Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/q3408v34

ASSOCIATION OF VITAMIN D DEFICIENCY WITH TUBERCULOSIS IN ADULT PATIENTS REPORTING TO A TERTIARY CARE HOSPITAL

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Abstract
Background: Tuberculosis is a life threatening disease and lack of vitamin D has been linked to an increased risk of tuberculosis.
Objective: The aim of the current study was to explore the association of vitamin D deficiency with tuberculosis in adult patients.
Methodology: The current case control study was carried out at the Department of medicine, Bolan medical college/ Bolan medical complex hospital Quetta. The study duration was one year from July 2023 to August 2024 after taking permission from the ethical committee of the institute. A total of 52 individuals with lung infections were enrolled and 52 age and gender matched controls were also included. For the identification of tuberculosis the sputum of each individual was examine through the gene Xpert technology. Vitamin D insufficiency was diagnosed based on serum 25-hydroxvitamin D level <50 nmol/l. SPSS version 20 was used for analyzing the data.
Results: When comparing the mean vitamin D levels between the participants and controls, there was a statistically significant difference (with a $p<0.001$). It was shown that 18 (34.6%) controls and 49 participants (94%) had insufficient vitamin D. (95%, Odd's Ratio = 3.8) 0.001, with a $p<0.001$), CI corresponds to 2.423—5.999. MDR Tuberculosis participants had mean vitamin D level was 22.38 ± 16.60 nmol/l, although the variation was deemed insignificant ($p > 0.05$). Sensitive individuals with TB had mean levels of vitamin D in their serum of 18.55 ± 9.99 nmol/l.
Conclusion: Participants with recent tuberculosis diagnoses showed signs of severe vitamin D insufficiency. Although a link between vitamin D deficiency and TB has been reported, its causative function has not been demonstrated.

Key words: Association; Vitamin D deficiency: Tuberculosis

Introduction

A serious disease known as tuberculosis (TB) has long been a global public health concern and a recognized medical emergency in 1993. Approximately 1/3 of the global population suffers from tuberculosis.[1] Three million people worldwide die due to TB each year, out of an estimated 10 million cases. Ninety-five percent of the global burden of this illness falls on developing nations. Pakistan is home to 61% of all TB cases in the WHO's Eastern Mediterranean Region and is ranked fifth out of 2nations with the greatest TB burden. In 2012, the incidence and prevalence rates of tuberculosis (TB) were elevated at 231/100,000 and 376/100,000, respectively.[1] Pakistan is ranked fifth among the nations with the greatest number of incident tuberculosis cases in 2012 (0.3–0.5 million) and fourth among the twenty-seven high multidrug- resistant TB burden countries.[2] A number of lines of evidence have emerged in the last several years that point to a potential connection between vitamin D deficiency and tuberculosis.[3] It is thought that vitamin D (Vit D) has a significant role in macrophage activation & the consequent inhibition of tuberculosis development.[4] Insufficient amounts of vitamin D are a regular occurrence worldwide, particularly in developing countries. The cause of these low levels varies according to dietary fortification laws, demographic characteristics, geographic location, and season. Lack of vitamin D has been linked to an increased risk of TB.[5] A few studies have reported a correlation involving 25 hydroxyvitamin D levels and tuberculosis, one of which involved a Chinese participant.[6] Initially, research has shown asymptomatic vitamin D insufficiency (hidden hunger) in our country's healthy general population.[7] A cross-sectional research being conducted in Karachi shows that asymptomatic vitamin D insufficiency is frequent in Pakistan.[8] Pakistan was among the top five nations in 2011 for the highest number of tuberculosis cases.[9] Despite the high prevalence of TB and vitamin D insufficiency, there is a lack of research on the relationship between TB and vitamin D deficiency in the indigenous Pakistani population. There is little doubt that this case needs more investigation and careful examination to see whether there is any likely connection between the two illnesses. Therefore the current study was carried out to explore the Association of vitamin D deficiency with tuberculosis in adult patients reporting to a tertiary care hospital.

