ORIGINAL ARTICLE

Frequency and Association of Vitamin D Deficiency in Patients with Tuberculosis at 2 and 6 weeks Interval

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ABSTRACT

Objective: To determine the frequency and association of Vitamin D deficiency in patients with tuberculosis at 2 and 6 weeks interval.
Study Design: Cross sectional study.
Place and Duration: The study was done in medical department of District Headquarter Teaching Hospital Kohat from 1st June 2019 to 30th May 2020.
Methodology: One hundred and fifty outdoor patients of tuberculosis were selected. All the study patients were divided into two major groups. In group A patients' vitamin D level was obtained at 2 weeks and group B patients vitamin D level was obtained at 6 weeks interval after treatment. Tuberculosis was diagnosed by presence of acid fast bacilli in sputum smears, positive culture for Mycobacterium tuberculosis or demonstration of chronic caseating granulomatous inflammation in tissue specimens. Serum 25 hydroxyvitamin D [25 (OH) D3] levels were checked at 2 weeks and then at 4 weeks. A level < 75 ng/ml was considered Vitamin D deficiency. The results were analyzed on SPSS version
Results: Only 5 (6.6%) in group A and 7 (9.3%) patients in group B had vitamin D level of 61 or above. Around one third of study patients had vitamin D level of up to 30 in both groups. The average vitamin D level was found equal in both groups. In group A the average vitamin D level was 38.7 + 13.5 where as in group B it was 39.7 + 14.0. Later on, after six weeks interval the vitamin D levels were found different among both groups. When the average vitamin D levels after intervention were compared among the two groups, it was found out that Group B patients had significantly higher vitamin D status compared to group A (53.4 vs 61.2 respectively, p-value = 0.008).
Conclusion: There is significant deficiency of Vitamin D in patients with tuberculosis. This deficiency is more pronounced in females, and in patients who have started treatment the vitamin D deficiency improved.
Keywords: Tuberculosis. Vitamin D. Tuberculosis.

INTRODUCTION

The most common cause of mortality from one infectious disease in the world is tuberculosis, with 1,7 million deaths in 2004. This is attributed to ineffective disease prevention programmes, insufficient care, multiple drug resistance (MDR), widespread HIV co-infection with drug resistant TB (XDR-TB), and overcrowding and poor nutrition. It is caused by an aerobial Mycobacterium tuberculosis complex in rod shapes which does not form a spore and typically affects the lungs, although up to a third of other organs are involved. If the disease is untreated, 50% to 65% of the cases may die within 5 years.[1]

Tuberculosis in Britain is a modifiable disease, with 8,037 notifications in 2005, which is now relatively stable, in contrast to just over 5,000 years ago. The incidence in India was reported to be about 1.8 million in 2004. Tuberculosis in UK is 40 and four times higher than in the indigenous white population, respectively, among immigrants from the Asian sub-continent and from the West Indians. [2]

The World Health Organisation, 95 percent of which were reported in the developing countries of Asia (5.2 million), Africa (2.8 million), Middle East (0.7 million), and Latin America, reported more than 5.8 million new cases of tuberculosis (all types of tuberculosis) in 2009 (0.3 million). Further, in 2008 1,7 million (range 1,5-1,9 million) tuberculosis deaths were estimated, including 0,4 million HIV infected individuals. Out of an estimated 9,4 million new TB cases in 2009, 440.000 MDR-TB cases, which are at least a type of bacilli-resistant disease, may have formed in 2008, are estimated to be at least 4.5 million. Currently >90% of these cases are not detected in most settings worldwide due to lack of culture and drug susceptibility testing capability. Overall in India, China and the Russian Federation, 60 percent are MDR-TB cases.[3]

