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Research Article

Association of Serum Vitamin D Levels with the Risk of Suicidal Behavior in Ilam, Iran: A Brief Report

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Abstract

There are conflicting reports on the effect of serum vitamin D (VD) levels on the development of suicidal behavior. VD deficiency is prevalent in Ilam province, and this region has the highest suicide mortality rate in Iran. The present study aimed to evaluate a possible association between serum VD levels and the risk of suicide among the inhabitants of Ilam province. A total of 157 suicide attempters (case group) and 314 age- and sex-matched individuals (control group) without a history of suicide attempts were recruited into the study. Suicide attempters were admitted to the Emergency Department of Ilam Shahid Mostafa Khomeini Hospital (Ilam, Iran) between March 2018 and March 2019. The individuals in the control group were randomly selected from those referred to various medical laboratories in Ilam during the same period. The participants in both groups were aged 18-35 years, and none had a history of kidney, liver, or endocrine diseases. Serum VD levels were measured using the enzyme-linked immunosorbent assay method. Categorical and continuous variables were compared using the Chi square test and independent samples t test, respectively. Serum VD level in the control group (31.5±0.2 ng/mL) was significantly lower than in the case group (43.1±0.1 ng/mL) (P<0.001). The results of logistic regression analysis showed that an increase in serum VD score was associated with an increase in the likelihood of suicide attempts (OR=1.05, 95% CI=1.03-1.06, P<0.001). Our findings confirmed the role of VD deficiency in the development of suicidal behavior. However, it is not a significant factor in its pathogenesis

Kew Words: suicide; attempted; vitamin d deficiency; iran

Introduction

Suicide is a preventable public health problem with an estimated 800,000 deaths worldwide per year. [1] Development of suicidal behavior is associated with social, environmental, psychological, and biological risk factors. [2,3] A previous study reported a higher suicide rate in geographical areas with less exposure to solar ultraviolet radiation. [4] Vitamin D (VD) is synthesized in the skin by exposure to sunlight. Hence, researchers have been interested in evaluating the association between the risk of suicidal ideation and VD deficiency. VD is fat-soluble and can easily cross the blood-brain barrier, and its receptors are broadly expressed in the brain. [5] VD deficiency has been associated with symptom severity in patients with mood disorders (depression, bipolar disorder) and schizophrenia. [6] Previous studies showed a strong correlation between VD deficiency and increased risks of suicide. [7-9] In contrast, a study in Korea did not observe a significant association between VD and suicide ideation in Korean adults. [10]

Ilam province, at the of Iran, has the highest suicide mortality rate (19.53 per 100,000 population) in Iran. [11] It is also reported that VD deficiency and insufficiency are highly prevalent in this province. [12] Hence, the present study aimed to evaluate a possible association between serum VD levels and the risk of suicide in Ilam province.

Patients and Methods

A total of 157 suicide attempters (94 men and 63 women) aged 18-35 years were recruited in the study. These individuals (case group) were admitted to the Emergency Department of Ilam Shahid Mostafa Khomeini Hospital (Ilam, Iran) between March 2018 and March 2019. In addition, 314 age- and sex-matched controls (124 men and 190 women) who were referred to various medical laboratories in Ilam during the same period were recruited. A questionnaire was used to collect demographic characteristics. Participants

with a history of kidney, liver, or endocrine diseases were excluded. The study protocol was approved by the Ethics Committee of Ilam University of Medical Sciences, Ilam, Iran (code: IR.MEDILAM.REC.1398.165). Written informed consent was obtained from all participants.

A blood sample from each participant was collected between 8-10 AM and allowed to clot at room temperature for 60 min. The samples were then centrifuged at 3,500 rpm for 10 min to obtain serum supernatant. Sera were then stored at -20 °C until analysis. Serum VD was measured quantitively using an enzyme-linked immunosorbent assay kit (b213966, Abcam, Cambridge, MA, USA) according to the manufacturer's instructions. Briefly, dissociation buffer was added to wells coated with donkey anti-sheep IgG antibody. Then, standards and samples were added to the wells, and dissociation of VD from its binding protein was allowed to occur. A solution of alkaline phosphatase-conjugated VD was added followed by a solution of sheep monoclonal antibody VD complex. After one hour of incubation at room temperature, the wells were washed, and a p-Nitrophenyl Phosphate (pNpp) substrate solution was added. The plate was incubated for 30 min at room temperature, and then stop solution was added. Finally, the resulting yellow color was detected optically at 405 nm. Results of serum VD were classified as severe VD deficiency (<12 ng/mL), moderate VD deficiency (<20 ng/mL), VD insufficiency (<30 ng/mL), and VD sufficiency (D≥30 ng/mL). [13]

