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Evaluating the Link Between Vitamin D Deficiency and Tuberculosis in Adult Patients

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ABSTRACT

Background: Tuberculosis (TB) is a serious public health problem in Pakistan, where vitamin D deficiency is also very common as TB. Vitamin D has been implicated in the regulation of the immune system and its deficiency has been suggested to make an individual susceptible to infections such as TB.

Objective: To determine the association between vitamin D deficiency and tuberculosis in adult patients presenting to a tertiary care hospital.

Methodology: A case-control study was conducted among 72 adults (36 TB patients and 36 healthy controls) from January to December 2023. Serum 25-hydroxyvitamin D [25(OH)D] concentrations were measured, and participants were classified as vitamin D deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Statistical analysis was carried out using SPSS version 25.

Results: The average vitamin D status was substantially lower in TB cases (18.8 ng/mL) than in controls (31.5 ng/mL) ($p < 0.001$). Vitamin D deficiency was present in 86.1% of TB cases versus 25% of controls. The risk of having TB among those with vitamin D deficiency was 13.6 times greater (95% CI: 4.3–42.5). Both male and female TB patients had significantly reduced BMI and vitamin D status than controls.

Conclusion: Vitamin D deficiency is closely linked with risk of tuberculosis. These data are consistent with the potential of vitamin D to prevent and treat TB, and highlight the significance of screening and supplementation in high-risk individuals.

Keywords: Vitamin D Deficiency; Tuberculosis; Immune Function; Nutritional Deficiency

Introduction

Tuberculosis (TB) is a severe infectious illness that primarily occurs in the lungs but also has a tendency to spread to other organs like the bones, kidneys, and the brain. TB is caused by the bacterium Mycobacterium tuberculosis.[1] TB is transmitted from one individual to another by way of the air when an infected person with active TB coughs, sneezes, or speaks.[2] Despite the fact that there are drugs to cure TB, it is also a serious health issue in most countries, particularly in low-income countries such as Pakistan.

Pakistan is among the leading nations with the most TB cases worldwide.[3] Annually, thousands of individuals in Pakistan are diagnosed with TB. There are a number of factors that lead to the transmission of TB in our nation, including overcrowding in residences, poor diet, ignorance, poverty, and low access to quality healthcare.[4] Even with national strategies and campaigns towards the control of TB, the condition continues to impact a significant number of individuals.

In recent years, scientists and doctors have started to explore how certain nutrients and vitamins in our body can influence our chances of getting infections like TB. Among the most significant vitamins that scientists have researched in this regard is vitamin D. Vitamin D is an essential nutrient that helps in the body's ability to absorb calcium and maintain healthy and strong bones. It is produced primarily in the skin when exposed to sunlight, and it can be found in foods such as fish, eggs, and milk that has been fortified. In addition to bone development, vitamin D also plays a significant role in strengthening the immune system.[5] It aids in fighting infections by helping white blood cells and inducing the secretion of antimicrobial proteins. Researchers have found that vitamin D assists our immune cells, such as macrophages, to kill the TB bacteria by generating unique proteins like cathelicidin.

Lack of vitamin D causes brittle bones, high vulnerability to infections, and can cause diseases such as tuberculosis, particularly among individuals with nutritional deficiencies or lack of exposure to sunshine.[6] Several studies in various nations have established that individuals with TB tend to have lower blood levels of vitamin D than those who are healthy. This indicates that vitamin D deficiency may be a risk factor for the development of active TB disease.

In Pakistan, vitamin D deficiency is extremely prevalent. Research has indicated that around a huge majority of individuals, particularly women, kids, and older people, are low in vitamin D.[7] This is chiefly attributed to factors like reduced exposure to the sun, covering oneself for cultural or religious motives, poor nutritional habits, and insufficient knowledge regarding nutrition. Coincidentally, TB is also widespread in the nation. Since both vitamin D deficiency and TB has such a high prevalence in Pakistan, it would be useful to research whether the two are associated with each other.

