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ORIGINAL ARTICLE

Vitamin D Status in Patients with Pulmonary Tuberculosis: A Teaching Hospital Based Study

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ABSTRACT:

Background: This study was designed to determine the level of vitamin D in patients with pulmonary tuberculosis. **Methods:** We conducted a cross sectional study on 300 subjects (150 newly diagnosed pulmonary tuberculosis and 150healthy controls) was selected through non-probability purposive sampling according to inclusion and exclusion criteria. **Results:** The mean 25(OH) D level is 22.26±10.03in cases and 32.3±12.41in the controls. The difference between themeans of the cases and controls were statistically significant p = 0.002 (p < 0.05). **Conclusion:** Vitamin D deficiency is higher in patients with tuberculosis than healthy individuals. Vitamin D supplementation is warranted for patients of pulmonary tuberculosis.

Keywords: Vitamin D Deficiency, 25-hydroxyvitamin D, Mycobacterium Tuberculosis, Epidemiology, Pulmonary.

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INTRODUCTION

Tuberculosis (TB) is a major public health problem and cause of mortality globally. TB caused mainly by M. tuberculosis that most often affects lungs leading to pulmonary tuberculosis. The host susceptibility to tuberculosis infection depends on a complex interaction between host, bacteria and several factors such as poverty, malnutrition, overcrowding, and exposure to other pathogens. Previously, it has been estimated that about one-third of the world's population is infected with latent M. tuberculosis, and only 10% of which will develop the active disease. Approximately more than 95% of the estimated cases and deaths due to tuberculosis Vitamin D (Vit D) is synthesized in the skin during exposure to ultraviolet light and is also available in the diet, principally from fish. Besides having a crucial role in calcium homeostasis and mineral metabolism in bone, it is known to be involved in biological functions like cell differentiation, inhibition of cell growth and immunomodulation occur in low-income countries. Deficiency of vitamin D (25-hydroxycholecalciferol) has long been implicated inactivation of tuberculosis (TB).[1] Serum levels of vitamin D inTB patients are lower than in healthy controls.[2,3] Paradoxically, prolonged treatment of TB also causes a decline in serum vitamin D levels[2]. Several studies have suggested that vitamin D is a potent immuno modulator of innate immune responses by acting as a cofactor for induction of anti mycobacterial activity.[4-6] Approximately 95% of tuberculosis(TB) cases occur in developing countries with highest rates (100/100,000 or higher) observed in sub-Saharan Africa, India, China, andthe islands of Southeast Asia. Vitamin D is reportedof having potential role in immunomodulation.[7-11]Vitamin-D is an important effecter of macrophage functions and thus could behaving an important role in limiting growth or survival of intracellular pathogens like Mycobacterium Tuberculosis, Salmonella and all viruses.[9-12] The role of Vitamin D in preventing several malignancies is increasingly being recognized. Recent evidences link vitamin Ddeficiency to diseases like Diabetes, Hypertension, infections, autoimmune disorders and cancer.[13,14] Vitamin D modifies gene expression in the tissues where it acts by binding to specific receptors vitamin D binding receptors (VDR) and has several known actions and several more hither to unknown to us.[9-11] Present study was conducted to determine the occurrence and associated factors of vitamin D deficiency in pulmonary tuberculosis patients compared to community controls

MATERIALS AN DMETHODS

This cross-sectional study was conducted in Department of tuberculosis and respiratory medicine, Deccan College of Medical Sciences, Hyderabad. Total of 300subjects (150 newly diagnosed pulmonary tuberculosis and 150 healthy controls) was selected through non-probability purposive sampling according to inclusion and exclusion criteria. Informed consent was taken from all the study subjects. Newly diagnosed TB cases were includedin the study with age and sex matched apparently healthy controls. A New case of TB is defined as apatient who has never had treatment for TB or has taken anti-tuberculosis treatment(ATT) for less than1 month duration as per RNTCP guidelines. The cases were diagnosed based on clinical features, chest x-

ray, sputum smear examination, CBNAAT, FNAC, USG, CSF analysis, pleural and ascetic fluid study. Patients with apparently normal nutrition were selected to exclude the effect of malnutrition consequent to TB on vitamin D level. Children and patients with multi drug-resistant TB were not included in the study. Patients with chronic obstructive pulmonary disease (COPD), interstitial lung disease(ILD), active diarrhoea, history suggestive of mal absorption, pre-existing liver or renal diseases, human immune deficiency virus(HIV) infection, diabetes mellitus, osteoporosis, cytotoxic and immune suppressive drug treatment, malignancy were excluded from the study.

