB outcomes, particularly in drug-resistant TB. Our study did not explore genetic markers, highlighting a potential area for future research. The 72% deficiency rate, alongside 20% insufficiency, emphasizes the urgency of Vitamin D screening in TB patients—ideally at diagnosis and before ATT initiation. Our findings support recommendations to integrate nutritional assessment into standard TB care, promote population-wide nutritional improvement, and expand research funding on undernutrition-TB links. Studies on supplementation have yielded mixed results—some showing improved sputum conversion, others no impact on mortality. Nevertheless, safe supplementation could improve outcomes if implemented judiciously, especially in high-risk, resource-constrained settings.

Limitations and Future Directions

Our study lacked a control group, limiting causal inference. Seasonal variation and genetic data were not assessed, both of which may affect Vitamin D status. Furthermore, the single-centre design and sample size (n = 100) could limit generalizability.Another limitation of the study is regarding lack of follow up of cases with vitamin D deficiency in Pulmonary TB patients after supplementation. To assess regarding sputum smear conversion and chest x-ray resolution after vitamin D supplementation.

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