Statistical Analysis

GraphPad Prism 8 software (GraphPad Software, USA) and SPSS 18.0 software (IBM, USA) were used for graphics and data analysis. Categorical and continuous variables were compared using the Chi square test and independent samples *t* test, respectively. The matching of variables was based on age and sex. Logistic regression analysis was performed to ascertain the effects of serum VD. P values<0.05 were considered statistically significant.

Results

Per one suicide attempter, two controls were randomly selected and matched by age and sex (314 controls, 157 suicide attempters). The mean age of the participants in the case and control groups was 26.6±6.1 and 26.9±8.2 years, respectively, which was not statistically significant (P=0.971). Mean serum VD levels in the case and control groups are shown in **figure 1.** The mean serum VD level in the control group (31.5±0.2 ng/mL) was significantly lower than in the case group (43.1±0.1 ng/mL) (P<0.001). Moreover, in the control group, the serum VD level in men (33.7±0.3 ng/mL) was significantly higher than in women (30.13±0.1 ng/mL) (P<0.001). Similarly, in the case group, serum VD level in men (48.7±2 ng/mL) was significantly higher than in women (34.7±1.6 ng/mL) (P<0.001). Moreover, for both male and female participants, the mean male and female serum VD levels in the case group were significantly higher than in the control group (P<0.001).