If a link between vitamin D deficiency and TB is established, it may assist physicians and public health practitioners in better preventing and controlling TB. For instance, screening TB patients for vitamin D status and providing them with supplements if necessary may enhance their cure rate. It may also assist in decreasing the transmission and prevalence of TB in the community.

Hence, this study has been performed to determine if there is a correlation between vitamin D deficiency and tuberculosis in adult patients who present to a tertiary care hospital in Pakistan. The aim is to identify the role of vitamin D in TB and to observe if vitamin D level correction could improve the management of the disease.

Objective

To determine the association between vitamin D deficiency and tuberculosis in adult patients presenting to a tertiary care hospital.

Methodology

This was a case-control study done among 72 patients at the Department of Medicine, Rehman Medical Institute between January 2023 and December 2023. Newly diagnosed adult patients of 18 years and older with pulmonary tuberculosis were included. Diagnosis was made according to clinical symptoms, radiological presentation, and microbiological confirmation from sputum smear or GeneXpert testing. Consecutive patients were enrolled as they came to the outpatient or inpatient department. Patients with prior anti-tubercular treatment of more than two weeks, extrapulmonary TB, on vitamin D supplements in the past three months, or with chronic illness like kidney disease, liver disease, HIV, or malignancy were excluded. Pregnant and breastfeeding women were also excluded from the study.

Following informed written consent, data were gathered on a standardized questionnaire encompassing demographic data, clinical symptoms, dietary, sun exposure, smoking status, and comorbidities. Blood samples were taken to assay serum 25-hydroxyvitamin D [25(OH)D] levels by the chemiluminescent immunoassay method. Vitamin D was defined as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL).

All the collected data were entered and were analyzed using SPSS version 27 software. Descriptive statistics including mean and standard deviation were computed for continuous variables and frequencies and percentages for categorical variables. The relationship between vitamin D status and tuberculosis was determined using the Chi-square test and independent t-test, where a p-value of less than 0.05 was taken as statistically significant. Ethical clearance of the study was granted by

the research department of RMI, and patient confidentiality was maintained in the course of the research.

Results

Both groups were of similar gender and age, so they were appropriate matches. TB patients, though, had much lower vitamin D (18.8 ng/mL) compared to healthy individuals (31.5 ng/mL) with the difference being quite evident and significant. Additionally, 86% of TB patients were deficient in vitamin D, whereas only 25% of the control group was facing this issue. This indicates that the deficiency in vitamin D was far more prevalent in individuals with TB. The findings indicate that individuals low in vitamin D are approximately 13 times as likely to have TB, indicating a robust correlation between vitamin D deficiency and tuberculosis (Table 1).

Table 1. Comparison of Mean Vitamin D Levels and Deficiency Status Between TB Patients and Controls

Variable	Cases (n=36)	Controls (n=36)	p-value
Mean Age (years)	42.7 ± 13.9	41.9 ± 12.7	0.73
Male Gender, n (%)	20 (55.5%)	20 (55.5%)	1.00
Female Gender, n (%)	16 (44.4%)	16 (44.4%)	1.00
Mean Vitamin D (ng/mL)	18.8 ± 9.8	31.5 ± 11.2	<0.001
Vitamin D Deficient, n (%)	31 (86.1%)	9 (25.0%)	<0.001
Odds Ratio for Vitamin D Deficiency	OR = 13.6 (95% CI: 4.3–42.5)	-	

Among men, TB patients had significantly lower vitamin D levels (19.3 ng/mL) than healthy men (32.9 ng/mL), and 85% of them were deficient compared to 20% in the control group. Their mean BMI was also lower (21.0 vs. 24.0). Female TB patients also had lower vitamin D levels (18.2 ng/mL) than healthy women (29.9 ng/mL), and 87.5% of them were deficient, compared to 31.2% of healthy women. Their BMI was also lower (20.3 compared with 24.3). These findings indicate that male and female TB patients had significantly lower vitamin D concentrations and BMI compared with healthy individuals, indicating a strong association between undernutrition, vitamin D deficiency, and tuberculosis in both the sexes (Table 2).

