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# EVALUATING VITAMIN-D INSUFFICIENCY IN PATIENTS WITH PULMONARY TUBERCULOSIS: A CASE-CONTROL STUDY

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## ABSTRACT

**Objective:** To ascertain the incidence and affiliation between deficient Vitamin-D levels and patients with Tuberculosis.

**Methodology:** This case-control study, conducted at Liaquat University of Medical & Health Sciences, Pakistan in the duration from May, 2023 to April, 2024, aimed to evaluate 25-Hydroxy Vitamin-D levels in newly diagnosed tuberculosis (TB) patients. Involving 110 participants, Group A comprised 55 recently identified TB patients (18-65 years) confirmed by sputum Gene Xpert method, while Group B included 55 age-and-gender-matched controls. Exclusions applied to those with recent surgery, bone disease, or renal impairment. Demographic data (age, gender, BMI, smoking) were collected via a proforma. Venous blood samples measured Vitamin-D levels, with insufficiency defined as <25 ng/ml. Data were analyzed using SPSS version 22, employing t-tests and chi-square tests with a significance threshold of $p < 0.05$.

**Results:** In this case-control study, 55 newly diagnosed tuberculosis (TB) patients and 55 age-and-gender-matched controls were compared. The TB group had a significantly lower average BMI (22.1 kg/m²) than the control group (25.0 kg/m²). Vitamin D levels were markedly lower in TB patients (21.8 ± 5.0 ng/ml) compared to controls (30.9 ± 8.9 ng/ml), with 78.18% of TB patients being vitamin D deficient, versus 27.27% in the control group ($p < 0.001$). Among TB patients, 85.45% had drug-sensitive TB, with 85.11% of these being vitamin D deficient, while 14.55% had multidrug-resistant TB, with 62.5% exhibiting vitamin D deficiency. This study highlights a significant association between TB and lower vitamin D levels.

**Conclusion:** Our study discovered that many tuberculosis patients had low levels of vitamin D compared to healthy individuals, including those with drug-sensitive and multidrug-resistant TB. This suggests that giving extra vitamin D might help prevent and treat tuberculosis, especially in countries

like Pakistan where the disease is a significant health concern. More research is necessary to confirm how vitamin D supplements could benefit tuberculosis treatment.

**Keywords:** Tuberculosis, Vitamin-D, Multi drug resistant TB, Drug-sensitive TB.

## Introduction

Tuberculosis (TB) still remains an important international health concern, caused by the Mycobacterium tuberculosis complex infection, the *Mycobacterium tuberculosis* (MTB) in particular.1 The global report on TB from the World Health Organization (WHO) states that in 2014, TB killed 1.5million individuals globally (1.1 million of whom were HIV-positive and 0.4 million of whom were HIV-negative).2 TB impacted 9.6 million people worldwide. Ethiopia, for instance, had an projected incidence rate of 207 per 100,000 individuals in the same year, placing it eighth out of the 22 overburdened nations in the world.3

Among the many variables affecting the occurrence and course of tuberculosis (TB), the presence of vitamin-D deficiency (VDD) has become a crucial focus of research. Humans get most of their vitamin-D from sunlight exposure, which helps the skin convert 7-dehydrocholesterol to vitamin-D3.4 After that, the liver metabolizes it to produce 25-hydroxy vitamin-D, which is subsequently converted by the kidneys into the bioactive frm 1,25-dihydroxy-vitamin-D3, which is is essential for macrophage activation, playing a vital role in restricting MTB growth.5-6

Insufficient levels of Vitamin-D (<30 ng/dL) are an unexceptional problem, particularly in developing nations.7 Season, geography, demographics, and dietary fortification initiatives can all have an impact on the prevalence of this deficiency.8 A number of studies, including one on Chinese adults with tuberculosis of the lungs, have linked low levels of 25-hydroxy vitamin-D to tuberculosis (TB), suggesting that VDD may pose to be a risk factor in the pathophysiology of this disease.9

Pakistan, with its high TB burden, was among the top five countries with the most TB cases in 2011. Despite this significant burden, asymptomatic VDD is prevalent in Pakistan.10 However, there has been a scarcity of studies precisely inspecting the association between deficient Vitamin-D and TB in Pakistan.

In order to close this knowledge gap, this research will examine the relationship between insufficient levels of serum vitamin-D and pulmonary tuberculosis in patients from Pakistan. This will provide important new information about the possible function of vitamin-D in the treatment and prevention of tuberculosis.

## Objective

To ascertain the incidence and affiliation between deficient Vitamin-D levels and patients with Tuberculosis.

## Methodology

This case-control study was conducted at Liaquat University of Medical & Health Sciences, Pakistan in the duration from May, 2023 to April, 2024. All subjects provided informed written agreement, and the institution's ethical committee approved the study. A total of 110 participants were taken, comprising 55 new tuberculosis (TB) patients aged between 18 to 65 years in Group-A, and 55 age-and-gender-matched control individuals in Group-B.

