The Association between Depression and Vitamin D and Parathyroid Hormone Levels in Adolescents

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Abstract

Background: Depression, a challenging disorder, affects 1–6% of adolescents and early onset often predicts more serious manifestations in later life. Elevated Parathyroid hormone (PTH), parathormone levels have reported among adults with depression. In this study, the roles of 25(OH) D (vitamin D) and parathormone during adolescence, in which the frequency of depression is high, were studied.

Materials and Methods:
Patients who were followed-up jointly at both clinics and whose 25(OH) D and PTH levels were evaluated and questioned "Depression Scale for Children" for depression at the same time, were included in the study. Cases’ socio-demographic data, 25(OH) D and PTH levels and Depression Scale’ scores were recorded.

Results: Depression was diagnosed in 35 (25.3%) of the 138 patients. No differences were found between vitamin D and parathormone in terms of age and gender in groups either with or without depression. Negative correlation was found between the vitamin D levels and depression score in the group with depression (r=-0.368; P=0.03). A significant and positive correlation was found between the PTH levels and depression score (r=0.399; P=0.018). A significant and negative correlation was found between 25(OH) D and PTH levels.

Conclusion:
Even if clinical depression is absent, the frequency of depressive symptoms is increased with decreased vitamin D levels and increased PTH levels, independent of other factors. The prevention of depression, specifically in adolescents, is important to decrease possible suicidal and homicidal thoughts that might arise during adulthood, and substance abuse. Maintaining vitamin D support during adolescence, as with the first year of life, is necessary for both the prevention and treatment of depression.

Key Words: Adolescents, Depression, Vitamin D, Parathormone, Prevention.


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1-INTRODUCTION
Depression is a challenging disorder and its treatment is frequently difficult. Although seen less frequently in childhood, its incidence rises markedly with adolescence. The reason for this is that during the adolescence period, biological, psychological and social change is accelerated and starts to interact intensely with each other as the adolescent attempts to establish a place in the social world and tries to create and realize his/her own plan and aims. Currently, a larger number of adolescents have been reported as having mental health problems (1). Depression affects 1–6% of adolescents worldwide and early onset often predicts more severe manifestations later in life (2, 3). Depression in adolescents is very important since it increases the risk of suicidal behavior, homicidal ideation, cigarette smoking and addiction to alcohol and other substances during late adolescence and adulthood (4, 5). Adolescence is also a period in which mental health problems are evaluated relatively less frequently. In addition, centers for adolescents’ mental health problems are inadequate both in terms of quantity and quality. Prevalence of mental health problems among adolescents and a demonstration of its associated factors are important for both planning and offering mental health services. Although it is an important health problem, the number of studies on depression in adolescence remains inadequate.

25(OH) D is a solid and a reliable marker of body vitamin D that reflects both food ingestion and synthesis is the skin (6). 25(OH) D provides calcium and phosphate balance together with parathormone (PTH) (7). In addition, vitamin D receptors have been found in the areas of the brain related with the development of depression (8). The association between vitamin D and depressive findings and other psychiatric diseases has been investigated (9). A high concentration of vitamin D receptors can be found in the amygdala, a region that controls emotions and behavior in humans, the thalamus, the hypothalamus, the dorsal raphe nucleus, the dorsal nucleus of the vagus nerve and motor neurons located both cranially and spinally, suggesting effects on sensory pathways, the endocrine-autonomic system and the motor system (8). Thus, symptoms of depression such as fatigue, mood regulation, motor function and pain, might be related to effects of vitamin D deficiency. Two prospective studies have found that a higher concentration of 25(OH) D in older adults were associated with a lower risk of depression (10). In addition, some studies (9, 10, 11) have reported higher PTH among adults with depression.

Although there has been research on the association of 25(OH) D and depression in adolescence, to our knowledge, no study has been published evaluating the role of 25(OH) D together with adolescent depression and PTH levels. While common, serum 25(OH) D and PTH abnormalities are highly treatable, which may enable the prevention of depression. Examining this association in childhood/adolescence is important because confounding by alcohol, smoking and mood-altering drugs is somewhat less likely than in adult studies and also, because it is increasingly recognized that depression can emerge in childhood/adolescence (3) and its prevention may be best started at this age. The objective of this study, which was designed to consider the reasons defined above, and to define the role of 25(OH) D and PTH during adolescence, in which the frequency of depression is high.

