

Examine the Vitamin D Deficiency in Patients with Pulmonary Tuberculosis

MUHAMMAD SAQIB MUSHARAF¹, ASAD JAVED², AMIR WAHEED³, SAIMA RIAZ⁴, WASEEM AHMAD KHAN⁵, MUHAMMAD NAIM ASHRAF⁶

¹Assistant Professor Pulmonology, Al Aleem Medical College, GDTH Lahore

²Senior Registrar, Department of Pulmonology, Al Aleem Medical College, GDTH Lahore

³Assistant Professor Pulmonology, Sialkot Medical College

⁴Senior Registrar Medicine, Avicenna Medical College, Lahore

⁵Senior Registrar Pulmonology, Amna Inayat Medical College/Kishwar Fazal Teaching Hospital, Sheikhpura

⁶Associate Prof Pathology, Al Aleem Medical College, Lahore

Correspondence to: Dr Saqib Musharaf, Email: drmsaqibm@gmail.com, Cell: 03134800767

ABSTRACT

Aim: To determine the level of vitamin D in patients with tuberculosis and compare it without tuberculosis patients.

Study design: Cross-sectional/Observational

Place and duration: Pulmonology Department, Al Aleem Medical College, Gulab Devi Teaching Hospital, Lahore from January, 2019 to June, 2019.

Methods: Total 70 patients of both genders presented with pulmonary tuberculosis with ages 20 to 70 years and 70 patients non tuberculosis with same age range were enrolled in this study. Sputum examination by gene Xpert method was used to examine the tuberculosis. Blood sample was taken from all the patients to examine the vitamin D level. Serum hydroxyl vitamin D 25 level less than 25ng/ml was considered as deficiency of vitamin D. Data was analyzed by SPSS 24.0.

Results: There were 46(65.71%) male and 24(34.29%) females in group I and 42(60%) males and 28(40%) females in group II. Mean age of patients in group I was 36.42±12.85 years and in group II it was 35.96±13.24 years. Vitamin D level was significantly low in tuberculosis patients as compared to healthy patients (22.79±5.14ng/ml Vs 31.76±9.52ng/ml) with p-value <0.0001. In group I 55(78.57%) and in group II 18 (25.71%) patients had vitamin D deficiency, a significant difference between both groups (P-value <0.001).

Conclusion: It is concluded that vitamin D deficiency is highly associated with pulmonary tuberculosis patients.

Keywords: Pulmonary Tuberculosis, Sensitive Tuberculosis, Multi-drug resistant, Vitamin D Level.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by the bacilli belonging to Mycobacterium tuberculosis complex, usually Mycobacterium tuberculosis (MTB)¹. TB remains a major global health problem. According to WHO global tuberculosis report, 9.6 million TB cases occurred and TB killed 1.5 million people (1.1 million HIV-negative and 0.4 million HIV-positive) worldwide in 2014². Ethiopia has ranked 7th among the world's 22 high burden countries with an estimated incidence rate of 207 per 100,000 population in 2014².

Various factors that could possibly affect the incidence and progression of TB have been reported, one of them is vitamin D deficiency (VDD)³⁻⁴ Exposure to sunlight is the main source of vitamin D for human and induces the conversion of 7-dehydrocholesterol to vitamin D₃ via pre-vitamin D₃ in the skin⁵. Vitamin D₃ is then converted to 25-hydroxy vitamin D (25(OH)D). In the liver and is further converted to the bioactive form of vitamin D, 1,25-dihydroxy vitamin D₃ (1,25(OH)₂D₃) in the kidney⁵. Vitamin D (VitD) is believed to have an important role in macrophage activation and the subsequent restriction of MTB growth⁶. Low levels of Vitamin D (<30ng/dL) is a common finding world over, specially prevalent in developing countries and varies depending on the food

fortification policies, demographic features, geographic location and season. Vitamin D deficiency has been implicated as a risk factor for tuberculosis (TB)⁷. An association between 25 hydroxy vitamin D (25[OH]D) levels and TB has been described in few studies including one on Chinese patients with pulmonary TB⁸. Pakistan was included in first five countries with maximum number of incidents of TB cases in 2011⁹⁻¹⁰. The present study was conducted to examine the low serum vitamin D level in patients with pulmonary tuberculosis.

