

The Relation between Polycystic Ovary Syndrome and Vitamin D Deficiency

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Abstract

Background: Vitamin D deficiency is common in women with polycystic ovary syndrome (PCOS). Vitamin D deficiency is a common health condition in the reproductive period of women and may escalate the symptoms of PCOS in women. **Objective:** The aim of this study was to investigate the association between serum Vitamin D levels in patients with PCOS compared to healthy controls. **Materials and Methods:** In the present case-control study, a total of 70 women diagnosed with PCOS were considered cases, and their Vitamin D levels and some other biochemical parameters were compared to 43 apparently healthy controls. The diagnosis of PCOS was established in line with the Rotterdam Consensus on Diagnostic Criteria for PCOS, including oligo or anovulation, clinical and biochemical signs of hyperandrogenism, and polycystic ovaries and exclusion of other etiologies (congenital adrenal hyperplasia, androgen-secreting tumors, and Cushing's syndrome). **Results:** The study revealed that patients with PCOS were significantly younger compared to the healthy controls; 26.57 versus 33.51; $P < 0.001$. Moreover, a higher percentage of patients had irregular menstruation (81.4%) and hirsutism (81.4%) compared to controls (4.7% and 4.7%, $P < 0.001$, respectively). The study revealed that the patients had a significantly lower level of Vitamin D and serum prolactin and higher levels thyroid-stimulating hormone compared to healthy control; 5.49 versus 17.83 ng/ml; 11.94 versus 8.57 IU/L; and 2.50 versus 1.72 IU/L, respectively. **Conclusion:** The present study suggests that patients with PCOS were more likely to have irregular menstruation and a lower level of Vitamin D compared to apparently healthy controls.

Keywords: Diagnosis, polycystic ovary syndrome, Vitamin D deficiency

INTRODUCTION

Vitamin D has an essential role in calcium homeostasis and bone metabolism. However, its role in a wide range of biological actions has been revealed over the past two decades. The roles include cell differentiation, cell growth inhibition, immunomodulation, and control of other hormonal systems. Vitamin D deficiency is a common health condition in the reproductive period of women life.^[1]

Polycystic ovary syndrome (PCOS) is a genetically complex endocrine disorder that its etiology is unclear with a complex pathophysiology. According to the estimation of the World Health Organization, 116 million women (3.4%) worldwide have been affected by PCOS.^[2] The global prevalence of PCOS is profoundly different across geographic locations ranged between 2.2% and 26%.^[3] It has life-long effects on patients, and its prevalence in persons at reproductive age is between 5% and 10%.^[4]

The patient with PCOS is presented by oligomenorrhea or amenorrhea, hyperandrogenemia, anovulation, and insulin resistance (IR).^[5] It seems that it is one of the leading causes of anovulatory infertility. As previously mentioned, the exact cause of PCOS is not clear. However, few investigations have reported that Vitamin D deficiency may have a role in the development of metabolic syndrome because Vitamin D is essential for the formation of the adrenal cortex hormones. Therefore, the management of PCOS needs treatment of Vitamin D deficiency.^[6]

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Vitamin D deficiency is common in women with PCOS ranged between 67% and 85% as defined serum concentrations of 25-hydroxyvitamin D (25OHD) <20 ng/ml. Vitamin D deficiency may escalate the symptoms of PCOS in women. The lower Vitamin D in PCOS patients has been shown to associate with IR, lower pregnancy rate, ovulatory and menstrual irregularities, hirsutism, elevated cardiovascular disease risk factors, obesity, and hyperandrogenism.^[7] Currently, there is limited evidence on the association of Vitamin D levels with PCOS disease.^[7,8]

The present study aims to assess the association between serum Vitamin D levels in patients with PCOS compared to healthy controls in Duhok city.

MATERIALS AND METHODS

Research design and sampling

In the present case–control study, the individuals who attended the Gynecology and Obstetrics Clinic of Duhok Maternity Hospital for the medical checkup were consecutively screened for eligibility criteria. The individuals who attended the clinic for the following medical issues; complaining of infertility, obesity, and hirsutism. The individuals who met inclusion criteria and were diagnosed with PCOS on ultrasonography were considered in the case group, and those who were not diagnosed with any disease were included in the control group. The individuals in the control group were apparently healthy individuals. The baseline information and biochemical parameters were compared between the individuals in both groups. The data collection was performed over 1 year between November 20, 2017, and November 25, 2018.

Inclusion and exclusion criteria

The individuals met eligibility criteria if they were aged 18 years and older, body mass index (BMI) between 20 and 35 irrespective of sociodemographic aspects. The individuals with pregnancy reported as hypertensive or diabetic were excluded from the study.

Data collection and diagnosis

The general information was collected from the subjects were age, BMI, marital status, history of infertility, menstruation categorized as regular/irregular, hirsutism, acne, and alopecia through self-reported technique.