2-MATERIALS AND METHODS
2-1.Participants
For this study the medical records of the Adolescent Clinic and Child Psychiatry Clinic of the Medical School of Dicle
University, Diyarbakır-Turkey, were used, retrospectively. Patients who were followed-up jointly at both clinics and whose 25(OH) D and PTH levels were evaluated and questioned for depression at the same time, were included in the study. The consent form of the local ethics committee was received.

2-2. Clinical evaluation form
The sociodemographic data collected with these forms were gender, age, whether parents were alive, ages of parents, level of education, birth order of the child, presence of chronic disease, presence of trauma history, school success, regular drug use, body perception and regular physical exercise. Also, the 25(OH) D and PTH levels were recorded.

2-3. Depression Scale for Children (DSC)
The Depression Scale for Children is a self-evaluation scale developed by Kovacs (12) that can be applied for children between six and 17 years of age. It is completed either by reading the scale to the child or being read by the child. The scale including 27 items and there are three options for each item. The child is asked to choose the sentence that best describes him/her during the previous two weeks. Each item is given points, such as 0, 1, or 2, according to the severity of the symptoms; the highest point is 54. High points reflect the level or severity of the depression and the cut-off point of the scale is 19. The DSC scores for each case are recorded. A point of equal or more than 19 in DSC was accepted as “depression present” and scored as 1 and other points were accepted as “no depression” and scored as 0.

2-4. Parathormone (PTH) level
This was determined using ElectroChemiLuminescence (ECLIA) on Cobas e411 (Roche Diagnostics International Ltd, Basel, Switzerland).

2-5. 25(OH) D level
This was determined briefly using the High Performance Liquid Chromatography (HPLC) method and conducted using a Shimadzu model 20AT LC system (Chiyoda-Ku, Tokyo, Japan) equipped with one pump (LC-20AT), a 20 µL injection loop, column oven (CTO-10AS), and UV detector (SPD-20A). The system was controlled through a system controller (SCL-10A) and a personal computer, on which the CLASS-VP 5.0 chromatography workstation and a data processing system (Shimadzu, Kyoto, Japan) had been installed. The analytical separation was accomplished using a Shimadzu's VP-ODS columns with size of 250 mm × 4.6 mm and particle 5 micrometer (µm). The mobile phase was a mixture of methanol and double-distilled water (65:35, v/v). The flow rate was 2.0 mL/min and the column temperature was 30°C. The column effluent was monitored at 264 nm.

2-6. Data Analyses
The statistical evaluation was conducted using SPSS 16.0. Chi-square test and t-test were used for categorical variables and continuous variables, respectively. Regression analysis was applied to detect the level and direction of the association, which was detected in the group with depression. Separate regression analyzes were performed for the known risk factors for depression. P<0.05 was accepted as statistically significant.

3- RESULTS
Depression was diagnosed in 35 (25.3%) of the 138 patients participating in this study. No differences were present in terms of age and gender between the groups either with or without depression. In addition, no differences were found between the groups in terms of ages of the parents, number of siblings, birth order of the child, the presence of chronic disease, history of trauma, school success, regular
drug use, body perception and regular physical exercise (Table 1 and 2). The mean depression score of the group with depression was 24.06 ± 4.98 while it was 9.42 ± 4.56 in the group without depression.

No significant difference was found in the vitamin D levels between the groups (P=0.602). Nevertheless, while no correlation was found between vitamin D levels and depression score in the group without depression (r=0.03; P=0.749), a negative correlation was found between the vitamin D levels and depression score in the group with depression (r=-0.368; P=0.03). Regression analysis was conducted to detect the level and direction of this correlation in the group with depression. No significant result was found in the regression analyzes performed separately with known risk factors for depression. No statistically significant results were found when the groups were evaluated in terms of PTH. Nevertheless, a statistically significant and positive correlation was found between the PTH levels and depression score (r=0.399; P=0.018). The correlation between depression scores and 25(OH) D or PTH and is demonstrated in (Figure 1). A significant and negative correlation was found between 25(OH) D and PTH levels (r=-0.468; P=0.005).

