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FREQUENCY OF VITAMIN D DEFICIENCY AMONG ADULT TUBERCULOSIS PATIENTS AT AYUB TEACHING HOSPITAL ABBOTTABAD

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ABSTRACT

Introduction: Tuberculosis infects more than 1 in 3 individuals worldwide. Although the basic mechanism involved is not known but Vitamin D deficiency is associated with increased risk of getting infected with *Mycobacterium tuberculosis*. This study was conducted to determine the incidence of Vitamin D deficiency among adult tuberculosis patients visiting the OPD of Ayub Teaching Hospital, Abbottabad.

Materials & Methods: This cross sectional study was conducted in Ayub Teaching Hospital, Abbottabad, from January to June 2015 on 147 patients after approval from ethical committee; data were collected from the Medical Outpatients Department (OPD) through convenience sampling from consecutive patients after taking written informed consent from them. Blood specimens were obtained under strict aseptic technique and were immediately sent to standard laboratory to detect Vitamin D deficiency. Data were analyzed for descriptive statistics using SPSS, 20; the Chi Square test was used for comparisons of frequencies keeping $p \leq 0.05$ as significant.

Results: The ages of tuberculosis patients were from 18 to 65 years, with 83% between the ages of 31-60 years (mean age 44.23±11.65 years). Vitamin D deficiency was observed in 62(42.18%) patients, equally distributed by gender. There was no association with age, gender, site of tuberculosis, or dietary intake of Vitamin D rich foods.

Conclusion: Vitamin D deficiency is a frequent finding in patients with tuberculosis and occurs irrespective of age, gender, site of tuberculosis, or dietary intake of Vitamin D rich foods.

Keywords: Vitamin D; Pulmonary Tuberculosis; *Mycobacterium tuberculosis*; Extra-Pulmonary Tuberculosis.

The authors declared no conflict of interest. All authors contributed substantially to the planning of research (SM), data collection (IQ, FN), data analysis (SM, IQ) and write-up of the article (SM, FN) and agreed to be accountable for all aspects of the work.

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INTRODUCTION

Pakistan faces major health problems with Tuberculosis (TB) and is placed on 6th number worldwide in terms of contributing to the global burden of tuberculosis patients. According to World Health Statistics, 181 cases of tuberculosis are reported per100,000 population.[1]

According to WHO guidelines,[2] productive cough for more than 2 weeks, which may or may not be accompanied by other respiratory symptoms such as shortness of breath, chest pains, hemoptysis and/or constitutional symptoms (loss of appetite, weight loss, fever, night sweats, and fatigue) is suggestive of tuberculosis. Smear examination for AFB bacilli and chest X-ray suggestive for active tuberculosis (cavities, soft shadowing) confirms the diagnosis. When tuberculosis involves organs other than lungs such as lymph nodes, pleura, bones, joints, brain, skin, meninges, it is referred to as extra-pulmonary TB. Diagnosis of tuberculosis is made either by evidence of at

least one specimen confirmed with *Mycobacterium tuberculosis* or histological features suggestive of tuberculosis or even strong clinical evidence of extra-pulmonary involvement of tuberculosis.[2]

Although *Mycobacterium tuberculosis* is an intracellular pathogen residing within macrophages, yet these macrophages are the first line of defense against it and for proper functioning of the macrophages against *Mycobacterium tuberculosis*, Vitamin D plays significant role by boosting and activating the immune system through its active metabolite Vitamin D3 [1,25(OH)D3] that is thought to have a role in helping the macrophages inhibit the growth of *Mycobacterium tuberculosis*. Therefore Vitamin D deficiency causes an increased risk of developing tuberculosis.[3,4] Other respiratory diseases may also have decreased levels of Vitamin D. TB household contacts should be prophylactically given Vitamin D.[4]

BCG infection *in vitro* is shown to have been fought against well by the enhanced ability of the *ex vivo* macrophages receiving single oral dose of 2.5mg of Vitamin D.[5,6]

In a study conducted in a general hospital of Malawi,[7] 42.2% of patients reporting with tuberculosis also had Vitamin D deficiency; while a study from Uganda[8] showed 44.2% cases of Vitamin D deficiency in tuberculosis patients. Levels of serum 25-hydroxyvitamin D [25(OH)D] <75nmol/l was considered as hypovitaminosis, <50nmol/l was considered as Vitamin D deficiency and <25nmol/l was considered as severe Vitamin D deficiency in both these studies.

The objective of this pilot study was to determine the magnitude of Vitamin D deficiency in tuberculosis patients reporting to the Medical OPD of Ayub Teaching Hospital, Abbottabad; it would form the basis for further studies to determine the association between tuberculosis and Vitamin D deficiency in this population.

MATERIALS & METHODS

The cross sectional study was conducted in the Medical OPD of Ayub Teaching Hospital, Abbottabad from January to June, 2015. Non probability consecutive sampling was employed based on a calculated sample size. All patients with newly diagnosed tuberculosis aged 18-65 years including patients who had taken Anti Tuberculous Therapy (ATT) for less than two weeks were included in the study. Confounders such as patients taking anti-convulsants, multivitamins, retroviral therapy and those with chronic renal failure were excluded. Vitamin D deficiency was taken as serum [25(OH)D] level <50nmol/l and Pulmonary Tuberculosis as patients with suggestive history, smear positive sputum for AFB and Chest X-ray findings suggestive of active tuberculosis (cavities, soft shadowing); and when Tuberculosis involved other organs such as genitourinary tract, pleura, abdomen, skin, bones, joints, meninges and lymph nodes, referred to as extra-pulmonary tuberculosis.

Approval from hospital ethical committee was taken prior to conducting the study. Informed consents were taken from the patients prior to data collection.