Methodology

The current case control study was carried out at the Department of medicine, Bolan medical college/ Bolan medical complex hospital Quetta. The study duration was one year from July 2023 to August 2024 after taking permission the ethical committee of the institute. A case of tuberculosis (TB) was defined as one in which a healthcare professional made the diagnosis and chose to administer a full course of tuberculosis therapy to an individual. Pregnant women, nursing mothers, people with abnormal serum calcium levels, renal and hepatic impairments, previous bone disease, malabsorption syndrome, and people taking drugs were excluded. Using the G Power 3.1.6 programme , the sample size (n) was determined to be 104 (case control ratio > 1:1) (effect size = 0.5, alpha error probability = 0.05, and power = 90 percentage).Through non-probability successive sampling from the outpatient department, 52 newly diagnosed non-smoking patients with pulmonary TB who had not yet begun anti-tuberculosis medication were chosen and categorized as cases. The Gene Xpert method was used to detect pulmonary tuberculosis. After testing negative for tuberculosis on clinical and radiological examination, 52 age and gender matched non-smoking controls were chosen from the general population. A questionnaire was given to each participants that including demographic features, job description, and taking of diet rich in vitamin D and exposure to sunshine. Each subject body mass was also evaluated. 5ml of venous blood was taken from each participant in plastic serum and placed in ice boxes and sent to the lab for examination. The blood samples were centrifuged to obtain serum. These samples were further verified by well trained pathologist. Serum vitamin D levels below 50 nmol/l have been classified as deficient, but levels above 50 nmol/l were declared appropriate.

Analysis of Data

SPSS version 20 was used for analyzing the data. For each quantitative variable, the mean and standard deviation were used to represent the outcomes. Percentages and frequency measurements

have been used for qualitative variables. Mann Whitney/Independent Samples T-test based on the kind of data and the distribution of the variables, the U test and the chi-square test were used, if applicable. A p-value less than 0.05 was regarded as statistically significant.

