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Vitamin D Status in Women with Tuberculosis

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ABSTRACT
The study was conducted at the Phthisiatry Research-Practice Center in Yakutsk. 70 hospitalized women with confirmed TB diagnosis and 70 women with ruled out TB were observed. Informed consent was obtained from all participants in compliance with an ethics code. Apparently healthy state with no signs of acute diseases or exacerbation of chronic diseases was ensured at enrolment; no one was taking vitamin D at enrolment. Mean ages were 40.9 and 43.3 in respective groups. The study results have shown the presence of vitamin D deficiency in women with TB. Healthy women in our study likewise demonstrated abnormal vitamin D levels. The study results have shown the presence of vitamin D deficiency in women with TB. Healthy women in our study likewise demonstrated abnormal vitamin D levels. Normal vitamin D levels were observed only in 5.7 % of TB patients and in 11.4 % of healthy women.

Keywords: *Vitamin D, tuberculosis, women, Yakutsk*

1. INTRODUCTION

Vitamin D is one of the world's most extensively studied vitamins. Vitamin D deficiency causing huge number of serious health consequences has been observed in many parts of the globe. Until recently, vitamin D deficiency had been linked almost solely to a risk of rickets [11]. Based on latest studies, decreased vitamin D concentration could be potential risk factor for neoplasms [7, 9], cardiovascular diseases [3, 19, 23], diabetes mellitus [14, 17], arterial hypertension [5], autoimmune diseases [15], metabolic disorders [13], infectious diseases, developing due to weakened immunity, including tuberculosis (TB) [10]. High doses of vitamin D were widely used to treat TB during pre-antibiotic era, while vitamin D active metabolite, 1,25-dihydroxyvitamin D, had long been known to enhance immune response against mycobacteria in vitro. Additional administration of vitamin D was shown to result in increased expression of cathelicidine peptide in macrophages, and hence, strengthening of the innate immunity in patients with TB. As a potent modulator of innate immune response, vitamin D acts as co-factor inducing antimycobacterial activity, plays an important role in immune response by stimulating phagolysosomal fusion and by producing LL-37, an antimicrobial peptide with direct bactericidal activity and immunoregulatory function [1, 24].

2. PROBLEM STATEMENT

Problem of tuberculosis in women has been attracting increased interest of TB clinicians lately. Commonly acknowledged truth is that nation's health is dependent on women's health, and women with TB present high epidemiological risk, unlike men, because of closer contact with children [2]. Annually, more than 900 million women are estimated to be infected with *M.tuberculosis*, 2.5 million women – newly diagnosed with TB, and 1 million women – die of TB. Development of active TB disease is influenced by many contributing factors: unfavorable social and economic living circumstances, smoking, alcohol abuse, stress, chronic diseases etc. TB is often associated with nutrient deficiency, including vitamin D deficiency, as well. Correlations between vitamin D deficiency and TB have been increasingly studied lately [16, 21, 25].

Australian study among African immigrants found vitamin D deficiency in 78 % of infected individuals, and lower vitamin D levels were associated with high probability of latent, active, or past TB infection [8]. A study in Castellon, Spain [4] comprising 202 contacts and 42 TB patients showed that only 20.3 % had sufficient serum levels of 25(OH)D (≥30 ng/mL).

Study of vitamin D levels in TB patients from Mwanza, Tanzania, showed the presence of vitamin D hypovitaminosis in 39.6 %; of them, 4.3 % had deficient levels [6].

Case-control study among 166 TB patients and 219 controls in Vietnam showed a 35.4 % prevalence of vitamin D deficiency in males with TB, compared to 19.5 % in control group [12]

A cohort study in Pakistan [18] found low vitamin D levels to be associated with the progression to active TB among healthy family contacts. Median vitamin D level was 9.1 ng/mL in an entire cohort of 128 participants; 9.6 ng/mL in 100 contacts without TB disease; 7.9 ng/mL in 20 patients who developed TB; 4.6 ng/mLin 2 patients with extensive TB who were receiving anti-TB medications at enrolment; 5.1 ng/mLin 6 contacts with a past history of TB. 100 family contacts without TB disease had vitamin D levels, which were significantly higher than in 28 participants with a history of confirmed TB in the past. Median vitamin D levels were significantly lower in 74 female patients, then in 54 male patients. After stratification by vitamin D levels, deficient level was present in 79 % (<20 ng/mL), insufficient level in 14 % (20–30 ng/mL), normal level in 7 % (>30 ng/mL). Vitamin D deficiency in female patients in this cohort presumably could be explained by low socio-economic status, malnutrition, traditional/cultural backgrounds, low exposure to sunlight.