Diagnosis of the polycystic ovarian syndrome

The diagnosis of PCOS was established in line with the Rotterdam Consensus on Diagnostic Criteria for PCOS. The revised diagnostic criteria of PCOS were in 2003 were oligo or anovulation, clinical and biochemical signs of hyperandrogenism, and polycystic ovaries, and exclusion of other etiologies (congenital adrenal hyperplasia, androgen-secreting tumors, and Cushing's syndrome).^[9] A 5 cc of venous blood was taken from each patient for measurements of biochemical parameters. The biochemical measurements were performed at the laboratory of Duhok Maternity Hospital.

Statistical methods

The descriptive purposes of the study were presented in mean and standard deviation or frequency and percentage. The prevalence of hirsutism, menstruation regularity, acne, and alopecia was presented in frequency and percentage. The difference in baseline information between the subjects in PCOS and healthy groups were examined in the independent *t*-test, Chi-square, or Fishers' exact tests. The difference in biochemical parameters between two study groups was examined either in independent *t*-test or Mann–Whitney U-test. The significant difference was determined in a $P < 0.05$. The statistical calculations were performed in Statistical Package for Social Sciences version 24:00 (SPSS 24; IBM Corp; USA).

Ethical considerations

The ethical clearance of the present protocol was obtained from the Health Ethics Committee of the Kurdistan Board for Medical Specialties. The individuals were included in this study were not undergone any invasive medical procedure or surgery. In addition, informed verbal consent was taken from all patients before study inclusion.

RESULTS

Of the total 113 individuals included in the study, 70 (64.92%) of them were diagnosed as PCOS, and the remaining 43 individuals (38.05%) were apparently healthy. The PCOS patients were significantly younger than the healthy controls; 26.57 versus 33.51, $P < 0.001$. Besides, the PCOS patients were more likely to be single (31.4%) compared to the healthy controls (4.7%; $P = 0.001$). The PCOS patients were more likely to have irregular menstruation (81.4%) compared to healthy controls (4.7%; $P < 0.001$). While the individuals in both PCOS and healthy were not different in BMI (26.07 vs. 27.32; $P = 0.429$), a history of infertility (45.7% vs. 44.2%; $P = 0.874$), acne ($P = 0.287$), and alopecia ($P = 1.00$) [Table 1].

The comparison of biochemical parameters between PCOS and healthy groups was shown in Table 2. The analysis showed that patients in PCOS had a significantly lower level of Vitamin D (14.16 vs. 17.83 ng/ml; $P = 0.010$), and a higher level of serum prolactin (23.22 vs. 17.66 IU/L; $P = 0.046$) and thyroid-stimulating hormone (2.50 vs. 1.72; $P = 0.004$), respectively. However, there was no significant difference in random blood sugar ($P = 0.168$), follicle-stimulating hormone ($P = 0.243$), serum testosterone ($P = 0.197$), T3 ($P = 0.250$), T4 ($P = 0.136$), and luteinizing hormone ($P = 0.735$).

DISCUSSION

The aim of the present investigation was to compare the Vitamin D level between the persons who were diagnosed with PCOS compared to a sample population of apparently healthy controls. The study found that the patients had a significantly lower level of Vitamin D. Furthermore, they were more likely to have irregular menstruation.

Table 1: Comparison of baseline and clinical characteristics between polycystic ovary syndrome and healthy groups

Subjects' characteristics (n=113)	Normal (n=43)	PCOS (n=70)	P (two-sided)
Age (year), mean (SD)	33.51 (7.08)	26.57 (7.07)	<0.001*
BMI, mean (SD)	27.32 (4.99)	26.07 (4.84)	0.429*
Marital status, frequency (%)			
Single	2 (4.7)	22 (31.4)	0.001**
Married	41 (95.3)	48 (68.6)	
History of infertility, frequency (%)	19 (44.2)	32 (45.7)	0.874**
Menstruation, frequency (%)			
Regular	41 (95.3)	13 (18.6)	<0.001**
Irregular	2 (4.7)	57 (81.4)	
Hirsutism, frequency (%)	2 (4.7)	57 (81.4)	<0.001**
Acne, frequency (%)	0 (0.0)	3 (4.3)	0.287***
Alopecia, frequency (%)	0 (0.0)	1 (1.4)	1.00***

*Independent *t*-test, **Chi-square and, ***Fisher's exact tests were performed for statistical analyses. The bold numbers show a significant difference.

