Serum Vitamin D Levels in Fertile and Infertile Women with Polycystic Ovary Syndrome

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Key words
hormones, infertility, ovary

Materials and Methods
274 infertile and 111 fertile women with polycystic ovary syndrome were included in this retrospective study. Infertile and fertile groups were matched by age, body mass index and homeostasis model assessment of insulin resistance. Anthropometric, clinical and laboratory characteristics of the women were recorded. Serum 25(OH)D₃ levels were used to assess serum vitamin D levels.

Results
No significant differences were detected between groups in terms of anthropometric, clinical and laboratory features except for serum 25(OH)D₃ levels and the incidence of vitamin D deficiency. Vitamin D levels were significantly lower and vitamin D deficiency was more common in the infertile group compared to the fertile group. When the groups were stratified into obese/non-obese or insulin resistance positive/negative, infertile obese and infertile insulin resistance-positive women had the lowest serum 25(OH)D₃ levels.

Conclusion
Serum vitamin D levels are lower in infertile women with polycystic ovary syndrome compared to fertile women. When insulin resistance or obesity was present, vitamin D levels were reduced further. Thus, in polycystic ovary syndrome, lower vitamin D levels may play a role in the pathogenesis of fertility problems.
Introduction

Infertility is an important issue in public health. It affects approximately 48.5 million couples worldwide and has significant psychological, medical and economic consequences [1]. Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in approximately 9 to 18% of women of reproductive age and the leading cause of female infertility [2, 3]. The etiology of PCOS is not fully understood and is probably the result of a complex interaction of environmental and genetic factors. Insulin resistance (IR) and hyperandrogenism have been shown to be key pathophysiological mechanisms. Clinically, PCOS may be associated with reproductive (hyperandrogenism, menstrual irregularity, oligo-ovulation or anovulation, infertility), metabolic (dyslipidemia, type 2 diabetes, cardiovascular risk factors) and psychological symptoms (depression, anxiety, lower quality of life) and can be a major health burden [4].

Vitamin D is a steroid hormone synthesized by the skin when exposed to ultraviolet light. A small amount of total vitamin D is obtained through diet and/or supplements. The main biological function in the human body is to protect calcium homeostasis and promote bone mineralization. It also affects a variety of functions such as cell differentiation, apoptosis, antiproliferation, immunosuppression and anti-inflammatory. Vitamin D carries out all these functions mainly through vitamin D receptors. Vitamin D receptors have not only been detected in calcium regulatory tissues such as the intestines and the skeletal and parathyroid glands but also in many other reproductive organs such as the ovaries (especially granulosa cells), uterus, placenta, testis, hypothalamus and the pituitary gland [5]. This has been interpreted as vitamin D having some effect on reproductive processes in women and men [6]. PCOS women have a higher risk of vitamin D deficiency. The prevalence of vitamin D deficiency in the general adult population is 20–48%, while the prevalence in PCOS women is 67–85% [7]. Several studies have been conducted in this context to investigate the relationship between vitamin D status and well-known PCOS comorbidities. Most studies have focused on vitamin D and metabolic conditions and reported that low levels of vitamin D are associated with an increased risk of type 2 diabetes, IR, metabolic syndrome and cardiovascular disease [8, 9]. However, there are not enough studies that show the relationship with female fertility. Therefore, we aimed to compare serum vitamin D levels in fertile and infertile women with polycystic ovary syndrome to evaluate whether vitamin D may play a role in the pathogenesis of fertility problems in women with polycystic ovary syndrome.

Materials and Methods

Study design and population

This retrospective case-control study was conducted in Zekai Tahir Burak Women’s Health Education and Research Hospital, a tertiary, referral teaching and research hospital in Ankara, the capital city of Turkey. Women diagnosed with PCOS and referred to the Reproductive Endocrinology and Infertility Department because of complaints related to PCOS over a 2 year-period were enrolled in the study. The Institutional Review Board of the hospital approved the study. Due to the retrospective design of the study, informed consent was not obtained from the subjects.

For all participants, the diagnosis of PCOS was made by expert gynecologists based on the Rotterdam criteria, i.e., two out of three of the following features were required for a confirmation of the diagnosis:
1. oligo-ovulation and/or anovulation,
2. clinical and/or biochemical signs of hyperandrogenism, and
3. the presence of polycystic ovaries on ultrasound examination [4].