A study in a military hospital in Kharian among 105 TB patients and 255 healthy controls showed mean vitamin D levels of 23.23±6.81 ng/mL (TB cases) and 29.27±8.89 ng/mL (controls), respectively. Vitamin D deficiency was determined in 57 % of TB cases vs. 33 % in control group. Mean vitamin D levels in women with TB were significantly lower (20.84 ng/mL), compared to men (25.03 ng/mL, p=0.002). Meanvitamin D levels in patients with multi-drug resistant TB were lower to a mean of 15.41±4.67 ng/mL (p<0.0001). (Iftikhar R., Kamran S.M., Qadir A. et al., 2013).

A study in Manipal, India sought for associations between vitamin D deficiency and recently diagnosed pulmonary TB among 50 individuals with TB and 50 controls. Serum vitamin D levels were found to be significantly lower in TB patients (19 ng/dL), compared to control group (25 ng/dL). Vitamin D deficiency was present in 27 out of 50 patients with TB (54 %), and only in 13 (26 %) healthy participants. Among TB patients with vitamin D deficiency, 44 % had high AFB counts (AFB 3 +) based on sputum smear microscopy results [22].

Vitamin D deficiency among TB patients is highly prevalent. Based on current research, mean levels of vitamin D in women appear to be lower, than in men. In view of this, we conducted a study on vitamin D levels in women with TB.

3. RESEARCH QUESTIONS

The study was conducted at the Phthisiatry Research-Practice Center in Yakutsk. 70 hospitalized women with confirmed TB diagnosis and 70 women with ruled out TB were observed. Informed consent was obtained from all participants in compliance with an ethics code. Apparently healthy state with no signs of acute diseases or exacerbation of chronic diseases was ensured at enrolment; no one was taking vitamin D at enrolment.

ELISA was performed to determine vitamin D 25(OH) in serum, using assay kits from Euroimmun (Germany). Concentration of serum 25(OH)D was assessed based on the following criteria: optimal level (30–100 ng/mL); abnormal level (20–30 ng/mL); vitamin D deficiency (10–20 ng/mL); severe vitamin D deficiency (less than 10 ng/mL).

Statistical processing was done using IBM SPSS Statistics v24.0 software suite. Descriptive statistics are presented as median with interquartile range: Me (Q1; Q3). Nonparametric Mann-Whitney test was used to do comparisons between groups.

The aim of this paper is to study vitamin D levels in women diagnosed with TB. The methods used in this research are conventional laboratory and clinical study methods, and case-control study design.

4. RESULTS

Table 1. Mean patient age

Parameter	TB patients, n=70	Healthy, n=70	p
Mean age, years	40.94 (19.118)	43.26 (16.466)	0.229

Mean age did not differ between both groups.

Table 2. Serum vitamin D concentrations

	TBpatients	Healthy	p
25(OH)D concentration, ng/mL	16.1 (9.925; 22.078)	14.9 (9.275; 21.34)	0.389

Vitamin D status in women was assessed using clinical guidelines developed by the Russian Association of Endocrinologists, based on international evidence.

Median 25(OH)D concentration was16.1 ng/mL in TB patients, and 14.9 ng/mL in healthy controls, and wasclassified as vitamin D deficiency. No statistically significant differences in serum 25(OH)D levels were found between TB patients and healthy women (p=0.861, Mann-Whitney test).

Table 3. Distribution of vitamin D levels, n (%)

Level	TB patients, n (%)	Healthy, n (%)
0–9.9 ng/mL (severe deficiency)	17 (24.3 %)	24 (34.3 %)
10–19.9 ng/mL (deficiency)	32 (45.7 %)	28 (40 %)
20–29.9 ng/mL (abnormal level)	17 (24.3 %)	10 (14.3 %)
30–70 ng/mL (normal level)	4 (5.7 %)	8 (11.4 %)

Table 4. Clinical forms of tuberculosis, n (%)

Diagnosis	n=70 (%)	Mean vitamin D level
Focal TB	10 (14.3 %)	17.6
InfiltrativeTB	45 (64.3 %)	17.2
DisseminatedTB	8 (11.4 %)	17.5
Other	7 (10 %)	17.07

Women with 25(OH)D deficiency made majority both among TB patients and among healthy women: 45.7 % (32) and 40 % (28), respectively. Interestingly, severe deficiency was observed more often in healthy women (34.3 %; 24). Normal levels of 25(OH)D were observed only in 5.7 % of TB patients and in 11.4 % of healthy women.

Mean 25(OH)D levels in all clinical forms of TB were consistent with vitamin D deficiency.

5. CONCLUSION

The study results have shown the presence of vitamin D deficiency in women with TB. Healthy women in our study likewise demonstrated abnormal vitamin D levels. Normal vitamin D levels were observed only in 5.7 % of TB patients and in 11.4 % of healthy women.

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