Vitamin D status among adolescent females with polycystic ovary syndrome

Abstract. Background. Polycystic ovary syndrome (PCOS) is a complex disorder affecting the hypothalamic-pituitary-ovarian axis and leading to menstrual irregularities and hyperandrogenism. Studies have suggested that low vitamin D levels may play a role in the pathogenesis of PCOS. There is currently insufficient data regarding association of serum vitamin D levels and PCOS in adolescent females. The purpose of the study was to compare 25-hydroxyvitamin D levels in adolescent females with and without PCOS. Materials and methods. Participants were categorized as having PCOS or as controls based on National Institutes of Health PCOS diagnostic criteria. Exact logistic regression analysis was done to compare normal (≥ 30 ng/mL) versus low (< 30 ng/mL) serum 25(OH)D levels in the PCOS and control groups. Data regarding the participant’s age, body mass index (BMI) percentile, serum 25(OH)D levels, and the season the blood was drawn were recorded in the database. Results. Eighty-two participants (32 were in the PCOS group and 50 were in the control group) met the inclusion criteria and were categorized as either PCOS or control. All participants in PCOS group had BMI greater than the 85th percentile. Therefore, participants with BMI percentile of less than 85th in the control group were excluded from analysis. The mean age of participants was 17.3 years. Vitamin D deficiency and insufficiency were frequently diagnosed in our study population. Sufficient 25(OH)D levels were found in only 7 of 82 participants (8.5 %). The majority of participants with BMI greater than 95th percentile were vitamin D deficient with statistical difference in mean 25(OH)D levels based on each category of BMI percentile. Vitamin D deficiency was noted among 65.6 % of participants with PCOS versus 38.0 % in the control group. The mean serum 25(OH)D level was 16.02 ng/ml in the PCOS group and 22.80 ng/ml in the control group. The difference in 25(OH)D levels between the groups was statistically significant (P = 0.036). Conclusions. Vitamin D deficiency was noted among 65.6 % of participants with PCOS versus 38.0 % in the control group. The mean serum 25(OH)D level was 16.02 ng/ml in the PCOS group and 22.80 ng/ml in the control group. Keywords: vitamin D; polycystic ovary syndrome; adolescents

Introduction
Polycystic ovary syndrome (PCOS) is a heterogeneous disorder characterized by hyperandrogenism and chronic anovulation [1]. Depending on diagnostic criteria, 6 to 20 % of reproductive aged women are affected [2]. PCOS is a complex disorder affecting the hypothalamic-pituitary-ovarian axis and leading to menstrual irregularities and hyperandrogenism marked by elevated serum androgen levels and clinical features such as hirsutism, acne, or alopecia [3].

PCOS is often associated with obesity and insulin resistance leading to metabolic disturbances including impaired glucose tolerance (IGT), type 2 diabetes mellitus (DM), and dyslipidemia with future risk of cardiovascular disease [4]. Other associated health concerns include infertility, endometrial hyperplasia, and cancer. PCOS is a predominant cause of infertility and a common gynecological concern affecting 7 to 15 % of women in reproductive age [5].

The etiology of this syndrome remains largely unknown, but mounting evidence suggests that PCOS might be a complex multigenic disorder with strong genetic and environmental influences, including diet and lifestyle factors [6].

Recently, it has been reported that vitamin D deficiency was a common complication of PCOS and vitamin D status was associated with reproductive ability, metabolic alterations,
and mental health of PCOS patients [7]. The serum cholecalciferol level is correlated with metabolic risk factors in PCOS women [8].

Vitamin D is thought to regulate gene transcription through vitamin D receptors (VDR) that are widely distributed in tissues including ovaries [9]. VDR-related genetic polymorphisms have been linked to serum levels of luteinizing hormone, sex hormone binding globulin, testosterone, and insulin [10].