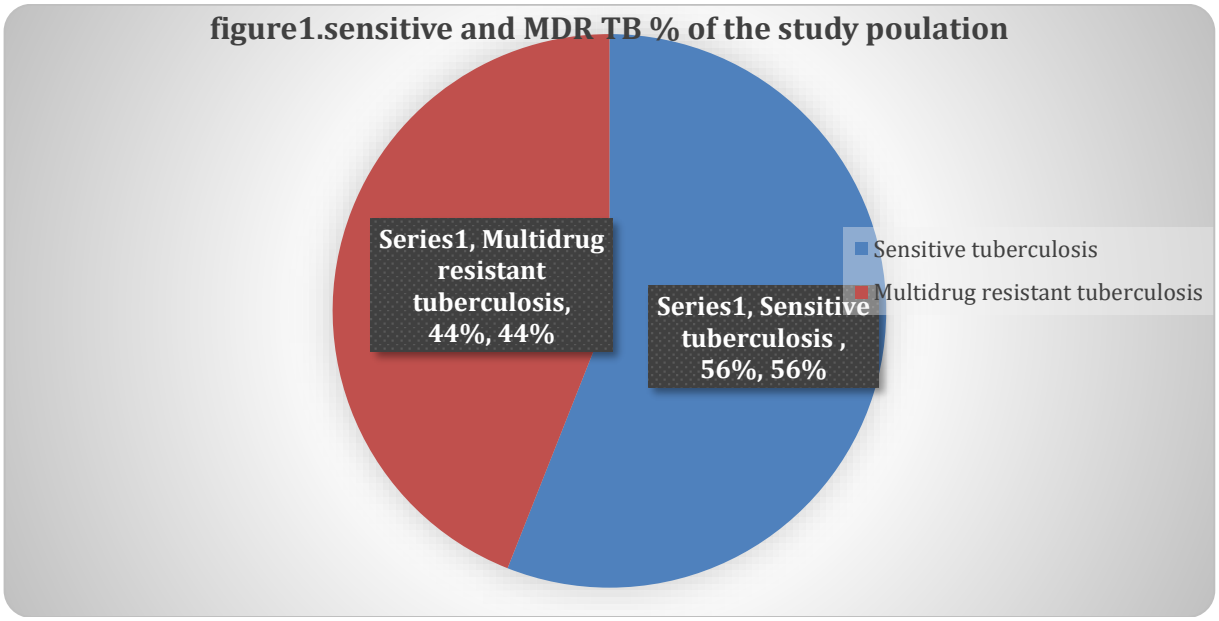
Results

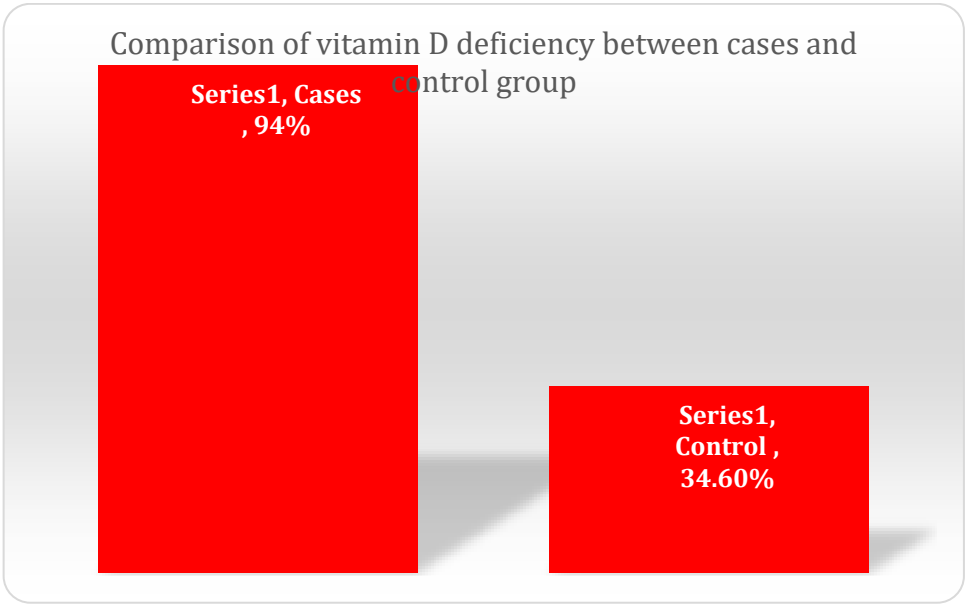
52 male and female matched controls (62% males and 38% women in each group) were compared to the 52 cases. The controls had a mean age of 38.41(14.12) [median (Interquartile range) =33.00 (28)] years, whereas the cases had a mean age of 39.48(14.21) [median (Interquartile range) =34.00 (27.00)] years. In terms of age ($p>0.05$) and gender ($p>0.05$), both groups were comparable. 32 (61.5%) of the actual cases and 33 (62.4%) of the controls were from urban regions, with the remaining controls being from rural areas (with a $p>0.05$). Vit D deficiency was discovered in 49 cases (94.2%) and 18 controls (34.6%) (With a $p<0.001$). The adjusted odds ratio (odds = 3.8, 95% confidence interval (CI) = 2.423—5.999, $p<0.001$) showed that those diagnosed with Tuberculosis had a 3.8-fold increased likelihood of having a vitamin D deficiency in comparison to the controls. When comparing individuals to the controls, it was discovered that the cases' mean serum vitamin D value was lower as described in **table 1.** The vitamin D levels of the women in the two groups were considerably lower than those of the men. Vitamin D insufficiency was seen in 19 out of Twenty (95% of them) women Tuberculosis victims as well as 30 out of 32 (93.5%) male Tuberculosis individuals (with a $p>0.05$). While vitamin D levels were lesser in female participants than in men, the difference was not statistically significant ($p > 0.05$). Through the use of gene Xpert, it was discovered that 29 out of 52 (56%) individuals suffering from tuberculosis had sensitive Tuberculosis and that 23 (44%) cases had Multidrug resistant tuberculosis in incident cases of tuberculosis as shown in **figure 1**. When comparing MDR people with tuberculosis to susceptible individuals with Tuberculosis , the mean blood vitamin D concentration was found to be lower; however, the difference was not statistically significant (with a $p>0.05$) **.** The average Body mass index for the study participants was 20.313 (3.273) kg/m2, whereas the controls had 24.683 (2.414) kg/m2 ($p<0.001$). The mean BMI for individuals with a vitamin D deficit (<50 nmol/l) was 20.314 (3.324) kg/m2, whereas the mean BMI for persons with appropriate blood vitamin D levels (>50 nmol/l) was 20.289 (2.818) kg/m 2 ($p>0.05$). In sensitive TB cases, the mean (Standard deviation) Body mass index was 20.629 (3.755) kg/m2, but in Multidrug resistant tuberculosis cases, the value was 20.062 (2.879) kg/m2 (with a $p>0.05$).**Table 1)**

Table 1.The research group's clinical and demographic features

Features	Measurement	**Cases**	**Controls**	**Value of P**
Vitamin D (Nanomoles / liter)	Mean (standard deviation)	20.67 (14.06	57.91(18.19)	$< 0.001^{M}$
	Interquartile range (Median)	16.26 (12.97)	65.50 (29.0)	
Deficiency of vitamin D	N (%)	49 (94.20)	18 (34.6)	$< 0.001^{C}$
Men	Mean Vitamin D (standard deviation)	21.29 (15.72)	62.96 (15.71	$< 0.001^{M}$
	Median Vitamin D (Interquartile range)	16.80 (13.31)	68.95(21.51)	
Women	Mean Vitamin D (standard deviation)	19.72 (11.22)	49.84 (19.35)	$< 0.001^{M}$
	Median Vitamin D (Interquartile range)	15.65 (11.59)	48.95 (31.88)	