BIOCHEMICAL ANALYSIS

An overnight fast 5 ml of venous blood sample was drawn from ante-cubital vein. The blood was centrifuged at 4000 rpm for ten minutes and serumobtained was frozen at -20oC. The serum was used for estimation of blood 25-hydroxy vitamin D3. The vitamin D3 was measured by ADVIA Centaur CP System for estimation of 25-OHD3 tem from bloods era. The normal, insufficiency and deficiency of Vitamin D3 were defined as; normal levels (>30ng/dl), vitamin D3 insufficiency (20-30 ng/dl)and vitamin D3 deficiency (<20ng/dl). Study was approved by the ethics committee of the institute. The data was recorded on a pre-structured proforma.

STATISTICAL ANALYSIS

All values were expressed as mean ± S.D. Data was analyzed on SPSS version18 Continuous and categorical variables were analyzed by student'st-age group. Test and chi square test respectively. The significant p-value was taken at ≤ 0.05.[Table 1].

RESULTS

The baseline characteristics ofstudy population are shown in table 2. Mean ±S.Dage of cases and control were 36.0±4.2 and 34±5.4years respectively. The obesity, BMI, smoking habit and chest x ray showing cavitations are shown in[Table 2]. Significant differences were observed for the obesity and smoking p-value 0.035 and 0.036respectively. Chest x ray revealed cavitary in 37(34.8%) of cases. Hemoglobin, RBC counts and Platelet counts revealed statistically significant difference between cases and controls. Low normal hemoglobin values were observed in most of study subjects in general and pulmonary tuberculosis patients in particular. Serum alkaline phosphatase, serum calcium and serum phosphate showed significant differences. 25 (OH) D levels were estimated from each subject in both cases and controls group and the mean value were calculated. Among the cases, 51 patients werefound to have Vitamin D deficient and 24 patientshad normal levels whereas among the controls, 19subjects had Vitamin D deficient and 56subjects had normal levels.

Table1: Age Distribution of Subjects in both Cases and Controls

Age in Years	Cases	Controls
<15	4	12
15-30	24	20
30-45	50	48
45-60	64	66
>60	8	4

Table 2: Baseline characteristics of laboratory findings

Variables	Cases	Controls	p-value
Ageinyear	38.0±4.2	36±5.4	0.04
BMI(kg/m2)	30±1.04	27±4.02	0.06
Obesity	29(%)	48(%)	0.025
Smokers	90(30%)	42(0.14%)	0.014
ChestX-ray cavity	74(24.66%)		
Hemoglobin(g/dl)	11.4±1.06	13.2±3.06	0.012
RBCcounts (x109µl-1)	3.6±2.2	4.4±3.06	0.024
WBCcounts(µl-1)	7686±148.2	7048±124.2	0.12
Platelets(x109µl-1)	3.6±1.01	3.4±1.06	0.06
Erythrocyte sedimentation rate	46.2±12.4	8.4±3.6	0.001
Alkaline phosphatase (iu)	104.2±4.04	92.6±8.04	0.001
Serumcalcium (mg/dl)	7.6±4.8	8.6±3.04	0.001
Serumphosphate (mg/dl)	2.4±1.00	2.8±0.2	0.07

Table 3: Distribution of 25(OH) D levels in cases andcontrols

Variables	Cases	Controls
Normal	48 (32%)	112
Deficient	102 (68%)	38

The study included 150 newly diagnosed TB cases and 150 age and sex matched healthy controls. Majority of the patients were in the 30 to 60year.

