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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 150 subjects (75 newly diagnosed pulmonary tuberculosis and 75 healthy controls) was selected through non-probability purposive sampling according to inclusion and exclusion criteria. **Results:** The mean 25(OH) D level is 24.46±12.03 in cases and 36.3 ±13.41 in the controls. The difference between the means of the cases and controls were statistically significant p = 0.002 (p < 0.05). **Conclusion:** 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.

Keywords: Pulmonary Tuberculosis and Vitamin D Deficiency.

INTRODUCTION

Deficiency of vitamin D (25-hydroxycholecalciferol) has long been implicated in activation of tuberculosis (TB).[1] Serum levels of vitamin D in TB 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 immunomodulator of innate immune responses by acting as a cofactor for induction of antimycobacterial 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, and the islands of Southeast Asia. Vitamin D is reported of having potential role in immunomodulation.[7-11] Vitamin-D is an important effecter of macrophage functions and thus could be having 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 D deficiency 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 hitherto unknown to us.[9-11] Only few studies on the role of vitamin D in tuberculosis have been done in Asian populations. There is paucity of literature addressing this issue in Indian population as well. This study was conducted to determine the level of vitamin D in patients with pulmonary tuberculosis.

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MATERIALS AND METHODS

This cross-sectional study was conducted in Department of Pulmonary Medicine and Paediatrics in K D Medical College & Hospital, Mathura, India during the period from March 2017 to April 2018. Total of 150 subjects (75 newly diagnosed pulmonary tuberculosis and 75 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 included in the study with age and sex matched apparently healthy controls. A New case of TB is defined as a patient who has never had treatment for TB or has taken anti-tuberculosis treatment (ATT) for less than 1 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 ascitic 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 multidrug-resistant TB were not included in the study. Patients with chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD), active diarrhoea, history suggestive of malabsorption, pre-existing liver or renal diseases, human immunodeficiency virus (HIV) infection, diabetes mellitus, osteoporosis, cytotoxic and immunosuppressive 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 serum obtained was frozen at -20oC. The serum was used for estimation of blood 25 -hydroxyvitamin D3. The vitamin D3 was measured by ADVIA Centaur CP System for estimation of 25-OHD3 tem from blood sera. 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 version 18 Continuous and categorical variables were analyzed by student's t-test and chi square test respectively. The significant p-value was taken at ≤ 0.05.

RESULTS & DISCUSSION

Table 1: Age Distribution of Subjects in both Cases and Controls

Age in Years	Cases	Controls
<15	2	6
15-30	12	10
30-45	25	24
45-60	32	33
>60	4	2

Table 2: Baseline characteristics of laboratory findings

Variables	Cases	Controls	p-value
Age in year	36.0±4.2	34±5.4	0.06
BMI (kg/m2)	28±2.04	25±4.02	0.08
Obesity	27(%)	46 (%)	0.035
Smokers	45 (41.9%)	21 (23.7%)	0.036
Chest X-ray cavity	37 (34.8%)		
Hemoglobin (g/dl)	11.2±2.06	13±4.06	0.021
RBC counts (x109 µl-1)	3.7±2.4	4.2±4.06	0.032
WBC counts (µl-1)	7785±158.2	7238±154.2	0.12
Platelets (x109 µl-1)	3.4±2.01	3.9±2.06	0.07
Erythrocyte sedimentation rate	47.2±14.6	8.±3.7	0.001
Alkaline phosphatase(iu)	107.3±6.04	94.7±10.03	0.001
Serum calcium (mg/dl)	7.8±4.9	8.7±3.07	0.001
Serum phosphate (mg/dl)	2.6±1.02	2.9±0.2	0.07

The study included 75 newly diagnosed TB cases and 75 age and sex matched healthy controls. Majority of the patients were in the 30 to 60 years age group [Table 1]. The baseline characteristics of study population are shown in table 2. Mean ±S.D age of cases and control were 36.0±4.2 and 34±5.4 years 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 0.036 respectively. 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 were found to have Vitamin D deficient and 24 patients had normal levels whereas among the controls, 19 subjects had Vitamin D deficient and 56 subjects had normal levels.

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

Variables	Cases	Controls
Normal	24(32%)	56(74.66%)
Deficient	51(68%)	19(25.33%)

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

Variables	Cases	Controls
Vitamin D Level	24.46±12.03	36.3 ±13.41

Statistically significant (p<0.05)

The mean 25(OH) D level is 24.46±12.03 in cases and 36.3 ±13.41 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 to 25.33% in the healthy controls. Vitamin D plays an important role in macrophage activation to restrict growth of mycobacterium. 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 cathelicidin 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, as assessed by 25[OH]2 D3 level, was significant in patients with TB, both in men and women.[19] As anti-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 randomised 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 immunomodulatory role in both innate and adaptive immunity. A meta-analysis of various studies has shown two-fold increased risk of active TB states in individuals with vitamin D deficiency.[20] Sasidharan PK et al from India conducted a study that demonstrated significant vitamin D deficiency in patients with active tuberculosis.[21] A study done by B Yuvaraj et al evidenced the association of decreased vitamin D levels with an increase sputum AFB load in patients with tuberculosis.[22] A study conducted on Indian children with intrathoracic tuberculosis by Khandelwal et al showed that majority of the children demonstrated low serum 25-hydroxyvitamin 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-dihydroxyvitamin 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 D therapy with ATT resulted in faster sputum smear conversion and radiological improvement in TB patients whereas a study conducted by Marineau et al showed that vitamin D supplementation did not significantly reduce the time to sputum culture conversion.[27,28] A study conducted in India by Peter Daley et al found that adjunctive vitamin D in the treatment of active tuberculosis did not reduce the time to sputum culture conversion.[29] In one published case report, simultaneous correction of vitamin D deficiency with ATT in an African-American female who presented with refractory, drug susceptible pulmonary tuberculosis resulted in clinical and microbiological improvement.[30] A meta-analysis was done by Lewis et al to assess the association of pulmonary TB with VDR FokI and TaqI polymorphisms.[31] Non-tuberculosis medical patients in present study were of other chronic illnesses such as congestive cardiac failure, diabetes mellitus, stroke and pneumonia. Cardiovascular disease and diabetes have also been reported with hypovitaminosis D.[32,33]

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. Literature search shows that vitamin D deficiency is much prevalent in India. Although many studies have evaluated for the association of vitamin D deficiency with tuberculosis, there are no uniform results and hence the correlation remains doubtful. The present finding also warrants further studies to determine whether Vitamin D supplementation can have a role in the prevention and treatment of tuberculosis in developing countries.

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