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SHORT COMMUNICATION

Relationship between vitamin D levels and brucellosis: a case-control study from Sanandaj, Iran

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ABSTRACT

Background and Objectives: Brucellosis is a zoonotic disease that is caused by the *Brucella* species. This disease is common in Iran and its incidence is increasing .This study measures serum vitamin D levels in patients with brucellosis and healthy people.
Materials and Methods: This research was conducted as a case-control study at Tohid Hospital, Sanandaj, Iran. The calculated sample size included 90 patients in the case group and 90 patients in the control group. The measurement of vitamin D levels in the case and control groups were performed by ELISA.
Results: The mean serum vitamin D level was 19.91 ng/ml in the case group and 22.87 ng/ml in the control group. (Serum vitamin D level <10 ng/mL is accepted as deficiency, 10-30 ng/mL as insufficiency, 30-100 ng/mL as sufficiency, and >100 ng/mL as toxicity).
Conclusion: There was no significant difference between the two groups in terms of vitamin D deficiency (p-value=0.097).

Keywords: Brucellosis; Vitamin D

INTRODUCTION

Brucellosis is a zoonotic disease that is caused by different species of *Brucella*. It is the most common zoonotic disease in the world (1). This disease is common in Iran and its incidence is increasing (2, 3). The four common species of *Brucella* are *B. abortus*,

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B. melitensis, *B. canis*, and *B. suis* (4). Brucellosis stimulates humoral and cellular immune systems. Antibodies facilitate phagocytosis by polymorphonucleocytes and phagocytes. Phagocytosed bacteria can survive in macrophage cells and cause persistent intracellular infections (5, 6). Vitamin D receptors are present on the surface of all immune cells, including supportive T cells, B cells, neutrophils, and macrophages (7). Vitamin D is a potent immunomodulator of the immune system. Macrophages and monocytes that are exposed to bacterial lipopolysaccharides or *Mycobacterium tuberculosis* express an upregulation in the vitamin D receptor gene as well as in the enzyme synthesizing vitamin D. The increase in the production of vitamin D leads to the synthesis of cathelicidin, which is a peptide that is able to eliminate *Mycobacterium tuberculosis* and other infectious agents (8-10). This study compared serum vitamin D levels between healthy people and patients with brucellosis to determine the potential role of vitamin D in the control of the disease.

MATERIALS AND METHODS

Our study was a case-control study that was conducted at Tohid Hospital, Sanandaj, Iran, which is also a province with a high incidence of brucellosis. The study was approved by the Ethics Committee of Kurdistan University of Medical Sciences (MUK. REC.1392.98). The calculated sample size included 90 patients in the case group (infected with brucellosis) and 90 patients in the control group (not infected with brucellosis). The measurement of vitamin D was performed using the ELISA method using IDS kits known as EUROIMMUN, which are manufactured in Germany from blood serum samples. All patients with brucellosis symptoms (fever, chills, sweating, fatigue, muscle aches, weakness, headache, and/or anorexia), Wright test ≥ 1.160, 2ME ≥ 1.80; and Coombs-Wright ≥ 1.80, were enrolled into this study. The subjects in the control group were selected from among those who were referred to the hospital laboratory for routine and periodic checkup tests and those who were not infected with brucellosis. The inclusion criteria for the control group were as follows: no brucellosis symptoms, no history of brucellosis, and negative brucellosis serology. Only those aged 12 years and older were enrolled into this study. The exclusion criteria were a history of vitamin D intake, a history of rheumatologic diseases, other bone, or articular diseases, and a history of calcium intake. Considering an accuracy of 5%, a power of 85%, a mean vitamin D level of 35 ng/ml in non-brucellosis group and 26 ng/ml in brucellosis group, and a standard deviation of 20 ng/ml, the calculated sample size was 90 subjects in each group. The subjects in the control group were matched in terms of age (equal to or less than 40 years of age and greater than 40 years of age), gender, and location (urban or rural).

Statistical analysis. A questionnaire was completed by subjects from both the case and control groups; and the collected data was entered into SPSS (ver 16). The variables were described using tables and charts. The Chi-square test was used to compare the qualitative variables between the two groups. The T-test was used to compare the quantitative values. Then, multiple regression was used to determine the factors affective for the serum vitamin D levels.