Table 4: Distribution of 25(OH) D levels in cases andcontrols

Variables	Cases	Controls
Vitamin D Level	22.26±10.03	32.3±12.41

Statistically significant (p<0.05)

The mean 25(OH) D level is 22.26±10.03 in cases and 32.3±12.41 in the controls. The difference between the means of the cases and controls were statistically significant p = 0.002 (p < 0.05). Our study confirmed a high prevalence of vitamin D deficiency, 68% in patients with TB with significant correlation compared to2 5.33% in the healthy controls. Vitamin D plays an important role in macro phage activation to restrict growth of my cobacterium. Several biological studies to detect effects of Vitamin D on immune system of the body show that Vitamin D has a definitive role in suppression of proliferation of Mycobacterium TB and generalized inflammatory response produced secondary to it.[16,17] Similarly, on triggering of toll-like receptors by molecules of the tubercle bacillus, the production of microbe- killing cathelicid in is impaired in the absence of adequate serum Vitamin D.[18] However in-vivo association between Vitamin D and tuberculosis is still a debatable issue. In this study, we found that Vitamin D insufficiency, asassessed by 25[OH]2 D3 level, was significant in patients with TB, both in men and women.[19] Asanti-tuberculosis chemotherapy can lower serum Vitamin D levels, so only those of tuberculosis patients were included who were yet to commence treatment.

Vitamin D has received attention as an important field of research in recent years. Many randomized controlled trials are done and going on to enlighten the association of vitamin D with various diseases with conflicting results. Vitamin D plays an important immune modulatory role in both innate and adaptive immunity. A meta-analysis of variousstudies has shown two-fold increased risk of active TB states in individuals with vitamin D deficiency.[20] Sasidharan PK etal from India conducted a study that demonstrated significant vitamin D deficiency in patients with active tuberculosis.[21] A study done by B Yuvaraj et alevidenced the association of decreased vitamin D levels with an increases putum AFB load in patients with tuberculosis.[22] A study conducted on Indian children within trathoracic tuberculosis by Khandelwal et al showed that majority of the children demonstrated low serum 25-hydroxy vitamin D levels.[23] A cohort study conducted in Pakistan found that vitamin D deficiency is associated with progression of latent TB to active disease in healthy household contacts.[24] A study done in China by Wei-Wei Gao et al found that patients with pulmonary tuberculosis had lower 1, 25-dihydroxy vitamin D concentrations than the healthy controls.[25] A study done on adult TB patients in Vietnam by Ho-Pham et al showed the prevalence of vitamin D deficiency in 35.4 and 45.3 percent of males and females respectively.[26] Nursyam et al showed that additional vitamin Dtherapy with ATT resulted in faster sputum smear conversion and radiological improvement in TBpatients whereas a study conducted by Marineau etal showed that vitamin D supplementation did not significantly reduce the time to sputum culture conversion.[27,28] Kibirige et al[29] conducted a study on 260 hospitalized adults with a confirmed diagnosis of TB. The serum concentrations of 25-hydroxyvitamin D or 25 (OH) D were determined by an electro chemilumniscence immune assay. Vitamin D deficiency, vitamin D insufficiency, severe and very severe vitamin D deficiency were defined as serum 25(OH) D concentrations of ≤ 20 ng/ml, 21–29 ng/ml, < 10 ng/ml and <5 ng/ml respectively. Results showed that majority of the study participants were males (146, 56.2%) and < 35 years (154, 59.2%). The mean age ± SD was 34.7 ± 9.5 years. Two hundred eight (80%) patients were HIV co-infected with a median CD4 count of 68 cells/mm3 (IQR: 17–165). The prevalence of vitamin D deficiency, vitamin D insufficiency, severe and very severe vitamin D deficiency among the hospitalized adult tuberculosis patients was 44.2%, 23.5%, 13.5% and 4.2% respectively. The median (IQR) vitamin D concentration in ng/ml was 22.55 (14.59-33.31). Vitamin D deficiency was more prevalent in patients with hypoalbuminemia (97.4%), anemia (86.1%), HIV co-infected patients with CD4 count <200cells/mm3 (83.2%) and hypocalcemia corrected for serum albumin levels (67%).Authors as accordance to our study also concluded that vitamin D deficiency is very common among hospitalized adult tuberculosis patients especially in patients with hypo albuminemia, anemia, HIV co-infected patients with CD4 count <200cells/mm3 and hypocalcemia corrected for serum albumin levels.

This cross-sectional study had some limitations. The sample size was not large enough; however, all the newly diagnosed patients were studied in one year. Furthermore, dietary intake, clothing coverage, the seasons' effects, and residences in the urban or rural were not considered

CONCLUSION

These findings suggest that, the patients with pulmonary tuberculosis are significantly Vitamin D deficient as compared to healthy controls. Vitamin D supplementation is warranted for patients of pulmonary tuberculosis.

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