Table 1: The Comparison of patients with and without depression in terms of numeric data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with depression mean± SD (n=35)</th>
<th>Patients without depression mean± SD (n=103)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case’ age (year)</td>
<td>12.79±1.87</td>
<td>12.73±1.81</td>
<td>0.869</td>
</tr>
<tr>
<td>Maternal age (year)</td>
<td>39.26±7.13</td>
<td>38.71±6.59</td>
<td>0.733</td>
</tr>
<tr>
<td>Paternal age (year)</td>
<td>43.04±7.58</td>
<td>42.93±6.61</td>
<td>0.946</td>
</tr>
<tr>
<td>Number of siblings</td>
<td>5.2±2.55</td>
<td>5.45±2.47</td>
<td>0.614</td>
</tr>
<tr>
<td>25(OH)D level (ng/ml)</td>
<td>14.7±7.4</td>
<td>14.04±4.41</td>
<td>0.602</td>
</tr>
<tr>
<td>PTH level (ng/ml)</td>
<td>44.7±21.7</td>
<td>44.4±22.1</td>
<td>0.937</td>
</tr>
</tbody>
</table>

Table 2: The Comparison of patients with and without depression in terms of categoric data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with depression (n, %)(n=35)</th>
<th>Patients without depression (n, %)(n=103)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>21(60)</td>
<td>48(47.5)</td>
<td>0.205</td>
</tr>
<tr>
<td>Male</td>
<td>14(40)</td>
<td>53(52.5)</td>
<td></td>
</tr>
<tr>
<td>The presence of known diseases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11(31.4)</td>
<td>40(38.8)</td>
<td>0.435</td>
</tr>
<tr>
<td>No</td>
<td>24(68.6)</td>
<td>63(61.2)</td>
<td></td>
</tr>
<tr>
<td>Trauma story</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3(8.8)</td>
<td>12(11.8)</td>
<td>0.637</td>
</tr>
<tr>
<td>No</td>
<td>31(91.2)</td>
<td>90(88.2)</td>
<td></td>
</tr>
<tr>
<td>School performance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>16(45.7)</td>
<td>46(46)</td>
<td>0.756</td>
</tr>
<tr>
<td>Mild</td>
<td>16(45.7)</td>
<td>39(39)</td>
<td></td>
</tr>
<tr>
<td>Well</td>
<td>3(8.6)</td>
<td>15(15)</td>
<td></td>
</tr>
<tr>
<td>Drug use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5(15.2)</td>
<td>15(15.3)</td>
<td>0.983</td>
</tr>
<tr>
<td>No</td>
<td>28(84.8)</td>
<td>83(84.7)</td>
<td></td>
</tr>
<tr>
<td>Body image</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>13(37.1)</td>
<td>31(31)</td>
<td>0.726</td>
</tr>
<tr>
<td>Positive</td>
<td>15(42.9)</td>
<td>51(51)</td>
<td></td>
</tr>
<tr>
<td>No comment</td>
<td>7(20)</td>
<td>18(18)</td>
<td></td>
</tr>
<tr>
<td>Regular sportive activities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15(42.9)</td>
<td>48(46.6)</td>
<td>0.702</td>
</tr>
<tr>
<td>No</td>
<td>20(57.1)</td>
<td>55(53.4)</td>
<td></td>
</tr>
</tbody>
</table>
**Figure 1**: The correlation between depression scores and 25(OH) D levels or PTH levels