RESULTS

Of all, 58 patients (64.4%) were male and 32 patients (35.6%) were female; the same ratio of male to female subjects was studied in the control group. Concerning the area of residence, 27 patients (30%) lived in urban areas and 63 patients (70%) lived in rural areas. The mean and standard deviation of serum vitamin D levels was 22.87 ± 13.23 ng/ml in the case group and 19.91 ± 10.43 ng/ml in the control group (p=0.097). The mean and standard deviation of vitamin D level was 22.72 ± 13.68 ng/ml in people living in in urban areas and 20.08 ± 11.19 ng/ml in people living in rural areas (p=0.334; Table 1).

After adjusting for other factors, the results of multivariate analysis showed no relationship between serum vitamin D levels and age, suggesting that with aging, there is an increase in the level of vitamin D deficiency. The results of this study showed no statistically significant correlation between vitamin D level and brucellosis; however, it is worth noting that the observed value was close to the level of significance (p=0.069; Table 2).

DISCUSSION

In this study, the mean serum vitamin D level

Table 1. Comparison of variables in the two studied groups

Variable	Controls (N=90)	Cases (N=90)	P-value
sex Male	58 (64.4%)	58 (64.4%)	1†
Female	32 (35.6%)	32 (35.6%)	
Location			
Urban	27 (30%)	27 (30%)	1†
Rural	63 (70%)	63 (70%)	
Vitamin D (ng/ml)	22.87 (±13.23)	19.91 (±10.43)	0.097††

† Chi-square test was used.

†† Independent t test was used.

(Serum vitamin D level <10 ng/mL is accepted as deficiency, 10-30 ng/mL as insufficiency, 30-100 ng/mL as sufficiency, and >100 ng/mL as toxicity).

was 22.87 ng/ml in the case group and 19.91 ng/ml in the control group, but there was no statistically significant difference between them (t=0.477, p value=0.097). The levels of vitamin D were insufficient in all subjects 21.97 ng/ml and for male subjects 21.07 ng/ml (t=0.477, p-value=0.634). In a study that investigated the effect of vitamin D on people with chronic hepatitis, it was found that vitamin D was effective in treating HCV and improved the treatment process (11). Salahuddin et al. found that consumed vitamin D supplementation accelerated clinical recovery with the results showing the role of vitamin D in the treatment of tuberculosis (12). Murdoch et al. investigated the effect of vitamin D supplements on upper respiratory tract infections in 322 healthy subjects. In their study, vitamin D with a dosage of 20,000 units was administered to patients and it was found that vitamin D was not effective in reducing the incidence of upper respiratory tract infections and did not affect its severity (13). Behice et al. showed that a significant difference was not found among clinical forms of the disease, vitamin D, and VDR levels (14). We expected that vitamin D would control brucellosis disease. In addition, we also expected to observe lower levels of Vitamin D in patients with brucellosis, but serum vitamin D levels did not differ significantly between both groups in this study. Based on the results of our study, serum vitamin D levels in patients with brucellosis and healthy subjects are not different. In other words, *Brucella* infection is probably a type of infection that is not affected by serum vitamin D levels. Based on the aforementioned, it seems necessary to conduct a future study to simultaneously measure the levels of TNF-γ or TNF-α, and vitamin D in the group with brucellosis and healthy subjects, and then compare them with each other to better make definitive statements about the effects of vitamin D on the cytokines expressed in brucellosis.

CONCLUSION

There was no significant difference between the two groups of cases and controls in terms of vitamin D deficiency (p-value=0.097). Depending on the type of infection and subsequent diseases, vitamin D has a different effect on cytokines. Moreover, vitamin D deficiency does not make a person vulnerable to brucellosis infection. However, it is necessary to conduct a future study to measure serum vitamin D levels and related cytokines (INF-gamma, TNF-a) in brucellosis patients and healthy subjects.

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Table 2. Relationship between vitamin D and brucellosis after adjusting for other factors

Variables	Unstandardized Coefficients		Standardized Coefficients	P-value	95.0% Confidence Interval for B	
	B	Std. Error	Beta		Lower Bound	Upper Bound
Constant	27.775	3.041		<0.001	21.774	33.777
Age	-0.109	0.055	-0.148	0.048	-0.218	-0.001
Sex	-1.298	1.854	-0.052	0.485	-4.958	2.362
Location	1.718	1.931	0.066	0.375	-2.093	5.528
Group	-3.248	1.772	-0.136	0.069	-6.745	0.250

The level of vitamin D was considered as the dependent variable.

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