The TB cases were recently identified patients who were not yet commenced on anti-tuberculosis treatment (ATT). Diagnosis was confirmed sputum Gene Xpert method. Drug susceptibility testing was performed on all TB patients to assess the presence of drug resistance.

The control group was made up of randomly chosen individuals who were of the same age and gender and were receiving standard medical examinations at the hospital outpatient department. A proforma was filled out by the patients and controls to gather information on specific demographics including age, gender, body mass index (BMI), and tobacco smoking. The study excluded participants with recent surgery, prior bone disease, or renal impairment.

Venous blood samples of 5ml were collected to measure 25-Hydroxy Vitamin-D levels. A pathologist confirmed each result. A level less than 25 ng/ml was taken as insufficient.
SPSS version 22 was utilized for data compilation and interpretation. For categorical data, the results were shown as a percentage and frequency, and for continuous variables, as a mean and standard deviation. T-tests and chi-square tests were implemented when needed, depending on the distribution and nature of the components. A significance level of less than 0.05 was used for the p-value.

**Results**

In the tuberculosis (TB) group, there were 35 men (63.64%) and 20 women (36.36%), while the control group had 33 men (60%) and 22 women (40%). The average age in the TB group was 37.4 years, and in the control group, it was 36.7 years. These age and gender differences between the groups were not statistically significant. The TB group had a lower average BMI of 22.1 kg/m² compared to 25.0 kg/m² in the control group, which was statistically significant. Smoking rates were similar between the TB group (61.82%) and the control group (54.55%), with no significant difference observed. [Table-1]

**Table-1: Study groups' demographic and clinical features**

| Characteristic | Group-A (TB) n=55 | Group-B (Controls) (n=55) | p-value |
|---|---|---|---|
| Males, n (%) | 35 (63.64%) | 33 (60%) | > 0.05 |
| Females, n (%) | 20 (36.36%) | 22 (40%) | > 0.05 |
| Mean Age (years) | 37.4 ± 11.8 | 36.7 ± 12.1 | > 0.05 |
| Mean BMI (kg/m²) | 22.1 ± 3.2 | 25.0 ± 3.4 | **< 0.05** |
| Smokers, n (%) | 34 (61.82%) | 30 (54.55%) | > 0.05 |

In tuberculosis patients, their vitamin D levels were much lower than those in healthy individuals (21.8 ± 5.0 ng/ml compared to 30.9 ± 8.9 ng/ml, $p < 0.0001$). A large majority of TB patients, 43 out of the group studied (78.18%), were deficient in vitamin D, while only 15 patients (27.27%) in the control group had this deficiency. This highlights a significant difference between the two groups in terms of vitamin D status ($p < 0.001$). [Table-2 & Figure-1]

**Table-2: Vitamin-D levels and its deficiency in study groups**

| Parameter | Group-A (TB) n=55 | Group-B (Controls) (n=55) | p-value |
|---|---|---|---|
| Mean Vitamin D Level (ng/ml) | 21.8 ± 5.0 | 30.9 ± 8.9 | < 0.0001 |
| Vitamin D Deficiency (<25 ng/ml), n (%) | 43 (78.18%) | 15 (27.27%) | < 0.001 |
| Normal Vitamin D Level (>25 ng/ml), n (%) | 12 (21.82%) | 40 (72.73%) | < 0.001 |