Long after the activation of tuberculosis, a lack of vitamin D (25-hydroxycholecalciferol) (TB). Vitamin D serum concentrations are lower in TB patients than in safe controls. Paradoxically, extended TB therapy causes serum vitamin D levels to decrease as well. Vitamin D, an effective immunomodulator of innate immune responses by serving as an activation cofactor for antimycobacterial activity has been suggested in several studies. Pakistan ranks eighth among the 22 countries with the highest incidence of TB.[4]

A study conducted by Najeeha T in Pakistan showing a correlation between deficiency in vitamin D and progression of tuberculosis. Most (79%) people had deficiencies. In another Henrik F study, hypo-vitaminsis D showed a 41.2 percent deficit; vitamin D was 0,8 percent

extreme (<25 nmol/L), vitamin D was moderate (25-50 nmol/L), and vitamin D was low (50–75 nmol/L) at 30%. Low vitamin D levels were associated with 5-fold increased risk for tuberculosis[5]. The concentrations of serum 25 (OH) D did not vary among men (87.3 ± 31.1 nmol/L) or between men (86.1 ±34.2 nmol/L) and hypovitaminosis D, respectively, was 40.7 and 41.5%.[6]

Deficiency of Vitamin D (VDD) entails compromised immunity from mycobacteria and TB susceptibility (TB). In a study by Banda R and his colleagues 25 hydroxy-vitamin-D levels have been measured in 161 patients who had TB adults at Malawi Central Hospital, of whom 120 (74.5%) had daily ~75 nmol/l (hypovitaminosis D), sixty-eight (42%) had daily +50 nmol/l (VDD) and 13.6% had nmo-and 6.8% of nmol/l (Severe VDD).[7, 8]

A deficiency in vitamin D (VDD) is linked to mycobacterial immunity and increased tuberculosis susceptibility. The lack of vitamin D is also related to a weak treatment response. Therefore, we not only boost the treatment response but also avoid the reoccurrence of disease by supplying vitamin D to people taking anti-tuberculosis drugs.

MATERIALS AND METHODS

This cross-sectional study was conducted at in/out patient department of General Medicine, District Headquarter Teaching Hospital Kohat from 1st June 2019 to 30th May 2020.150 outdoor patients of tuberculosis with ages 20 to 60 years were enrolled. Patients detailed demographics were recorded after taking written consent. Patients with obesity, Crohn's disease patients, patients with celiac disease, patients with chronic liver disease and patients with renal failure were excluded.

All the study patients were divided equally into two major groups. In group A patients vitamin D level was obtained at 2 weeks and group B patients vitamin D level was obtained at 6 weeks interval after treatment. Tuberculosis was diagnosed by presence of acid fast bacilli in sputum smears, positive culture for Mycobacterium tuberculosis or demonstration of chronic caseating granulomatous inflammation in tissue specimens. Serum 25 hydroxyvitamin D [25 (OH) D3] levels were checked at 2 weeks and then at 4 weeks. A level < 75 ng/ml was considered Vitamin D deficiency.

The data was analyzed by SPSS software version 16. Descriptive statistics were calculated for all variables like age, gender, plasma Vitamin D3 level. Frequency and percentage were presented for qualitative variables like sex, plasma Vitamin D3.

RESULTS

The mean age of patients was 33.3 + 16.1 years in group A and 36.5 + 16.5 years in group B. Almost 70.0% of the study patients in both groups were younger than 40 years of age. (Table 1)

Female gender was found predominant in this study. In group A 58.7% patients were female and in group B 52.0% patients were females whereas 41.3% and 48.0% patients in group A and B were males respectively. (Table 2)

All the study patients were divided into two major groups. In group A patients vitamin D level was obtained at 2 weeks and group B patients vitamin D level was obtained at 6 weeks interval after treatment. Almost all the study patients with tuberculosis had low vitamin D status in both groups. At two weeks interval, only 5 (6.6%) in group A and 7 (9.3%) patients in group B had vitamin D level of 61 or above. Around one third of study patients had vitamin D level of up to 30 in both groups. In group A, 20 (26.6%) patients had vitamin D level between 31 and 45 compared to 24 (32.0%) in group B. Similarly, another 20 (26.6%) in group A had vitamin D level between 46 and 60 whereas in group B 18 (24.0%) had so. (Table 3)