MATERIALS AND METHODS

This cross-sectional/observational study was conducted at Pulmonology Department, Al Aleem Medical College, Gulab Devi Teaching Hospital, Lahore during from the period January, 2019 to June, 2019. A total 140 patients of both genders with ages 20 to 70 years were enrolled in this study. 70 patients with pulmonary tuberculosis diagnosed through sputum examination by gene Xpert method (group I) and 70 patients without tuberculosis taken as controls (group II). Patients detailed demographic including age, sex, smoking status and body mass index (BMI) was recorded after taking informed consent. Patients with renal failure, patients with bone disorders and those recently undergoing surgery were excluded.

5ml blood sample was taken from all the patients to examine the serum vitamin D level. Serum hydroxyl vitamin

Received on 17-08-2019

Accepted on 23-01-2020

D 25 level less than 25ng/ml was considered as deficiency of vitamin D. All the data was analyzed by SPSS 24.0. Mean±SD was applied. Frequencies and percentages were recorded in tabulation form. Chi-square test and student t' test was done to compare the vitamin D level. P-value <0.05 was set as statistically significant.

RESULTS

There were 46(65.71%) male and 24(34.29%) females in group I and 42(60%) males and 28(40%) females in group II. Mean age of patients in group I was 36.42±12.85 years and in group II it was 35.96±13.24 years. No significant difference was observed regarding age and gender between both groups with p-value >0.05. Mean BMI in group I was 21.34±3.45kg/m² and in group II it was 24.71±3.36 kg/m², a significant difference was observed between both groups (p-value <0.05). In group I 43(61.43%) patients were smokers while in group II 39(55.71%) patients were smokers, no significant difference was observed (p-value >0.05). (Table 1)

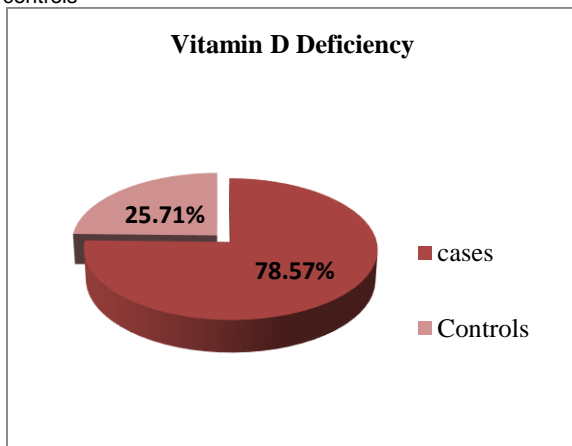
Table 1: Demographical details of all the patients

Characteristics	Group I (Cases)	Group II (Controls)	P-value
Mean Age (Yrs)	36.42±12.85	35.96±13.24	>0.05
Mean BMI (kg/m)	21.34±3.45	24.71±3.36	0.001
Gender			
Male	46 (65.71%)	42 (60%)	>0.05
Female	24 (34.29%)	28 (40%)	
Smokers			
Yes	43 (61.43%)	39 (55.71%)	>0.05
No	27 (38.57%)	31 (44.29%)	

Table 2: Comparison of Vitamin D level between both groups

Characteristics	Group I (Cases)	Group II (Controls)	P-value
Mean Vitamin D Level (ng/ml)	22.79±5.14	31.76±9.52	<0.001

Figure 1: Frequency of Vitamin d deficiency among cases and controls



According to the vitamin D level, patients with tuberculosis had significantly low serum vitamin D level as compared to healthy controls (22.79±5.14ng/ml Vs 31.76±9.52ng/ml) with p-value <0.0001 (Table 2).

In group I 55 (78.57%) and in group II 18(25.71%) patients had vitamin D deficiency, a significant difference between both groups (P-value <0.001) (Figure 1).

Among all tuberculosis patients, 58(82.86%) patients had sensitive tuberculosis, in which 50(86.21%) patients had Vit D deficiency and 8(13.79%) patients had normal vitamin D level >25ng/ml. 12(17.14%) had multidrug resistant tuberculosis in which 5(41.67%) patients had vitamin D level <25ng/ml while 4(33.33%) patients had vitamin D level >25ng/ml (Table 3).

