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The Assessment of Vitamin D Serum Level in Patients With Pulmonary and Extra-Pulmonary Tuberculosis in Karaj, Iran, During 2017-2018.

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Abstract

Background: It is important to determine the type of tuberculosis and its related factors in order for effectively treating a disease and reducing its side effects in the society.

Objective: This study aimed to determine vitamin D level in patients with pulmonary and extra-pulmonary tuberculosis in Karaj, Iran in 2017-2018.

Materials and Methods: In this observational study, 102 patients suffering from pulmonary and extra-pulmonary tuberculosis disease were availably selected in Karaj, Iran in 2017-2018. They were examined and, then, their vitamin D level were assessed and compared according to the type of tuberculosis.

Results: The study results showed that vitamin D level was normal in 39.2% of the case study population, but it was abnormal in 60.8% of it (18.6% deficiency and 42.2% insufficiency). Vitamin D deficiency was 15.8% in pulmonary tuberculosis patients and it was 22.2% in extra-pulmonary tuberculosis ones, showing no significant difference ($P>0.05$) statistically.

Conclusion: According to the obtained results, hypovitaminosis-D was detected in more than half of the patients with pulmonary and extra pulmonary tuberculosis, which was not associated with the type of tuberculosis. Seemingly, the patients needed the same amount of – or even more – food, medical supplements, sports, and sunlight compared to healthy people.

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Background

Tuberculosis, caused by *Mycobacterium tuberculosis*, *Mycobacterium bovis* or *Mycobacterium africanum*, is one of the most common infectious diseases affecting people in different countries, especially in Iran.[1,2] The prevalence of the disease varies from area to area, and from patient to patient with different diseases and background conditions; therefore, different studies should be conducted to examine it in different areas.[2,3] Tuberculosis, as a global urgency, requires comprehensive studies and more serious actions. Moreover, the failure of fighting programs against tuberculosis in most developing countries in recent years has been a serious matter demonstrating that treating tuberculosis is a multidimensional problem which has various aspects such as side effects as well as drug resistance and effectiveness.[1,3] Given the above-mentioned arguments, it is important to perform an appropriate measurement in order for properly addressing tuberculosis dimensions in Iran. This issue is a matter of importance due to the global increase in the number of people infected with tuberculosis, and the increased cases of antibiotic resistance observed even among children.[4,5] The first step to carry out the appropriate measurement is to identify relevant factors influencing tuberculosis in order to design necessary programs. One of the contributing factors identified in the field is vitamin D.

Several studies have discovered a relationship between low level of vitamin D and tuberculosis prevalence, but they failed to find any inverse relationship between these two factors.[6-8] The results from these studies might be explained by the fact that the active form of vitamin D causes an increase in the capacity of macrophages in suppressing *Mycobacterium tuberculosis* cellular growth. Moreover, it has been revealed that insufficient amount of vitamin D disrupts the production of peptides such as cathelicidin produced by Toll-like receptors.[9] Vitamin D reinforces the function of monocytes and macrophages in the body, and by doing so, it acts as an agent to build up innate immunity against infectious factors. This property of vitamin D may play an important role in protecting the body against tuberculosis in which the attack of macrophages is considered a crucial factor in suppressing

pathogens.

The function of vitamin D begins with connecting to the nuclear receptors on the cells. Thus both the low level of vitamin D and the anomaly in structure may cause a disorder in the host immunity against TB bacilli. Maintaining a balance between calcium and phosphorus in the body is the most well-known function of vitamin D.[10]

The results from some researches have indicated that vitamin D deficiency is more common in patients with tuberculosis. Therefore, this study aimed to examine vitamin D level in patients with pulmonary and extra-pulmonary tuberculosis in Karaj, the capital of Alborz province in Iran, in 2017-2018.

Materials and Methods

Sample Size

Following the statistical formula, 100 people were selected and included in the study consciously. The selected people were those who had referred to Imam Ali hospital in Karaj during a period from 2017 to 2018 and had been examined by the infectious disease specialist.

Three samples of the morning sputum were collected from every suspected patient for microscopic examination and direct slide observation. When the smear was positive, sputum culture was performed and, afterwards, the patient was considered as tuberculosis patient based on the results of the examination and observation, as well as on the approval of the infectious disease specialist.

Patients unwilling to participate in the study and those having a history of taking anti-tuberculosis drugs or vitamin supplements, as well as those with underlying conditions such as diabetes or cancer were excluded from the study. Before beginning the treatment, blood samples were taken from all patients and vitamin D3 level was determined using blood tests and ELISA kit made by Beckman, USA. The obtained results are presented as follows:

Vitamin D serum levels below 10 nmol/mL were considered deficient, those between 10 to 30 nmol/mL were regarded insufficient, and those above 30 nmol/ml were described sufficient.