The average vitamin D level was found equal in both groups. In group A the average vitamin D level was 38.7 + 13.5 where as in group B it was 39.7 + 14.0. (Table 4)

Later on, after interval of 6 weeks vitamin D levels were found different among both groups. In group A, 19 (25.3%) patients had levels between 30 and 40, another 15 (20.0%) patients had levels between 41 to 50 whereas majority of the cases had 34 (45.3%) had the levels of 61 or above. Comparatively, in group B, 10 (13.3%) patients had vitamin D levels of 30 to 40; another 18 (24.0%) patients had levels between 41 and 50 whereas 38 (50.6%) patients had the levels of 61 or above. It was found that group B still had significantly less cases that group B having very low levels of vitamin D (p-value =0.05). (Table 5)

When the average vitamin D levels after intervention were compared among the two groups, it was found out that Group B patients had significantly higher vitamin D status compared to group A (53.4 vs 61.2 respectively, p-value = 0.008). (Table 6)

Table 1: Age of patients in the two study groups

	Group A (n=75)	Group B (n=75)
Age (years)		
Up to 20	22 (29.3%)	11 (14.6%)
21 to 30	13 (17.3%)	24 (32.0%)
31 to 40	17 (22.6%)	15 (20.0%)
41 to 50	7 (9.3%)	8 (10.6%)
51 to 60	9 (12.0%)	9 (12.0%)
61 or above	7 (9.3%)	8 (10.6%)
Mean + SD	33.3 + 16.1	36.5 + 16.5

Table 2: Gender of patients in the two study groups

	Group A (n=75)	Group B (n=75)
Gender		
Male	31 (41.3%)	36 (48.0%)
Female	44 (58.7%)	39 (52.0%)

Table 3: Baseline vitamin D status in patients between two study groups

	Group A (n=75)	Group B (n=75)
Up to 25	10 (13.3%)	13 (17.3%)
26 to 30	20 (26.6%)	13 (17.3%)
31 to 45	20 (26.6%)	24 (32.0%)
46 to 60	20 (26.6%)	18 (24.0%)
61 or above	5 (6.6%)	7 (9.3%)

Table 4: Baseline vitamin D status in patients between two study groups

	Group A (n=75)	Group B (n=75)
Mean + SD	38.7 + 13.5	39.7 + 14.0

Table 5: Comparison of Vitamin D level at 6 weeks interval between two study groups

	Group A (n=75)	Group B (n=75)	p-value
30 to 40	19 (25.3%)	10 (13.3%)	0.05
41 to 50	15 (20.0%)	18 (24.0%)	n.s.
51 to 60	7 (9.3%)	9 (12.0%)	n.s.
61 or above	34 (45.3%)	38 (50.6%)	n.s.

Table 6: Comparison of Vitamin D levels in patients between two study groups

	Group A (n=75)	Group B (n=75)	p-value
Mean + SD	53.4 + 17.7	61.2 + 18.5	0.008

DISCUSSION

In macrophage activation and limiting growth of mycobacteria, vitamin D (Vit D) plays an important role. Vit D's definitive function for suppressing Mycobacterium TB proliferation and generalised inflammatory responses that are secondary to the immune system has been shown by several biological studies for the effect of Vit D on the body's immune system. The microbe-killing of cathelicidin, in the absence of sufficient Vitamin D serum, is analogous to the triggering of toll-like receptors with tubercular bacillus molecules. The in vivo vitamin D association, however, remains a debatable issue. In this research, we have found that insufficiency of vitamin D in male and female TB patients is high, as assessed by 25(OHD) levels. Since the serum vitamin D level can be reduced as antituberculosis chemotherapy, only those patients who have yet to begin treatment have been included

In his study Martineau et al[9] found that 82 percent of the 500 inmates of the study had vitamin D deficiencies, 11 percent of whom had vitamin D deficiency. One of the study areas also suggested a substantial decrease in the growth of the mycobacteria by supplementing vitamin D with one oral dose of 2.5 mg (100,000 IU).