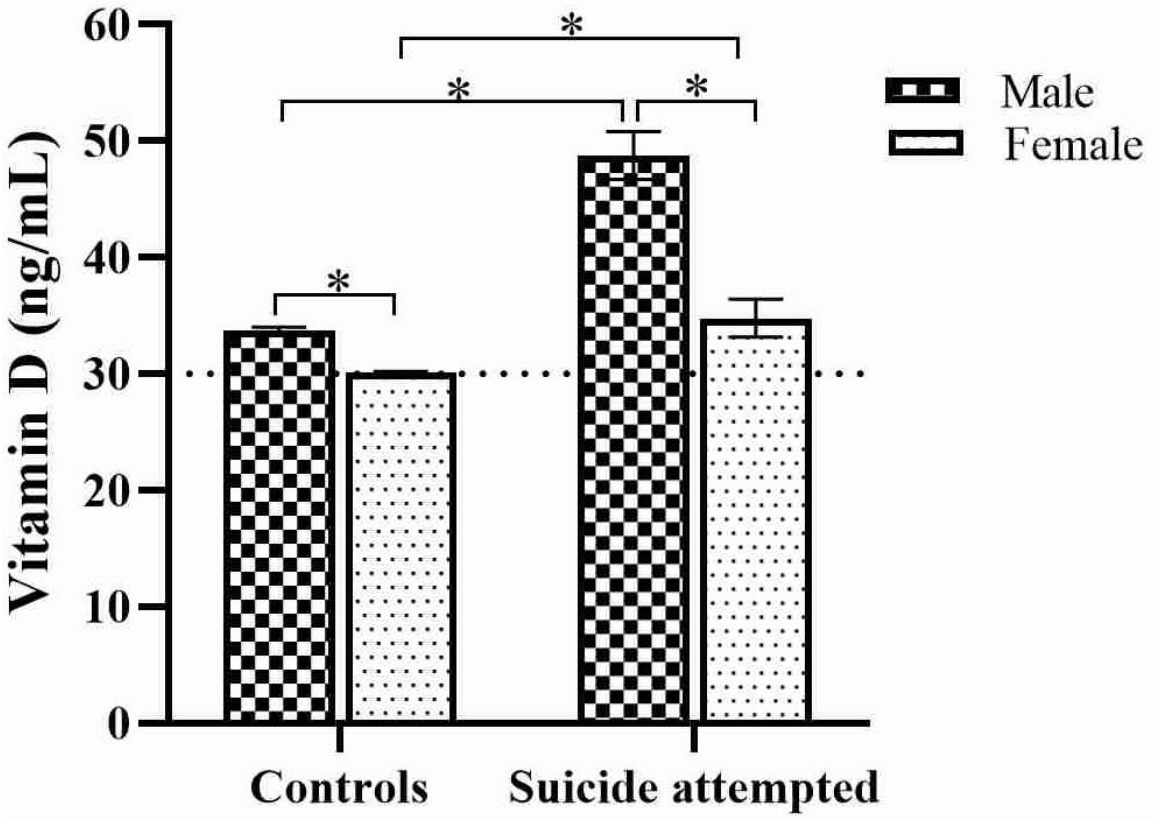

Figure 1. The graph shows the serum vitamin D levels in the control and case groups. *Significant difference between the groups (P<0.001). Values are expressed as mean±SEM (standard error of the mean).

The frequency of severe and moderate VD deficiency in the control group was 10 (3.2%) and 41 (13.0%), respectively. The frequency of severe and moderate VD deficiency in the case group was 2 (1.3%) and 16 (10.2%), respectively. Logistic regression analysis was performed to ascertain the effects of serum VD and VD status in the case group compared to the control group. The increase in serum VD scores was associated with an increase in the likelihood of suicide attempts (OR=1.05, 95% CI=1.03-1.06, P<0.001) (**table 1).**

Variable	β	OR	95% CI		P value
			Lower	Upper	
Serum VD	0.048	1.050	1.032	1.067	<0.001
Severe VD deficiency (<12 ng/mL)	-	-	-	-	-
Moderate VD deficiency (<20 ng/mL)	0.187	1.20	0.235	6.17	0.822
VD insufficiency (<30 ng/mL)	-0.054	0.277	0.348	1.92	0.227
VD sufficiency (≥30 ng/mL)	-0.965	0.503	0.570	2.95	0.570
VD: Vitamin D; OR: Odds ratio; CI: Confidence interval; P<0.05 was considered statistically significant.					

Discussion

The results showed a high frequency of moderate VD deficiency and a low frequency of severe VD deficiency in the control and case groups, respectively. The difference in the frequency of severe and moderated VD deficiency between the groups was not statistically significant. However, for both men and women, the mean serum VD level in the case group was significantly higher than in the control group.

Previous studies indicated that severe VD deficiency increased the risk of suicide. Umhau and colleagues evaluated the suicide rate among US military personnel and reported a higher risk of suicide in African Americans than other ethnicities. Given very low serum VD levels (<15.5 ng/mL) in African Americans, they concluded VD deficiency may play a role in increased risk for suicide. [8] Fond and colleagues also reported that serum VD levels below 10 ng/mL increased the severity of symptoms and risk of suicide in schizophrenia patients. [7] In another study, Gokalp and colleagues reported lower serum VD levels in those who attempted suicide (12.3±6 ng/mL) than the controls (19.4±10 ng/mL). [14] In a study of suicide ideation among Korean adults, Kim and colleagues concluded that serum VD levels higher than 10 ng/mL did not impact suicidal ideation. However, lower levels significantly increased the risk of suicide. [15]

In line with a previous study in Ilam (Iran) that reported VD deficiency is prevalent in this province, [12] we found a higher frequency of VD deficiency in the control group. Furthermore, the frequency of severe VD deficiency in the case and control groups were the same, confirming the effect of VD on the risk of suicide. The results also showed that only a small portion of those in the control and case groups were suffering from severe VD deficiency. This means that VD deficiency is not a significant factor in the pathogenesis of suicidal behavior in Ilam province.

Conclusion

VD deficiency plays a role in the development of suicidal behavior; however, it is not a significant factor in its pathogenesis. Further studies are required to identify the main risk factors associated with the high suicide mortality rate in Ilam province.

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Authors' Contribution

M.B: Study design, acquisition of data, and the draft version of the manuscript. S.A and Y.M: Acquisition of data. Y.V: Data analysis. S.S: Study design, data analysis and interpretation, the draft version of the manuscript. All authors were involved in reviewing the manuscript for important intellectual content and final approval for publication. They agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest:

None declared.

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