Results

The average age of patients was 44 including the range of 14 to 87 years. The average level of Vitamin D was 29.5 ng/ml including the range of 3.2 to 86 (Table 1). According to the study results, -55.9% of the patients had pulmonary tuberculosis (50% with positive pulmonary Smear tuberculosis and 5.9% with negative one). Moreover, -13.7% of the patients had lymphatic tuberculosis. The prevalence of different types of -tuberculosis is shown in Table 2.

According to Table 3, vitamin D level was abnormal in 60.9% of the patients (18.6% deficient and 42.2% insufficient cases), but it was normal in 39.21% of them.

Patients information were studied based on their age. Majority of the patients with pulmonary TB were those aged 14 to 24 (14 cases), and the least number of the patients with pulmonary TB were those aged 45 to 54, and 75 to 84 (4 cases) (Table 4).

Most patients with extra-pulmonary TB were within the age-group 35 to 44 years (4 cases), and the least number of the patients in this group were within 45 to 54 years. There was no one infected with extra-pulmonary TB aged

Table 1 . The Average Range of Age and Vitamin D Level in Patients

	Minimum	Maximum	Average
Age	14	87	44.2
Vitamin D	3.24 ng/mL	86 ng/mL	29.4 ng/mL

Table 2. The Frequency Distribution of Tuberculosis in Patients

Tuberculosis type	Number	Percent
Pulmonary smear positive TB	51	50
Pulmonary smear negative TB	6	5.9
Lymphatic TB	14	13.7
Skin TB	3	2.9
Salivary meningitis	5	4.9
Visceral fascia TB	5	4.9
Spine TB	3	2.9
Bone TB	2	2
Urinary tract TB	3	2.9
Others	10	9.8
Total	102	100

Table 3. Frequency Distribution of Vitamin D Level in Patients

Vitamin D Level	Number	Percent
Deficiency	19	18.6
Insufficiency	43	42.2
Sufficiency	40	39.2
Total	102	100

Table 4. Comparing Vitamin D Average in Pulmonary and Extra-Pulmonary TB

TB Type	Number	Minimum	Maximum	Average
Pulmonary	57	3.24	86	31.27
Extra- pulmonary	45	4	75	27.16

P value >0.05.

Table 5. Comparing Vitamin D Level in Positive Smear TB With Negative Smear TB

Type of TB	Number	Low Level	High Level	Average
Smear positive TB	51	3.2	86	31.27
Smear negative TB	6	10	63	31.33
Extra-pulmonary	45	4	75	27.16

P value >0.05.

75 to 84 or 85 and older (Table 5).

Examination of vitamin D level based on the age of the patients with pulmonary TB showed that patients aged 14-24 and 35-44 (71.4%) had the most abnormal level, and those aged 75-84 (25%) had the least abnormal level.

In patients with extra-pulmonary TB, the highest abnormal level of vitamin D was found among patients aged 45-54 (75%), and its lowest level was observed among those aged 65-74 (33%). Vitamin D level was investigated based on the gender in patients with pulmonary and extra-pulmonary tuberculosis. Vitamin D level was abnormal in 66.7% of male patients with pulmonary TB (20% deficient and 46.7% insufficient), but it was normal in 33% of them. In 48.1% of female patients, vitamin D level was abnormal (11% deficient and 37% insufficient); and in 51.9% of them, it was normal. Vitamin D level was determined normal for 62.5% of male patients with extra-pulmonary TB (25% deficient and 37.5% insufficient), as well as for 37.5% of female ones. It was also abnormal in 65.5% of female patients (20.7% deficiency and 44% insufficiency) but normal in 34.5% of them. There was 15.8% of vitamin D level deficiency in pulmonary and 22.2% in extra-pulmonary TB, which indicated no statistically significant difference (P>0.05). Vitamin D level insufficiencies for pulmonary and extra-pulmonary TB were 42.1% and 42.2%, respectively, which showed no statistically significant difference (P>0.05). Vitamin D deficiencies for pulmonary tuberculosis and extra-pulmonary tuberculosis were 57.9% and 64.4%, respectively, which suggested no statistically significant difference (P>0.05). The average amount of vitamin D was 31.3 nanogram/ml in pulmonary, and 27.2 nanogram/ml in extra-pulmonary TB, which demonstrated no statistically significant difference (P>0.05) (Table 4).

Vitamin D deficiencies in positive smear TB and negative smear TB were 15.7% and 16.7%, respectively, which revealed no statistically significant difference (P>0.05). Decreased vitamin D in positive smear TB and negative smear TB were 56.9% and 166.7%, respectively, which displayed no statistically significant difference (P>0.05). The average amounts of serum vitamin D were 31.27 nanogram/ml in positive smear TB, and 31.33 nanogram/ml in negative smear TB, which showed no statistically significant difference (P>0.05) (Table 5).