Current literature suggests a correlation between low vitamin D levels and insulin resistance (IR) in women with PCOS [11]. Limited evidence supports beneficial effect of vitamin D supplementation on IR, menstrual dysfunction, and fertility [12–14].

Vitamin D deficiency is highly prevalent in infertile PCOS women [15, 16]. Studies hypothesize that vitamin D deficiency in PCOS seems to be associated with obesity [17, 18]. There is currently insufficient data regarding association of serum vitamin D levels and PCOS in adolescent females [3]. It is unknown if adolescent females with PCOS have higher prevalence of vitamin D deficiency than do adolescent females without PCOS.

The purpose of the study was to compare prevalence of vitamin D deficiency in adolescent females with and without PCOS.

Materials and methods

The study sample of adolescent females aged 15–19 years included 82 participants; 32 were in the PCOS group and 50 were in the control group.

The study was approved by the Ukrainian Research and Scientific Centre of Endocrine Surgery, Transplantation of Endocrine Organs and Tissues institutional review board. Serum 25(OH)D levels were obtained using liquid chromatography–tandem mass spectrometry, which is a standard method at the institutional laboratory.

Exclusion criteria included history of vitamin D deficiency; current vitamin D supplementation; increased risk of vitamin D deficiency secondary to current medication including steroids, antiretrovirals, antiepileptics, or antifungals; or chronic medical conditions such as chronic kidney disease, osteoporosis, osteopenia, cystic fibrosis, or inflammatory bowel disease. Chart review was performed to collect information on menstrual pattern, clinical signs of hyperandrogenemia such as hirsutism, and serum free testosterone level.

The participants were categorized as in either the PCOS or the control group based on National Institutes of Health (NIH) PCOS diagnostic criteria (chronic anovulation characterized by oligomenorrhea, primary or secondary amenorrhea, clinical or biochemical hyperandrogenemia with exclusion of other mimicking conditions) [19].

All participants in the PCOS group had chronic anovulation with elevated serum free testosterone. Conditions such as hyperprolactinemia, congenital adrenal hyperplasia, thyroid disease, and androgen-secreting tumors were effectively excluded by collecting information on prolactin, 17-hydroxyprogesterone, thyroid-stimulating hormone (TSH), and dehydroepiandrosterone sulfate levels.

Data regarding the participant’s age, body mass index (BMI) percentile, serum 25(OH)D levels, and the season the blood was drawn were recorded in the database. Serum 25(OH)D levels were defined as deficient if the levels were 20 ng/ml or less, insufficient if levels were between 21 and 29 ng/ml, and sufficient if levels were 30 ng/ml or greater [20]. BMI percentile was used as a marker for adiposity; using the Centers for Disease Control and Prevention criteria for BMI percentile, participants were categorized as normal (<85th percentile), overweight (85th–95th percentile), obese (95th–99th percentile), and morbid obese (>99th percentile) [21]. Serum 25(OH)D levels were compared between the PCOS and control groups based on BMI percentile.

Statistical Analysis

Logistic regression analysis was done to compare normal (≥30 ng/ml) vs low (<30 ng/ml) serum 25(OH)D levels in the PCOS and control groups. Effects of BMI percentile were controlled in the model. All data management and analyses were carried out using the Statgraphics Plus 5.0 software. Values of P < 0.05 were considered statistically significant.

Results

82 participants (32 were in the PCOS group and 50 were in the control) group met the inclusion criteria and were categorized as either PCOS or control. All participants in PCOS group had BMI percentile greater than the 85th percentile. Therefore, participants with BMI percentile of less than 85th in the control group were excluded for analysis. The mean age of participants was 17.3 years.