PCOS: Polycystic ovary syndrome, SD: Standard deviation, BMI: Body mass index

Table 2: Comparison of biochemical parameters between polycystic ovary syndrome and healthy groups

Biochemical parameters (n=113)	Normal (n=43)	PCOS (n=70)	P (two-sided)
Vitamin D (ng/mL)	17.83 (8.00)	14.16 (5.49)	0.010
RBS (mg/dL)	103.62 (8.66)	98.09 (14.53)	0.168
FSH (IU/L)	7.89 (8.06)	5.73 (3.21)	0.243
Serum prolactin (IU/L)	17.66 (8.57)	23.22 (11.94)	0.046
Serum testosterone (ng/dL)	0.68 (0.39)	3.60 (9.16)	0.197
TSH (IU/L)	1.72 (1.20)	2.86 (2.50)	0.004
T3 (mIU/L)	2.75 (2.65)	8.32 (19.90)	0.250
T4 (mIU/L)	65.66 (37.09)	92.02 (35.85)	0.136
Serum progesterone (ng/mL)	1.89	3.22 (3.39)	NA
LH (IU/L), median (IQR)	4.70 (4.10)	5.70 (6.48)	0.735*

*Mann-Whitney U-test was performed for the statistical analysis of LH and the independent *t*-test for other parameters. The bold numbers show significant differences. The number is in mean and SD except LH which were in median and IQR. IQR: Interquartile range, FSH: Follicle-stimulating hormone, RBS: Random blood sugar, TSH: Thyroid-stimulating hormone, T3: Triiodothyronine, T4: Thyroxine, SD: Standard deviation, NA: Not available, LH: Luteinizing hormone

The association between Vitamin D levels and various PCOS symptoms including IR, hirsutism, and infertility have been documented in the literature.^[10-13]

Pal *et al.*^[12] explored the association between Vitamin D status and diagnosis of ovulatory disturbances and PCOS in a population of otherwise healthy infertile women in a cross-sectional study. They found 7% of persons with normal Vitamin D (>30 ng/ml) only in their study individuals. There were a significantly lower serum Vitamin D levels in women with ovulatory disturbances and PCOS compared to those with other infertility etiologies. Interestingly, they found that each unit increase in Vitamin D level was attributed to reducing the likelihood of PCOS diagnosis by 96% ($P = 0.015$), and for ovulatory infertility by 87% ($P = 0.038$).

Yılmaz *et al.*^[14] determined the relation of serum 25-OHD levels to hormonal, clinical, and metabolic profile in patients

with and without PCOS. In this regard, they included 48 normal-weight women with PCOS, 36 overweight women with PCOS, and 56 normal-weight control in the study. The blood samples were taken in the follicular phases between days 2 and 5 of the menstrual cycle following an overnight fast. They found that normal and overweight women with PCOS had a lower level of circulating 25-OHD levels compared to normal-weight controls. The levels of 25-OHD were reported to associate negatively with waist circumference, waist-to-hip ratio, free testosterone, and modified Ferriman–Gallwey scores.

The literature reported that Vitamin D deficiency in women with PCOS is between 67% and 85%, with a serum concentration of 25OHD <20 ng/ml.^[7] The high prevalence of Vitamin D deficiency has been associated with metabolic syndrome, which may have a great effect on public health.^[15] Low Vitamin D levels may escalate the PCOS symptoms, such as ovulatory, menstrual irregularities, infertility, IR, hyperandrogenism, and obesity. In addition, it elevates the risk of cardiovascular diseases.^[16]

Vitamin D supplementation lowers the abnormally elevated serum levels of anti-Müllerian hormone and raises serum soluble anti-inflammatory receptor for advanced glycation end-products in Vitamin D-deficient women with PCOS.^[17] Particular, Vitamin D and calcium supplementation along with metformin therapy in women diagnosed with PCOS could lead to the beneficial impacts on menstrual regularity and ovulation.^[17]

The present study found that patients with PCOS were more likely to have irregular menstruation compared to healthy controls. Irregular menstruation has been reported to be the risk factor of PCOS in the literature as well. For instance, Shan *et al.*^[18] explored the risk factors of PCOS in 285 cases of PCOS in comparison with 580 healthy controls in a case–control study. The menstrual irregularity of mother (odds ratio [OR]: 2.557) was found to be one of the risk factors for PCOS. Other risk factors were a family history of infertility

(OR: 11.953), family history of diabetes (OR: 7.008), bad mood (OR: 2.852), menstrual cycle disorder (OR: 5.824), and lack of physical activity (OR: 1.866).

Majority of PCOS patients experience the onset of irregular menstruation as adolescence, and endocrine dyscrasia along any part of the hypothalamic-pituitary-gonadal axis may result in irregular menstruation and anovulation.^[19] Besides, the irregular menstruation of the mother has been shown to contribute to a higher risk of PCOS of the daughter.^[20]

The exact reason for PCOS is inconclusive owing to its complexity. The literature has reported the interaction between genetic and environmental factors as the possible risk factors.^[21]

Strength and limitation of the study

The strong point of the study could be traced in its design and the strict inclusion, and exclusion criteria were applied to the subjects in both the study groups. However, the study was not exempt from the limitation. The difference in findings reported in the present investigation with those reported in the literature may back to the different diagnostic criteria of PCOS or various geographic locations.

CONCLUSION

The present study suggests that patients with PCOS were more likely to have irregular menstruation and a lower level of Vitamin D compared to apparently healthy controls. The early screen, diagnosis, and treatment of PCOS are recommended to decrease the incidence rate in this region.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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