Discussion

Tuberculosis (TB) is a bacterial disease that directly affects the lungs but can also involve other organs. TB spreads from one person to another by airborne droplets. TB usually develops slowly, presenting symptoms like a chronic cough, chest pain, weakness, fever, and unintentional weight loss. Though it is a treatable disease if the correct antibiotic is provided, TB still remains a major public health problem, particularly in developing nations.[8] Factors such as malnutrition, compromised immune systems, and less than adequate access to healthcare services, which cause it to continue and be highly transmittable. In spite of the large-scale efforts to prevent its spread, TB continues to be widespread due to several biological, environmental, social, and economic reasons.

The present work showed a highly significant and statistically confirmed relation between tuberculosis and vitamin D deficiency. Patients with TB showed significantly low serum levels of 25-hydroxyvitamin D compared to controls (18.8 ng/mL vs. 31.5 ng/mL, $p < 0.001$). Additionally, 86.1% of TB patients were vitamin D deficient, in contrast to only 25% of controls. The odds ratio determined (13.6; 95% CI: 4.3–42.5) shows that vitamin D-deficient individuals are more than thirteen times at risk of getting TB. A study by Pareek et al. (2015) documented that Vitamin D deficiency may potentially raise the risk of tuberculosis infection extending beyond the lungs, particularly in dark-skinned people and in women.[9] This implies that vitamin D aids the body to regulate TB infection. This provides a suggestion of possible causation between vitamin D status and TB infection.

The results are biologically coherent. Vitamin D play an important role in the regulation of immunity and defense against infection, including TB. It participates in the activation of macrophages and in antimicrobial peptide production, such as cathelicidin and defensins, which can kill Mycobacterium tuberculosis. In individuals with vitamin D deficiency, the immune response's capacity to respond to TB bacilli effectively can be severely impaired,

Table 2. Gender-wise Comparison of Vitamin D Levels and BMI in TB Cases and Controls

Gender	Group	Mean Vitamin D (ng/mL)	Vitamin D Deficient (%)	Mean BMI (kg/m²)
Male	TB Cases	19.3 ± 10.2	17 / 20 (85.0%)	21.0 ± 2.8
	Controls	32.9 ± 10.6	4 / 20 (20.0%)	24.0 ± 2.5
Female	TB Cases	18.2 ± 9.3	14 / 16 (87.5%)	20.3 ± 2.8
	Controls	29.9 ± 11.7	5 / 16 (31.2%)	24.3 ± 2.8

and thus, either activation from latent TB infection or an increased severity of active TB occur. A study by Selvaraj in 2015 reported that the active vitamin D, $1,25(OH)_2D_3$, enhances the immune response by increasing the activity of macrophages, such as phagocytosis and the release of antimicrobial peptides such as cathelicidin and defensins that contribute to the killing of Mycobacterium tuberculosis. It also induces autophagy and controls cytokine secretion, reinforcing the body's defense against TB.[10] Vitamin D supplementation during treatment for TB is likely to minimize inflammation and enhance recovery.

This study also pointed out that both the male and female patients with TB had lower BMIs and vitamin D status compared to their respective controls. For instance, male TB patients had a mean of 21.0 for BMI and a mean of 19.3 ng/mL for vitamin D, whereas male controls were found to have a BMI of 24.0 and vitamin D of 32.9 ng/mL. In females, TB patients had a BMI of 20.3 and a vitamin D level of 18.2 ng/mL compared to 24.3 and 29.9 ng/mL in controls respectively. A cohort study from Tanzania investigated the association between vitamin D status and outcomes of TB treatment among 677 patients, including both HIV-positive and HIV-negative. Vitamin D deficiency was associated with increased risk of TB relapse, decreased levels of T-cells in HIV-positive individuals, and increased decline of BMI, but no correlation with death or HIV disease progression was observed. The study identifies the possibility of vitamin D sufficiency in enhancing outcomes of TB.[11]

Aibana et al. (2019) reported in their study that low baseline vitamin D status as a risk factor for developing tuberculosis (TB), especially among HIV-positive individuals. This meta-analysis of multiple studies established a dose-response relationship, wherein the most severe vitamin D deficiency carried the highest risk of TB. These observations show the possible contribution of vitamin D to TB prevention and necessitate trials of supplementation.[12] Similarly, Ho-Pham et al. (2010) also had the experience that the majority of their patients with TB were vitamin D deficient and that deficiency was an independent strong predictor of TB. Their observations closely mirror those in our study.[13]

