

# Prevalence of Vitamin D Deficiency in Patients with Active Tuberculosis at a Tertiary Care Hospital: A Cross-Sectional Study

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## ABSTRACT

**Background:** The immune system's adaptive and innate responses can both be modified by vitamin D's powerful immunomodulatory effects. In recent years, vitamin D deficiency in tuberculosis patients has been reported in the medical literature. **Objective:** To determine the association between Vitamin D deficiency and active pulmonary tuberculosis. **Study Design:** It was a case control study. **Settings:** Research was carried out at PNS Hafeez, Islamabad. **Duration:** Duration of study was 6 months from August 2020 to January 2021. **Methods:** Sixty-six male and female patients aged 18 to 55 who had been diagnosed with active pulmonary tuberculosis were paired with sixty-six healthy controls. Vitamin D deficiency was diagnosed when the serum level was found to be less than 25 ng/ml. Vitamin D insufficiency prevalence was used as the outcome variable for this analysis. Each participant gave their informed consent in writing. **Results:** Patients' ages ranged from 18 to 55, with a mean age of 34.779.98. Fifty-seven men (43.2%) and seventy-five women (56.6%) made up the patient population. Patients' body mass index (BMI) was anything from 18.5 to 28.9, with a mean of 23.12 2.82. As many as 49 (37.1%) patients were heavy smokers. Clinically active tuberculosis patients had a substantially lower serum vitamin D level than controls (19.566.64 vs. 23.726.42 ng/ml; p0.001). Deficits in vitamin D were more common in cases than in controls (72.7 vs. 39.4 %; p0.001; OR=4.10; 95% CI=1.97-8.54). **Conclusion:** A lower mean serum vitamin D level and a higher prevalence of vitamin D deficiency were found to be associated with active pulmonary tuberculosis, with an (OR) odds ratio of 4.1 supporting routine screening of these patients for vitamin D status to prompt identify and, consequently, monitor patients with vitamin D deficiency in subsequent clinical practice.

**Keywords:** Vitamin D deficiency, Active tuberculosis, Pulmonary tuberculosis.

## INTRODUCTION

Tuberculosis is a disease that is most often caused by an infection with *Mycobacterium (M.) tuberculosis*, causes an estimated 1.5 million deaths in 2014.<sup>1</sup> Roughly 10 million persons contracted tuberculosis in 2020 with 1.4 million succumbing to it.<sup>2,3</sup> In 2019, TB was found to be most prevalent in South-East Asia (44%), followed by Africa (25%), the Western Pacific (18%), the Eastern Mediterranean (8.2%), the Americas (2.9%), and Europe (2.5%).<sup>2</sup> Active 1,25-dihydroxyvitamin D has been known to influence immune responses and anti-proliferative effects for over 20 years. When no effective antitubercular

medications were available at the time, high doses of this substance were employed to treat tuberculosis.<sup>4</sup> Recent years have brought more knowledge about vitamin D and its role in the pathogenesis and potential prevention of human disease, including tuberculosis.<sup>5</sup>

Vitamin D has been shown to play an essential biological role in bone metabolism. But 1,25-dihydroxy vitamin D3 (1,25D3), the active form of vitamin D, also exerts pleiotropic effects on the immune system.<sup>6</sup> Human monocytes/macrophages contaminated with *Mycobacterium TB* produce more autophagic peptides and proteins after being exposed to 1,25-

dihydroxyvitamin D3. Nitric oxide synthase is downregulated by vitamin D metabolites, which in turn inhibits mycobacterial development.<sup>7</sup>

As a powerful immunomodulator, vitamin D has an effect on both the adaptive and innate immune responses. As in other impoverished countries, vitamin D insufficiency is present in the asymptomatic population of Pakistan. Because women are more likely to be housebound and undernourished than men, they are disproportionately affected by this deficit.<sup>8</sup> Vitamin D3, the active form, is created when skin is exposed to sunshine. A higher rate of TB was seen in populations that got less sunlight. It has been shown that a lack of vitamin D raises the likelihood that you may get active TB.<sup>9</sup>

Vitamin D is known to influence the body's monocyte-macrophage system, which is important for warding off mycobacterium tuberculosis infection by blocking the intracellular reproduction and killing of the bacteria with the aid of antigen-presenting cells.<sup>10</sup> Vitamin D also has a role in the overexpression of the antimicrobial peptide cathelicidin, which enhances the intracellular M. tuberculosis killing capacity. Cathelicidin synthesis in reaction to macrophage receptor activation by M. tuberculosis antigen is reduced in vitamin D deficiency. Vitamin D3 supplements were studied for their potential to aid in the treatment of tuberculosis. Contacts of tuberculosis patients who received a single dosage of vitamin D had a greater increase in their in vitro immunity to Mycobacterium.<sup>11</sup>

Previous research<sup>12</sup> had limitations since they included people with cancer and hidden chronic illnesses. Vitamin D deficiency in tuberculosis patients will be investigated in this study, providing a new perspective from which to assess the potential benefits of vitamin D supplementation in the treatment of this disease.