Table 3: Clinical presentation and vitamin D level in TB patients

Variables	Sensitive TB (n=58)	MDR TB (n=12)	P-value
Vitamin D Deficiency			
Yes	50 (86.21%)	5 (41.67%)	<0.001
No	8 (13.79%)	4 (33.33%)	

DISCUSSION

Pulmonary tuberculosis is one of the most common disease found all over the world with high rate of mortality and morbidity¹¹. Many of studies have been conducted to examine the vitamin D level in patients with tuberculosis and its association with tuberculosis, because vitamin D plays an important role in prevention of any infectious diseases¹²⁻¹³. The present study was also conducted aimed to examine the association of vitamin D level in patients with tuberculosis. In this regard 140 patients were enrolled and divided into two groups. 70 patients with tuberculosis and 70 patients without tuberculosis taken as controls. There were 46(65.71%) male and 24(34.29%) females in cases group and 42 (60%) males and 28(40%) females in control group. Mean age of patients in group I was 36.42±12.85 years and in group II it was 35.96±13.24 years. No significant difference was observed regarding age and gender between both groups with p-value >0.05. These results showed similarity to many of previous studies in which male patients population was high 60% to 75% as compared to females and majority of patients had ages above 40 years¹⁴⁻¹⁵.

In our study, mean BMI in group I was 21.34±3.45 kg/m² and in group II it was 24.71±3.36 kg/m², a significant difference was observed between both groups (p-value <0.05). In group I 43 (61.43%) patients were smokers while in group II 39(55.71%) patients were smokers, no significant difference was observed (p-value >0.05). A study by Iftikhar R et al¹⁶ reported low BMI in tuberculosis patients as compared to healthy controls (20.43±2.06 Vs 23.62± 2.35kg/m²).

In present study we found that patients with tuberculosis had significantly low serum vitamin D level as compared to healthy controls (22.79±5.14ng/ml Vs 31.76±9.52ng/ml) with p-value <0.0001. In group I 55 (78.57%) and in group II 18 (25.71%) patients had vitamin D deficiency, a significant difference between both groups (P-value <0.001). A study by Mashhaddi FS et al¹⁷ reported similarity to our study findings regarding serum vit D level in tuberculosis patients in which they reported Mean vitamin D was significantly lower (20.688 ±14.065nmol/l) in cases as compared to the controls (57.917±18.197nmol/l) (p<0.001). Another study conducted by Workineh M et al¹⁸ reported that patients with tuberculosis had significantly low

serum vitamin D level as compared to non-tuberculosis patients 30.1 ± 19.3 nmol/L Vs 38.5 ± 20.9 nmol/L, $P = 0.005$. They also reported patients with tuberculosis had high frequency of vitamin D deficiency as compared to without TB patients (83.3% Vs 67.1%). Several other studies demonstrated that patients with tuberculosis had high rate of vitamin D deficiency as compared to healthy patients^{19,20}.

In our study, 58 (82.86%) patients had sensitive tuberculosis, in which 50 (86.21%) patients had vit D deficiency and 8(13.79%) patients had normal vitamin D level >25 ng/ml. 12(17.14%) had multidrug resistant tuberculosis in which 5(41.67%) patients had vitamin D level <25 ng/ml while 4(33.33%) patients had vitamin D level >25 ng/ml. These results were comparable to many of previous studies^{21,22}.

CONCLUSION

Vitamin D plays an important role in the prevention and treatment of tuberculosis. We concluded from this study that patients with pulmonary tuberculosis had significantly low serum vitamin D3 level as compared to healthy controls.