The case-control study in Bangladesh conducted by Sah et al. (2021) also reported that pulmonary TB patients had significantly lower vitamin D levels in their serum than healthy controls. Vitamin D deficiency (<20 ng/mL) was linked to a 5.21-fold increased risk for developing TB. The results point to a high correlation between low vitamin D and TB, where vitamin D supplementation in the affected patients appears to be necessary.[14] Likewise, in a longitudinal study from Lahore, by Junaid et al. (2015) identified that more than half of the patients of pulmonary TB had severe vitamin D deficiency (<25 nmol/L), which was associated with sputum smear conversion delay during treatment. Female sex, winter season, and bilateral disease were more frequently associated with deficiency. However, genetic variants within VDR, DBP, and CYP2R1 were not significantly associated with vitamin D status or response to treatment. These results highlight the role of vitamin D deficiency but not associated genetic polymorphisms in TB treatment outcomes.[15]

A prospective cohort study in Spain by Arnedo-Pena et al. (2015) concluded that a greater level of serum vitamin D was linked with reduced risk of tuberculosis infection conversion (TBIC) in contacts of TB patients. Mean vitamin D levels were significantly lower in participants who developed TBIC (20.7 ng/mL) than in the non-cases (27.2 ng/mL). The risk of TBIC decreased by 6% for every 1 ng/mL increase in vitamin D. These results indicate that sufficient vitamin D levels might provide protective effects against latent TB infection.[16] Similarly, in one study it was reported by Carwile et al. (2022) that undernutrition is the most important risk factor for tuberculosis (TB), causing 15% of cases, twice that of HIV. Undernourished people are more likely to develop active TB, more severe disease, and poor outcomes of treatment, including higher mortality. Nutritional interventions can enhance treatment success and lower mortality.[17]

The gender-based analysis in the current research also contributes a vital aspect. While both male and female TB patients were deficient in vitamin D, females had slightly lower mean levels. This may be attributed to cultural norms like veiling and remaining indoors, which restrict exposure to the sun, which is the main source of vitamin D. Moreover, old eating habits and socioeconomic disparities may also decrease vitamin D consumption in women.

This has consequences for targeted public health interventions that might have to triage women and other high-risk groups for vitamin D screening and supplementation.

The low BMI in TB patients versus controls as seen in our observation is to be expected and has been repeatedly described in the literature. Undernutrition is a well-documented risk factor for TB and could potentially be associated with vitamin D status since poorly nourished individuals are likely to be deficient in more than one micronutrient. Also, TB itself causes cachexia and weight loss, thereby contributing to nutritional deficiencies. Hanrahan et al. (2010) reported that in South African HIV-infected adults, higher BMI is linked with a lower risk of both tuberculosis. Overweight and obese participants had significantly lower hazard ratios for TB and mortality.[18] This research highlights the need to identify and treat vitamin D deficiency as a potentially modifiable risk factor for TB. Given the high burden of both diseases in Pakistan, screening and supplementation of vitamin D as part of TB control programs could yield substantial public health gains. Future research needs to investigate the effect of vitamin D supplementation on incidence of TB, treatment outcomes, and prevention of relapse to inform more definite recommendations for clinical practice and public health policy.

Conclusion

This research provides a substantial link between vitamin D deficiency and tuberculosis in adults in Pakistan, with vitamin D-deficient individuals having more than thirteen times the probability of contracting TB. The findings support the biological plausibility of the protective function of vitamin D in TB through immune modulation. Since both diseases are highly prevalent in Pakistan, public health policy must involve routine screening for vitamin D deficiency in TB patients and high-risk groups, as well as the consideration of vitamin D supplementation as an adjunct to TB prevention and treatment programs. Additional longitudinal and interventional research is needed to assess the effect of vitamin D supplementation on TB incidence, treatment response, and relapse prevention.

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