## METHODS

After receiving approval from the hospital ethics committee and research department, total 132 patients (66 cases and 66 controls) from the August 2020 to January 2021 were include in this study who meet the inclusion criteria.

In this study, cases of newly diagnosed pulmonary tuberculosis were defined as those with age restrictions of 18 to 55 years, sputum assessment by microscopy or cultures, and both genders. The individuals in the control group were chosen from those who reported to our hospital's outpatient department for a standard medical checkup and were age- and sex-matched. Renal impairment, bone disease, cancer, undetected chronic illness, and recent surgery were excluded from the study. These patients had recently been diagnosed with tuberculosis but had not yet begun therapy. Their written

informed permission was obtained. Patients were divided into two groups depending on the selection criteria. Members of Group A were recently diagnosed cases of active tuberculosis who sought treatment at the medical center's outpatient clinic or inpatient hospital. Individuals in Group B served as a control group, and they were chosen at random from patients who came to our hospital's outpatient department for preventative care. The levels of 25 (OH) D3 were measured in a 0.2 cc venous blood sample. Each patient's results were recorded in a standard format using Performa. A pathologist confirmed all of the findings. Vitamin D deficiency was defined as a serum concentration of less than 25 ng/ml throughout the duration of the trial.

All the collected information of study variables was put into SPSS version 19.0 and analysed. Age and Vitamin D levels, have been shown by mean SD. Categorical variables, such as gender and vitamin D deficiency have been shown by frequency and percentage. The vitamin D deficiency in two groups has been compared using the Chi-square ( $\chi^2$ ) test. P value < 0.05 has been thought to be significant. Odd ratio >1 has been taken significant with 95% confidence interval. Stratification has been used to control the effects of things like age, BMI, gender, and smoking. Odd's ratio has been worked out after stratification.

## RESULTS

The patients' ages ranged from 18 to 55 years old, with a mean of 34.77±9.98. The majority of the patients (n=87, 65.9%) were in the 18–36 age range. There were 75 patients, or 56.8% women, and 57 men, for a male to female proportion of 1:1.3. With a mean BMI of 23.12 ± 2.82 kg/m<sup>2</sup>, the range of these individuals' BMIs was 18.5 kg/m<sup>2</sup> to 28.9 kg/m<sup>2</sup>. 49 patients (37.1%) smoked, as reported in Table 1.

**Table 1: Characteristics of the study sample at a baseline**

Variables	Characteristics	Study Sample n=132
Age	Mean ± SD	34.77 ± 9.98
	18-36 years	87 (65.9%)
	37-55 years	45 (34.1%)
Gender	Male	57 (43.2%)
	Female	75 (56.8%)
BMI (Kg/m <sup>2</sup> )	Mean ± SD	23.12 ± 2.82
	<20 Kg/m <sup>2</sup>	25 (18.9%)
	20-25 Kg/m <sup>2</sup>	72 (54.5%)
	>25 Kg/m <sup>2</sup>	35 (26.5%)
Smoking Status	Smoker	49 (37.1%)
	Non-Smoker	83 (62.9%)

As demonstrated in Table 2, both research groups were equivalent of mean BMI (p=0.576), age (p=0.952), gender (p=0.861), BMI (p=0.614), and smoking status (p=0.589).

**Table 2: Characteristics of the study sample of both groups**

Variables	Characteristics	Cases n=66	Controls n=66	P value
Age	Age (years)	34.82 ± 9.98	34.71 ± 10.06	0.952
	18-36 years	43 (65.2%)	44 (66.7%)	0.854
	37-55 years	23 (34.8%)	22 (33.3%)	
Gender	Male	29 (43.9%)	28 (42.4%)	0.861
	Female	37 (56.1%)	38 (57.6%)	
BMI	Mean ± SD	22.99 ± 2.83	23.26 ± 2.83	0.576
	<20 Kg/m <sup>2</sup>	13 (19.7%)	12 (18.2%)	0.614
	20-25 Kg/m <sup>2</sup>	38 (57.6%)	34 (51.5%)	
	>25 Kg/m <sup>2</sup>	15 (22.7%)	20 (30.3%)	
Smoking Status	Smoker	26 (39.4%)	23 (34.8%)	0.589
	Non-Smoker	40 (60.6%)	43 (65.2%)	
Vitamin D	Vitamin D level (ng/ml)	19.56 ± 6.64	23.72 ± 6.42	<0.001*

Chi-square ( $X^2$ ) and independent sample t-test results showed that the difference that was found was statistically significant.