4- DISCUSSION

Adolescence is a period in which the tendency to depression is relatively increased due to sudden changes in feelings, thoughts and social relations. Adolescents with depression may exhibit signs such as social withdrawal, decreased attention and efficacy, impairment in relations with friends, decrease in school success, truancy and abandoning home, a tendency for substance and alcohol use and suicidal thoughts and attempts. These signs increase the risk of suicidal behaviors, homicidal thoughts, cigarette smoking, and addiction to alcohol and other substances (13, 14). It is remarkable that with adolescents, alcohol and substance addiction starts at a mean of 4.5 years after the depressive disorder begins; therefore the prevention of depression during adolescence provides an important opportunity for deterring addiction in adulthood (15). Thus, the definition of factors that might cause depression in adolescence is the first step in the treatment. Depression can result from genetic, hereditary, biological, psychosocial, and nutritional factors. One of the important factors contributing to depression is nutritional deficiencies; specifically a deficiency of niacin, omega fatty acids, iron, zinc, vitamin C, selenium, and folic acid (16). Evidence from studies on animals also supports the role of vitamin D in the expression of monoamines likely to be involved in depression, including norepinephrine, serotonin and dopamine (17, 18). Hoogendijk et al. (9) showed that in the elderly a decreased level of vitamin D and increased PTH correlates with the incidence of depression and its severity. However, in this study, the association of depression, vitamin D and PTH was investigated in adolescents.
Vitamin D deficiency is a worldwide problem that has been common in one third to half of the adult population of both developing and developed countries (19). Yet, recent investigations have revealed that dermal synthesis does not satisfy the daily requirements of the body for this vitamin and various factors, including latitude, insufficient exposure to sunlight, seasonal characteristics, the use of sun-blocking creams, and different types of clothing may result in the insufficient intake of vitamin D (20, 21). In a recent study conducted in Turkey (22), negative correlations were observed between vitamin D levels and season and also between vitamin D levels and age. The need for Vitamin D increases due to rapid growth during adolescence. The presence of Vitamin D deficiency during adolescence, in which there is already a tendency for depression, is high and increases the dilemmas of the periods.

Studies conducted on adults with depression, their children, and adolescents with depression, has demonstrated that family relations were more conflicted and negative, communication problems were encountered more frequently, feelings were expressed less frequently and a reduced presence of supportive behavior (15, 23). In addition, it has been reported that for children whose mothers had insufficient basic functions, the risk increases for any psychiatric disorder, independent of the mother’s psychiatric condition (24). In this present study, no significant difference was found in terms of the family environment between the two groups.

Depressive disorders are more frequently seen in women. On the other hand, the role of gender in adolescents varies according to age. In many investigations gender has been reported not to be an important factor until late adolescence. On the other hand, during late adolescence, the females are reported as carrying a two-fold risk of depression compared with males (25, 26). In this present study, there was no significant difference in terms of gender between the two groups. Chronic diseases or the presence of regularly used drugs may increase signs of depression but no difference was detected in this present study.

The risk of new attacks has been demonstrated to increase in adolescents with depression and in adolescents with a low self-esteem, compared with normal controls even after treatment (15). The adolescents’ sense of self was similar between the two groups in this present study. This might be due to the mildness of the complaints in many of the cases.

A number of epidemiological studies have found associations between 25(OH)D concentrations and depression, independent of lifestyle and health factors (27-30). Many of these studies were conducted in middle-aged to elderly adults, due to the limited data available for adolescents (31). In this present study, the depression score was negatively correlated with vitamin D levels and positively correlated with PTH, independent of health problems and life-style in adolescents.

Studies have demonstrated higher PTH levels in adults with depression, while for the first time Anna et al. (2) established results that supported the presence of a relation between depression and vitamin D in adolescents. To our best knowledge, it is this present study that evaluates the association of depression with PTH in addition to vitamin D in the adolescent population.

5- CONCLUSION

In conclusion, even if clinical depression is absent, the frequency of depressive symptoms is increased with decreased vitamin D levels and increased PTH levels, independent of other factors. The prevention of depression, specifically
in adolescence, is important to decrease possible suicidal and homicidal thoughts that might arise during adulthood, and cigarette smoking and addiction to alcohol and other substances. Maintaining vitamin D support during the adolescence, as with the first year of life, is necessary for both the prevention and treatment of depression.

6- CONFLICT OF INTEREST: None.
7-ACKNOWLEDGMENT
There is no acknowledgment and grants received by authors.

8-REFERENCES
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Depression and Vitamin D Levels