REFERENCES

- Kumar V, Abbas AK, Fausto N, Mitchell RN. Robbins basic pathology. 8th ed. Philadelphia: Saunders Elsevier; 2007. p. 516–22.
- WHO. Global tuberculosis report. Geneva: WHO; 2015.
- Kim JH, Park JS, Cho YJ, et al. Low serum 25-hydroxyvitamin D level: an independent risk factor for tuberculosis? *Clin Nutr*. 2014;33(6):1081–1086.
- Gibney KB, MacGregor L, Leder K, et al. Vitamin D deficiency is associated with tuberculosis and latent tuberculosis infection in immigrants from sub-Saharan Africa. *Clin Infect Dis*. 2008;46(3):443–446.
- Steenhoff AP, Redwood A, Pettifor JM, et al. Vitamin D status in HIV-infected patients with and without tuberculosis: a pilot study. *J Acquir Immune Defic Syndr*. 2012;61(2):e21–e23.
- WHO. Global tuberculosis control: a short update to the 2009 report. Geneva: WHO Report; 2010.
- Mithal A, Wahl DA, Bonjour JP, Burckhardt P, Dawson-Hughes B. Global Vitamin D status and determinants of hypovitaminosis D. *Osteoporosis Int* 20; 2009:1807-20.
- Sheikh A, Saeed Z, Jafri SAD, Yazdani I, Hussain SA. Vitamin D levels in asymptomatic adults: a population survey in Karachi, Pakistan *PLoS One* 2012. 7:e33452.
- World Health Organisation. World tuberculosis report 2012. Geneva: WHO; 2012.
- Khan H. Prevalence of vitamin D deficiency in general population of Islamabad, Pakistan. *Ann Pak Inst Med Sci* 2013; 9(1):45-7.
- Tessema, B., Moges, F., Habte, D. *et al*. Vitamin D deficiency among smear positive pulmonary tuberculosis patients and their tuberculosis negative household contacts in Northwest Ethiopia: a case-control study. *Ann Clin Microbiol Antimicrob* 6, 36 (2017). <https://doi.org/10.1186/s12941-017-0211-3>.
- Norval M, Coussens AK, Wilkinson RJ, et al. Vitamin D status and its consequences for health in South Africa. *Int J Environ Res Public Health* 2016;13: pii: E1019.
- Jolliffe DA, Ganmaa D, Wejse C, et al. Adjunctive vitamin D in tuberculosis treatment: meta-analysis of individual participant data [published online February 6, 2019]. *Eur Respir J*. doi:10.1183/13993003.02003-2018.
- Wakayo T, Belachew T, Vatanparast H, Whiting SJ. Vitamin D deficiency and its predictors in a country with thirteen months of sunshine: the case of school children in central Ethiopia. *PLoS ONE*. 2015;10(3):e0120963. doi:10.1371/journal.pone.0120963.
- Mansoor S, Habib A, Ghani F, Fatmi Z, Badruddin S, Mansoor S, et al. Prevalence and significance of Vitamin D deficiency and insufficiency among apparently healthy adults. *Clin Biochem* 43; 2010:1431-5.
- Iftikhar R, Kamran SM, Qadir A, Haider E, Hassan BU. Vitamin D deficiency in patients with tuberculosis. *Journal of the College of Physicians and Surgeons-Pakistan: JCPSP* 2013; 23(10):780-3.
- Mashhaddi FS, Rahman UR, Azam N, Hashim R, Khan A, Fawad A. Association Of Vitamin D Deficiency With Tuberculosis In Adult. *Pak Armed Forces Med J* 2014; 64 (3):479-83.
- Workineh, M., Mathewos, B., Moges, B. *et al*. Vitamin D deficiency among newly diagnosed tuberculosis patients and their household contacts: a comparative cross-sectional study. *Arch Public Health* 75, 25 (2017). <https://doi.org/10.1186/s13690-017-0195-7>.
- Kim, J.H., Yim, J.J. Achievements in and challenges of tuberculosis control in South Korea. *Emerg Infect Dis*. 2015;21:1913–1920.
- Oh, Jongwon *et al*. Evaluation of vitamin status in patients with pulmonary tuberculosis. *Journal of Infection*, Volume 74, Issue 3, 272 – 280.
- ibana, O.; Franke, M.F.; Huang, C.C.; Galea, J.T.; Calderon, R.; Zhang, Z.; Becerra, M.C.; Smith, E.R.; Contreras, C.; Yataco, R.; et al. Vitamin E status is inversely associated with risk of incident tuberculosis disease among household contacts. *J. Nutr*. 2018, 148, 56–62.
- Koh, W.J.; Jeong, B.H.; Kim, S.Y.; Jeon, K.; Park, K.U.; Jhun, B.W.; Lee, H.; Park, H.Y.; Kim, D.H.; Huh, H.J.; et al. Mycobacterial characteristics and treatment outcomes in Mycobacterium abscessus lung disease. *Clin. Infect. Dis*. 2017, 64, 309–316.