The average amount of vitamin D was found in both groups in our sample. In Group A, the average level of vitamin D was 38,7 + 13,5, while in Group B it was 39,7 + 14,0.When compared to both groups, the average level of vitamin D was found to be substantially better in Group B than in Group A (53,4 vs. 61,2 respectively, p-value = 0,008).

Previously, the report of vitamin D deficiency from India alone was scattered and considered to be nonexistent and the usual levels of vitamin D did not come to any consensus. The medium value of safe controls was 19.4 ng/ml and the range was between 9 and 58 ng/ml [10]. Since there was no population data of 25 OH vitamin-D in the study area, a value less than 10 ng/mL, the lowest control amount, has been described as a definite deficiency. The mean value was 10.7 ng/ml with a range from 1–30 ng/ml in patients with tuberculosis. A research by Rajeev E et al [11] recently found that a value under 30ng/ml would be a defect; the normal range would be 20-100ng/ml and the preferred normal value range was 30-60ng/ml. Vitamin D intoxication only happens when the level is above 150ng/mL. Out of 35 patients with tuberculosis who had 25 30ng/mL hydroxide D3 and much less than the preferred ranges, only one patient was found to have vitamin D deficit in all patients with tuberculosis.

TB patients also have lower levels of vitamin D than the public in general. Many scientists have shown the impact of vitamin D on TB disease. A recent Spanish research by Tucker M[11] showed high levels of TB contacts with low serum 25(OH)D and indicated that enough 25(OH)D levels protect from the tuberculin skin test (TST), so the hypothesis that a vitamin D defective is a TB risk factor can be endorsed. A lack of sun-induced vitamin D synthesis is one of the key causes of globally VDD. In Germany, a survey of Suda T, Ueno Y y al showed that a high prevalence of vitamin D deficiency was found among immigrant children and teens of Turkish or Arab-Islamic origin[12].

In patients with TB, Masoud Nouri-Vaskehet al[13] has confirmed that vitamin D (25 vs.2 healthy patients; P <0.001) and serum levels are significantly higher compared to healthy patients in vitamin D vitamin levels (22.66 ± 15.17 vs 73.03 ± 25,6 ng/mL; P <0.001).

T y al [14], Najeeha. The risk of active TB progression in plasma vitamin D levels was analysed. Of the 100 household touch without diseases, over 4 years of follow up 8 (8%) have progressed to active disease. Progress of TB has been correlated significantly with lower levels of plasma-vitamin D. Out of 30 patients in the lowest tertile (less than 7 ng/ml), 1 (3%) of 32 with medium-tertile vitamin D (more than 7-13 ng/ml), no more than 30 with the maximum tertile (> 13 Ng/mL), a disease progressed in 7 (23%) The disease was more frequent. Of eight patients with advanced TB, six (75 per cent) were women with lowest tertile vitamin D levels.

In Pakistan, Raheel I and al[15] found that 35 (77 percent) out of 45 tuberculosis women had Vitamin D deficits, while 10 (23 percent) of other patients had Vitamin D deficiency. Female TB patients were lower than male TB patients (p=0.002) and that 35 (77 percent) had a Vitamin D insufficiency. Likewise, vitamin D deficiency occurred at 41.8% (46 of 110) of females in the control sample. Among the cases 82 were PT patients (78%) and 23 additional PT were PT patients TB patients TB patients (22 percent).

CONCLUSION

Tuberculosis patients are slightly worse than average people with vitamin D. In females, extrapulmonary and MDR tuberculosis, this deficiency is more severe. The present result also calls for further research to determine whether Vitamin D supplementation can or cannot be used in developing countries such as Pakistan to prevent and treat tuberculosis.

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