All baseline characteristics like age, sex, site of tuberculosis, dietary history (weekly intake of food with high concentrations of Vitamin D like fish, organ meat and eggs) were noted down on a Performa. Blood sampling was done to detect the levels of serum [25(OH)D] concentration. Values were noted down on the Performa. The levels of Vitamin D were classified as normal, hypovitaminosis, Vitamin D deficiency, and severe Vitamin D deficiency.

Data were entered into SPSS 20 and analyzed for descriptive statistics. Data were stratified

by age and sex. The Chi-square test was used to determine association between Vitamin D deficiency and independent variables keeping significance level as p≤0.05.

RESULTS

Out of 147 Tuberculosis patients, 80 were male and 67 female (1.24:1). The mean age of patients was 44.23±11.65 years; the age groups of patients are shown in Table 1; age 30 or less (20 patients, 13.6%), ages between 31-45 years (62 patients, 42.23%), ages between 46-60 (60 patients, 40.8%) and age above 60 years (5 patients, 3.4%).

Table 1: Demographic data of patients (n=147).

#	Variables	Frequency	Percent
1.	**Gender**		
	Male	80	54.4
	Female	67	45.6
2.	**Age Groups (years)**		
	≤ 30	20	13.6
	31- 45	62	42.2
	46- 60	60	40.8
	> 61	05	03.4
Total		**147**	**100.0**

Vitamin D deficiency (Table 2) was present in 62(42.18%) patients while 85(57.82%) did not have Vitamin D deficiency. Age-wise distribution of Vitamin D deficiency (Table 2) showed approximately equal distribution among the different age groups (p=0.686). However the majority of patients were in the age groups of 31-45 years (45.2%) and 46-60 years (41.9%). Gender distribution showed an equal frequency of Vitamin D deficiency in males and female patients (Table 2), but the difference from non-deficient patients was not statistically significant (p=0.226).

Table 2: Age and Gender Distribution of Vitamin D Deficiency (n=147).

Variables	Vitamin D deficiency		Total	p value
	Yes	No		
Age (in years)				
≤ 30	06 (09.7)	14 (16.5)	20 (13.6)	
31 - 45	28 (45.2)	34 (40.0)	62 (42.2)	0.686
46 - 60	26 (41.9)	34 (40.0)	60 (40.8)	
≥ 61	02 (03.2)	03 (03.5)	05 (03.4)	
Gender				
Male	31 (50.0)	49 (57.6)	80 (54.4)	0.226
Female	31 (50.0)	36 (42.4)	67 (45.6)	
Total	**62 (42.2)**	**85 (57.8)**	**147 (100.0)**	

Vitamin D deficiency was also stratified by site of tuberculosis and dietary history of Vitamin D intake (Table 3), but showed no significant differences (p=0.101 and 0.545 respectively).

Table 3: Distribution of Vitamin D deficiency by Site of tuberculosis and dietary Vitamin D Intake (n=147).

Variables	Vitamin D deficiency			p value
	Yes	No	Total	
Site of Tuberculosis				
Pulmonary	30 (49.2)	31 (50.8)	61 (41.5)	0.101
Extra pulmonary	32 (37.2)	54 (62.8)	86 (59.5)	
Dietary history				
Intake	28 (42.4)	38 (57.6)	66 (44.9)	0.545
No Intake	34 (42.0)	47 (58.0)	81 (55.1)	
Total	**62 (42.2)**	**85 (57.8)**	**147 (100.0)**	

DISCUSSION

There is an utmost need to better understand the underlying mechanisms for the progression of the disease so that further better strategies could be developed to eradicate TB from the world. Both innate[9] and adaptive[10] immunity is required for protection against infection from Mycobacterium tuberculosis. Mycobacterium tuberculosis[8] has infected 1/3rd of the population globally, 95% cases occurring in developing countries, out of which highest incidence rates occur in South East Asia and Sub Saharan Africa. According to WHO statistics,[11] Pakistan plays a significant role in contribution towards tuberculosis in the Eastern Mediterranean region and is placed on 6th number out of 22 countries globally in the category of high TB risk countries by contributing 43% of the disease.

Growth and spread of Mycobacterium tuberculosis is restricted by the vigilant action of the macrophages.[12-13] Worldwide, the Vitamin D deficiency is largely contributed by the developing countries and factors like food fortification, demographic features, geographic location and seasonal variations have important role. Vitamin D deficiency is considered to be one of the very significant risk factors for infection with Tuberculosis.[13]

It has been shown by several studies done for biological purposes that Vitamin D plays a significant role in immunity against *Mycobacterium tuberculosis*.[13,14]

Recently, it was stated that very low D3 levels are associated with both primary infection and reactivation by Mycobacterium tuberculosis.[14]

On a contrary note, there were some studies that showed higher levels[15,16] of Vitamin D in tuberculous patients than their control subjects.

A hypothesis exists regarding the dual relationship between Vitamin D deficiency and tuberculosis, so that both can cause each other but the evidence of Vitamin D deficiency causing tuberculosis is stronger because of requirement of Vitamin D levels to activate macrophage functions against Mycobacterium tuberculosis and boost up the immunity system. Additionally, Cathelicidin which is bactericidal in action has impaired production in the setting of decreased Vitamin D levels.[16-18]

Another mechanism suggests that when there are mutations in Vitamin D receptors, it causes further susceptibility to tuberculous infection.[14] Studies also suggest that Vitamin D deficient tuberculosis patients have poor outcome with anti-tuberculosis therapy.[19]

CONCLUSION

Vitamin D deficiency is frequently present in tuberculosis patients, irrespective of age, gender, site of tuberculosis, or dietary intake of Vitamin D rich foods.

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