Discussion

According to several studies including a cohort study by Gray et al,[11] the review studies by Talat et al,[12] another review study by Nnoaham and Clarke,[13] as well as the study by Workineh et al,[14] it was discovered that vitamin D deficiency was more common among people with TB. Taking the results from the given studies into account, this study was carried out to determine vitamin D level in patients with pulmonary and extra-pulmonary TB in Karaj, during a period from 2017 to 2018.

Our study result showed that vitamin D level was abnormal in 60.8% (18.6% deficiency and 42.2% insufficiency) of the case study population, but it was normal in 39.2% of the population. Vitamin D deficiency was detected to be 15.8% and 22.2% in pulmonary and extra-pulmonary TB, respectively, indicating no statistically significant difference.

In a study by Wingfield et al (ecologically done in England, 2014), 852 TB patients were examined and it was concluded that 57% of them had low level of vitamin D, and the level was assumed to be even lower among women and in cold seasons.[6]

In another study by Karampini et al, moreover, 65 TB patients whose diagnostic process had been performed during seven earlier months were examined and it was determined that 95% of TB patients suffered from vitamin D deficiency; but there was no considerable difference between men and women in terms of the deficiency. There was also no considerable difference between vitamin D level of extra-pulmonary TB patients and that of pulmonary ones.[15]

In this study, a significant difference was found between abnormal vitamin D level in pulmonary and extra-pulmonary TB based on the gender of patients. It is also worth mentioning that the season was not studied as a goal variable in this study. In an analytical study by Gray et al, 92 patients with TB as well as 236 patients with other diseases were investigated, and it was detected that vitamin D deficiency was more common among TB patients.[11]

In a study by Workineh et al on 126 patients recently diagnosed with smear positive TB, the average amount of vitamin D level in TB patients was determined to be considerably lower than that of control group.[14]

In the cohort study by Talat et al, 129 patients were studied among whom 79% had vitamin D deficiency.[12] Their study, compared to our study, produced more numbers, which could be attributed to the race and climate differences. In a review study by Chocanco-Bedoya and Ronnenberg, a relationship was discovered between vitamin D deficiency and the number of people who was infected with TB. However, more studies are still required to explore this issue thoroughly.[16] Their study results further point to the importance of our study and other similar studies.

In the review study by Nnoaham and Clarke, it was demonstrated that vitamin D level in non-TB people was 70% higher than that of TB patients.

In the meta-analytic study by Huang et al, it was argued that vitamin D deficiency was associated with the increased risk of getting infected by active TB in people with latent TB, as well as with the increased change in tuberculin skin tests. In addition, the downward trend of vitamin D level in patients with active TB – compared to patients with latent TB, was not statistically significant, which demonstrated that vitamin D deficiency was more than a risk factor for tuberculosis.[17] In another study by

Pareek et al on 462 British by descent, it was concluded that the average vitamin D level in patients with extra-pulmonary TB was lower than that of patients with pulmonary TB. It was also revealed that doubling vitamin D level resulted in decreasing the risk of getting infected by extra-pulmonary TB.[18] In this study, however, no relationship was found between vitamin D and different routes of TB infection.

According to Yuvaraj et al, vitamin D level in patients with TB had no statistically significant difference with that of healthy people in control group. Comparing positive smear patients with negative ones, however, an inverse relationship was found between vitamin D serum level and smear positive level.

But in the present study, no significant relationship was detected between vitamin D deficiency and positive or negative smear TB.[19]

Overall, our study result – compared to results from other studies in the field, revealed a vitamin D deficiency in more than half of the pulmonary and extra-pulmonary TB patients in Karaj, which was not associated with the TB type.

Conclusion

In this study, a vitamin D deficiency was found in TB patients (including pulmonary and extra-pulmonary TB) in Karaj, which was not associated with the TB type. Moreover, it was concluded that the vitamin D level in the majority of patients proved insufficient. The findings suggest that patients with pulmonary or extrapulmonary tuberculosis, in addition to medication and antibiotic therapy, need proper health and nutritional care, the use of supplements, sunlight, and proper physical activity to accelerate the healing process.

Authors' Contributions

AS supervised the resaerch. MHDT designed and performed experiments. SSH : performed experiments and write the paper. NA: cowrite the papar. RT: design and performed experiments and wrote the paper.

Ethics Approval

This study was approved by the Ethics Committee of Alborz University of Medical Sciences, Karaj, Iran [IR.ABZUMS.REC.1397.01].

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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