Vitamin D deficiency and insufficiency were frequently diagnosed in our study population. Sufficient 25(OH)D levels

<table>
<thead>
<tr>
<th>Vitamin D status</th>
<th>Group with PCOS (n = 32)</th>
<th>Control group (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deficient (≤20 ng/ml)</td>
<td>21 (65.6)</td>
<td>19 (38.0)</td>
</tr>
<tr>
<td>Insufficient (21–29 ng/ml)</td>
<td>9 (28.1)</td>
<td>26 (54.0)</td>
</tr>
<tr>
<td>Sufficient (&gt;30 ng/ml)</td>
<td>2 (6.2)</td>
<td>5 (10.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Mean serum 25(OH)D level (ng/ml)</th>
<th>Standard deviation</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS</td>
<td>32</td>
<td>16.02</td>
<td>4.92</td>
<td>15.00</td>
<td>6.00</td>
<td>34.00</td>
<td>0.036</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>22.80</td>
<td>6.24</td>
<td>19.00</td>
<td>5.00</td>
<td>42.00</td>
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</tr>
</tbody>
</table>
were found in only 7 of 82 participants (8.5%). The majority of participants with BMI greater than 95th percentile were vitamin D deficient with statistical difference in mean 25(OH)D levels based on each category of BMI percentile. Vitamin D deficiency was noted among 65.6 % of participants with PCOS versus 38.0 % of participants in the control group (Table 1).

The mean serum 25(OH)D levels was 16.02 ng/ml in the PCOS group and 22.80 ng/ml in the control group. The difference in 25(OH)D levels between the groups was statistically significant (P = 0.036) (Table 2).

Discussion

Our study was devoted to the study of vitamin D levels in adolescent females with PCOS. There was statistically significant difference in mean 25(OH)D levels between the PCOS and control groups. The majority of participants with PCOS were obese with low serum 25(OH)D levels. BMI percentile in adolescents has been found to correlate with 25(OH)D levels.

Vitamin D is fat soluble and regulates numerous processes in adipose tissue and their dysregulation leads to metabolic disorders [22]. Obese individuals may spend less time outdoors with less sun exposure and have insufficient vitamin D biosynthesis in the skin [17].

The many PCOS diagnostic models in the adolescent population used in clinical practice, commonly referred to as the NIH criteria, Rotterdam criteria, and androgen excess society criteria [23]. Rotterdam criteria were proposed specific to adolescents that includes the presence of all 3 major criteria: oligomenorrhea or amenorrhea for 2 years after menarche, clinical and biochemical hyperandrogenism, and increased ovarian volume of 10 cm3 or greater in 1 ovary [24].

There has been no consensus on diagnostic approach. PCOS falls under the domain of various pediatric subspecialties such as endocrine, adolescent medicine, and gynecology. These specialties often have different approaches to documenting clinical examination findings, androgen panel evaluation, and use of ultrasound when evaluating for polycystos and, ultimately, often subscribe to different PCOS diagnostic recommendations. We chose to use the NIH diagnosis model based on the clinical practice.

Limitation of the study was that a comparison of serum 25(OH)D levels involving participants with BMI in the normal percentile was not done as there were no normal BMI percentile adolescent females with PCOS in our study. Sample size in each group was smaller than the calculated sample size. A future, large-scale study that includes normal-BMI adolescent females with PCOS would be helpful to determine if there is an association between PCOS and vitamin D.

Conclusions

Vitamin D deficiency was noted among 65.6 % of participants with PCOS versus 38.0 % of participants in the control group.

The mean serum 25(OH)D levels was 16.02 ng/ml in the PCOS group and 22.80 ng/ml in the control group. The difference in 25(OH)D levels between the groups was statistically significant (P = 0.036).

Vitamin D deficiency in adolescent females with PCOS is related to obesity.

References


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Актуальность витамина D; синдром поликистозных яичников у девочек-подростков.

Витамин D может играть一定的 role в патогенезе СПКЯ.

Резюме. Учитывая вышеизложенное, в исследуемой популяции в более частой диагностике выявляли дефицит витамина D. Достаточная доза 25(OH)D у девочек-подростков.

Ключевые слова: витамин D; синдром поликистозных яичников; пилдитик