M Mann Whitney U test, C Chi Square test





Discussion

Vitamin D is crucial for both inhibiting the development of mycobacterium and activating macrophages. Numerous biological investigations aimed at identifying the impact of vitamin D on the body's immune system have demonstrated that this vitamin plays a crucial role in preventing the growth of Mycobacterium tuberculosis and the subsequent development of a widespread immune system response.[10-11] Similarly, insufficient blood Vitamin D inhibits the generation of microbe-killing cathelicidin upon the activation of TLRS with tubercle bacillus molecules.[12] Nonetheless, there is ongoing debate over the in vivo correlation between vitamin D levels and Tuberculosis. In our research, we revealed that both male and female individuals with Tuberculosis had significant levels of vitamin D deficiency. Only people suffering from it who had not yet started therapy were included since ant- tuberculosis chemotherapy can reduce serum Vitamin D levels. More than 20 years ago, a probable correlation between vitamin D & Tuberculosis was first revealed.[13]

However, different results have been obtained from advance research. Studies on African immigrants residing in Australia, [14] have demonstrated that tuberculosis people had lower 25 (OH) D levels and a greater incidence of vitamin D insufficiency than non-Tuberculosis individuals. African immigrants living in Australia, for instance, were shown to have significantly lower serum concentrations of vitamin D than inhabitants of London who did not have it, whether it was latent or active. It's possible

that a drop in blood Vitamin D levels triggers latent tuberculosis activation and impairs cell-mediated immunity, but it's also conceivable that tuberculosis itself causes low serum Vitamin D levels.[15] one of the risk factors for it is smoking. There is no proof that smoking directly affects vitamin D absorption, despite the fact that vitamin D is necessary for calcium absorption, which is impeded by smoking. Additionally, there was no discernible correlation between body mass index and changes in vitamin D levels in this investigation. Since a low body mass index is a common feature in Tubercle bacillus infected individuals and is also linked to vitamin D insufficiency, low body mass index is a significant confounder in the relationship between low vitamin D and tuberculosis. Since diabetic mellitus is becoming more common worldwide and since persons with this diseases are approximately four times prone than those without Diabetes to develop clinically severe chronic kidney disease [16]. Low vitamin D levels in peoples with tuberculosis need to be further investigated. Furthermore, compared to those with no kidney disease, people with chronic kidney disease or dialysis dependents are far more probable to experience low vitamin D levels.[17] The increased number of people with CKD from underlying causes like diabetes mellitus may require early attention to their body Vitamin D levels to reduce the risk of active tuberculosis. The prevalence of TB is high in CKD individuals in part because of impaired cell-mediated immunity, but if low serum Vitamin D levels also put it at risk to tuberculosis. Furthermore, this study found that around half of the normal female population had vitamin D insufficiency. This is highly important and raises concerns for healthcare since a sizable portion of the healthy population may not be receiving the advantages of vitamin D. The majority of homebound females, inferior nutritional status compared to males, the stigma surrounding tuberculosis (TB), which deters women from searching for early medical attention, vitamin D deficiency brought on by inadequate dietary intake and not enough exposure to sunlight as a result of substandard housing and the custom of wearing cloaked are all potential explanations for the female preponderance. Nonetheless, the frequency of vitamin D insufficiency was significantly lower than that of a different Karachi research.[8] Similar to this, the prevalence of vitamin D insufficiency in asymptomatic females was significantly lower in this study than in the premenopausal women's bone health survey conducted in Karachi in by Mansoor et al.[18] when 82.8% of the women had vitamin D deficiency. The discrepancy in the results might be explained by the smaller size, different cut off point of vitamin D deficient level, darker skin pigmentation in women of Karachi, and betal chewing practice.[19] According to the current research, vitamin D may help Tuberculosis individuals recover more quickly. The findings of Martineau et al., which showed that a single dosage of vitamin D enhanced immunity against Microbes in vitro in associations with people with TB, corroborate this discovery.[20]

Conclusion

Participants with recent tuberculosis diagnoses showed signs of severe vitamin D insufficiency. Although a link between vitamin D deficiency and TB has been reported, its causative function has not been demonstrated.

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