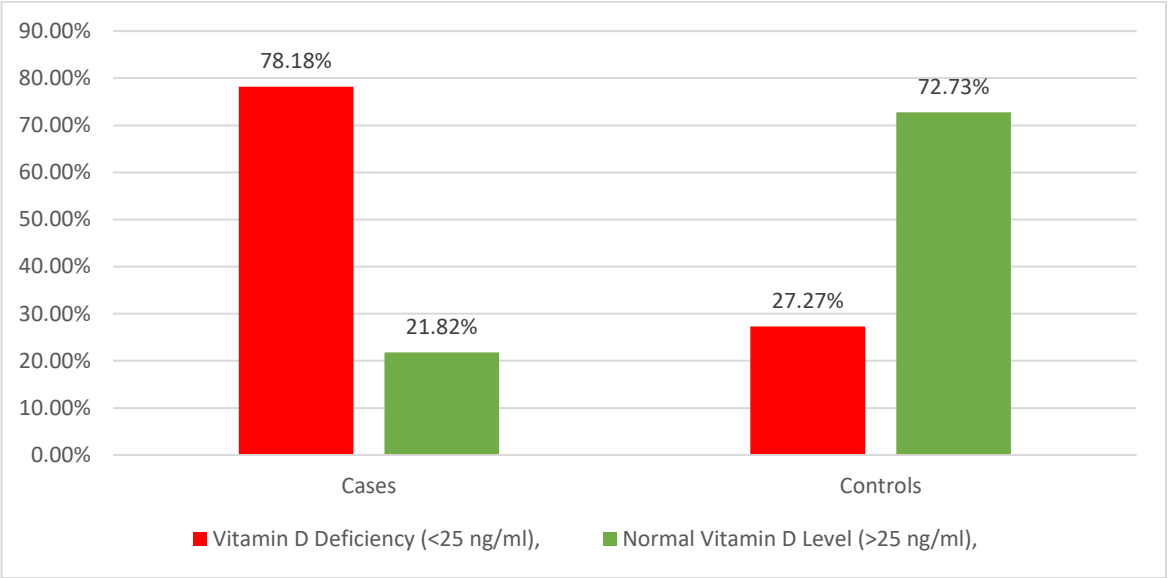


**Figure-1: Distribution of Study groups on the basis of Vit-D levels**

Among all tuberculosis patients, 47 (85.45%) had drug-sensitive tuberculosis, with 40 (85.11%) of these patients having vitamin D deficiency, and 7 (14.89%) having normal vitamin D levels (>25 ng/ml). Of the eight patients (14.55%) with multidrug-resistant tuberculosis, five (62.5%) had low vitamin D levels, while three (37.5%) had normal levels (>25 ng/ml). [Table-3]

**Table-3: Drug-sensitivity and Vit-D levels in TB patients**

| Parameter | TB-Group (n=55) | Vit-D Deficiency (<25 ng/ml) | Normal Vit-D Level (>25 ng/ml) | p-value |
|---|---|---|---|---|
| Drug-Sensitive TB, n (%) | 47 (85.45%) | 40 (85.11%) | 7 (14.89%) | <0.05 |
| Multidrug-Resistant TB, n (%) | 8 (14.55%) | 5 (62.5%) | 3 (37.5%) | <0.05 |

## Discussion

Pulmonary TB remains a significant worldwide health challenge, particularly in the developing nations and associated with substantial morbidity and mortality. Numerous studies have explored various factors influencing tuberculosis pathogenesis, including the role of vitamin-D levels due to its immunomodulatory properties.11-12

110 individuals were enrolled, of whom 55 were healthy controls and 55 were patients with a diagnosis of TB. Three quarters of the control group were female, with twenty (40%) and sixty percent of the males being TB participants. Statistically, no significant differences were identified ($p > 0.05$) between the TB group's and the control group's mean ages ($36.7 \pm 12.1$ years) and $37.4 \pm 11.8$ years, respectively. There is a comparable age distribution and a preponderance of males among tuberculosis patients, which is consistent with earlier research investigations by Mansoor et al. and Wakayo et al.13-14

Significant differences were noted in BMI between the TB group ($22.1 \pm 3.2$ kg/m²) and the control group ($25.0 \pm 3.4$ kg/m²), with the TB group demonstrating lower BMI values ($p < 0.05$). This finding of lower BMI in tuberculosis patients is coherent with the study results of Iftikhar et al, which may reflect disease-related metabolic alterations and nutritional deficiencies.15 Whereas, Smoking habits did not significantly differ between the TB group (61.82% smokers) and the control group (54.55% smokers).

Tuberculosis patients had much lower levels of vitamin D in their blood compared to healthy people ($21.8 \pm 5.0$ ng/ml vs. $30.9 \pm 8.9$ ng/ml, $p < 0.0001$). A significant majority of tuberculosis patients, 78.18%, were deficient in vitamin D (<25 ng/ml), while only 27.27% of the control group had this deficiency ($p < 0.001$). These results support earlier studies by Workineh et al. and Mashhaddi et al.,

emphasizing how vitamin D deficiency may affect susceptibility to and progression of tuberculosis.16-17

Moreover, 85.45% of patients with tuberculosis had drug-sensitive tuberculosis, and 85.11% of them had vitamin D insufficiency, which was a significant prevalence. By comparison, 14.55% of patients had tuberculosis that was resistant to several drugs, and a greater percentage of vitamin D insufficiency (62.5%) was noted. Similar to the findings mentioned by Jongwon et al., these data point to a possible link between vitamin D deficiency and the severity of tuberculosis, which calls for additional research to determine the consequences for outcomes of therapy and resistance patterns.18

In summary, our study adds to the evidence that low vitamin-D levels are associated with tuberculosis. It highlights the need to maintain optimal vitamin-D levels as part of tuberculosis treatment. Future research should investigate whether vitamin D supplements can improve outcomes and lessen the burden of tuberculosis on patients.

## Conclusion

Our study discovered that many tuberculosis patients had low levels of vitamin D compared to healthy individuals, including those with drug-sensitive and multidrug-resistant TB. This suggests that giving extra vitamin D might help prevent and treat tuberculosis, especially in countries like Pakistan where the disease is a significant health concern. More research is necessary to confirm how vitamin D supplements could benefit tuberculosis treatment.

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