As indicated in Table 3, patients with active tuberculosis had significantly lower serum vitamin D levels (19.56 ± 6.64 vs. 23.72 ± 6.42 ng/ml; p0.001) than controls.

**Table 3: Comparison of Vitamin D Deficiency between Cases and Controls**

Vitamin D Deficiency	Cases n=66	Controls n=66	P value	OR	95% CI
Yes	48 (72.7%)	26 (39.4%)	< 0.001*	4.10	1.97- 8.54
No	18 (27.3%)	40 (60.6%)			
Total	66 (100.0%)	66 (100.0%)			

Chi-square test, the difference between the observed and expected values was statistically significant, odds ratio, and 95% Confidence Interval

## DISCUSSION

Like other underdeveloped countries, vitamin D insufficiency is present in the asymptomatic Pakistani population. Patients with active tuberculosis have been documented to have vitamin D insufficiency. Existing studies may have been flawed due to selection bias; therefore, the current investigation was conducted to see if vitamin D insufficiency and active pulmonary TB are linked.<sup>13</sup>

Sixty-five percent of the patients were young adults between the ages of 18 and 36. Patients between the ages of 18 and 40 made up 67.6% of all tuberculous patients seen by Tariq *et al.* at Ayub Teaching Hospital in Abbottabad.<sup>17</sup> Saqib *et al.* (2011) found an identically high

prevalence of 79% in such Rawalpindi patients. Among patients in Ethiopia, the rate was found to be 72.8% by Tessema *et al.* (2017).<sup>18,19</sup>

The patients in this study had a mean age of 34.77 ± 9.98 years old when they participated. According to the findings of Mirza *et al.*, patients who sought treatment at the AFIP located in Rawalpindi, had a mean age of 34.08 ± 12.9 years (2015).<sup>14</sup> According to research carried out by Kamal *et al.* (2015), patients diagnosed with pulmonary tuberculosis in the Mansehra city all shared an identical mean age of 32.11 ± 9.1 years.<sup>15</sup> Wejse and colleagues also discovered that the typical age of patients with this condition in Sweden was 37.4 ± 13.7 years old.<sup>16</sup>

There were 57 male patients (43.2%) and 75 female patients (56.8%) in this study. Kamal *et al.* also found a female preponderance among tuberculosis patients in the Mansehra district. Patients at Ayub Teaching Hospital, Abbottabad, were more likely to be female, as was previously noted by Tariq *et al.*<sup>17</sup> Female preponderance was also documented by Dave *et al.* (2016) and Pho *et al.* (2012) among Indian TB patients.<sup>20,21</sup>

Patients' body mass indexes (BMIs) varied from 18.5 to 28.9, with a mean of 23.12 ± 2.82 Kg/m<sup>2</sup>, and 47 of them (37.1%) were regular smokers. Patients with this diagnosis who present to the Combined Military Hospital in Kharian have a comparable mean body mass index (BMI) of 23.62 ± 2.35 Kg/m<sup>2</sup>, as described by Iftikhar *et al.*<sup>22</sup>

Patients with active tuberculosis had a substantially lower serum vitamin D level than controls (19.56 ± 6.64 vs. 23.72 ± 6.42 ng/ml; p0.001). Furthermore, Iftikhar *et al.* found a significant difference between the mean serum vitamin D levels of tuberculosis patients (23.23 ± 6.81 ng/ml) and controls in the surrounding population (29.27 ± 8.89 ng/ml; p0.0001).<sup>22</sup> Sasidharan *et al.*<sup>23</sup> also found a significant difference (p0.005) between the mean serum vitamin D level of Indian tuberculous patients and controls (10.7 vs. 19.4ng/ml).

## CONCLUSION

A lower mean serum vitamin D level and a higher prevalence of vitamin D deficiency were found to be associated with active pulmonary tuberculosis, with an (OR) odds ratio of 4.1 supporting routine screening of these patients for vitamin D status to promptly identify and, consequently, monitor patients with vitamin D deficiency in subsequent clinical practice.

## LIMITATIONS

We did not take into account the influence of vitamin D supplementation on treatment result, which would have

further highlighted this link, and this is a major limitation of the current study.

## SUGGESTIONS / RECOMMENDATIONS

Future research should be appreciated on this topic.

## CONFLICT OF INTEREST / DISCLOSURE

None.

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