Hyperprolactinemia, thyroid dysfunction, and specific adrenal disorders were excluded clinically and, if necessary, biochemically. The case group consisted of infertile women with PCOS. Infertile women with PCOS were women who had tried to become pregnant but were unable to conceive despite at least 1 year of unprotected sexual intercourse. All of the women had not previously had any infertility treatment. Their tubes were open and the uterine cavity was normal in size as measured by hysterosalpingography. Their husbands also had normal spermiograms (with a sperm concentration of at least 15 million per milliliter, a motility of more than 40% and a morphology of more than 4% normal forms). The control group consisted of women with PCOS who had a biochemically confirmed pregnancy at the time of referral to the department for menstrual irregularity. None of these women received infertility treatment. Pregnant women whose pregnancy would not be able to reach 20 weeks of gestation were excluded from the control group. The case and control groups were matched by age, body mass index (BMI) and homeostasis model assessment of insulin resistance (HOMA-IR). Women who were older than 35 years, smoked, had a history of any systemic disease (i.e., hypertension, diabetes or cardiovascular disease), had previously taken vitamin D supplements, had taken oral contraceptives, glucocorticoids, antiandrogens, ovulation induction agents,
antidiabetic or antiobesity drugs, or other hormonal drugs in the previous 6 months or had other concurrent medical illnesses (i.e., renal disease or malabsorptive disorders) were excluded from the study.

**Anthropometric, clinical and laboratory data**

All the data in the study were obtained from hospital records. Women with insufficient data were also excluded. Standard anthropometric data (height, weight, waist circumference [WC] and hip circumference [HC]), systolic and diastolic blood pressure) of each participant were recorded. HC was measured as the widest circumference at the level of the buttocks. WC was measured as the smallest circumference at the level of umbilicus. Waist-to-hip ratio (WHR) was calculated by dividing WC by HC. BMI was calculated as weight/height² (kg/m²). A Ferriman–Gallwey score was used to evaluate the degree of hirsutism [10]. Blood samples to determine hormonal (total testosterone, free testosterone, dehydroepiandrosterone sulfate, sex hormone-binding globulin [SHBG], luteinizing hormone [LH], follicle-stimulating hormone [FSH], LH/FSH ratio, estradiol, prolactin, thyroid-stimulating hormone, anti-Mullerian hormone [AMH], 25(OH)D₃ and metabolic (fasting glucose, fasting insulin, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides) parameters were collected from the antecubital vein between 8:00 and 9:00 a.m. after at least 8 hours of fasting, preferably in the early follicular phase of the menstrual cycle (2nd or 3rd day) from both cases and controls. IR was estimated using the HOMA-IR (calculated as fasting plasma insulin in µ U/ml × fasting plasma glucose in mmol/L divided by 22.5) [11]. The free androgen index (FAI) was calculated as testosterone (nmol/L)/SHBG (nmol/L) x 100 [12].

Serum 25(OH)D₃ levels were used to assess serum vitamin D levels, because 25(OH)D₃ levels reflect both dietary intake and skin-synthesized vitamin D levels and do not change during the

| Table 1 Clinical characteristics of infertile and fertile women with PCOS. |
|---------------------------------|-----------------|----------------|---|
|                                | Infertile group (n = 274) | Fertile group (n = 111) | p   |
| Age (years)                    | 25.01 ± 3.58     | 25.47 ± 2.96    | 0.238 |
| BMI (kg/m²)                    | 27.57 ± 6.74     | 27.38 ± 6.57    | 0.725 |
| Waist-to-hip ratio             | 0.83 ± 0.06      | 0.81 ± 0.07     | 0.596 |
| Systolic blood pressure (mmHg) | 110.4 ± 9.1      | 111.8 ± 15.1    | 0.689 |
| Diastolic blood pressure (mmHg)| 71.9 ± 5.6       | 70.5 ± 8.6      | 0.752 |
| Ferriman–Gallwey score         | 8.66 ± 4.90      | 9.15 ± 5.08     | 0.462 |
| Fasting blood glucose (mg/dl)  | 91.24 ± 8.26     | 92.16 ± 9.86    | 0.346 |
| Fasting insulin (µIU/ml)       | 13.94 ± 8.28     | 12.80 ± 7.01    | 0.263 |
| HOMA-IR                        | 3.13 ± 0.89      | 3.08 ± 0.85     | 0.668 |
| Total cholesterol (mmol/l)     | 176.02 ± 34.54   | 176.81 ± 39.38  | 0.847 |
| High-density lipoprotein (mmol/l) | 54.88 ± 16.06   | 53.18 ± 13.87  | 0.229 |
| Low-density lipoprotein (mmol/l) | 97.77 ± 31.98   | 103.20 ± 53.38  | 0.229 |
| Triglycerides (mmol/l)         | 125.63 ± 46.20   | 133.08 ± 58.76  | 0.124 |
| Luteinizing hormone (IU/l)     | 9.38 ± 4.08      | 8.02 ± 4.03     | 0.157 |
| Follicle-stimulating hormone (IU/l) | 5.58 ± 2.18   | 5.41 ± 1.50     | 0.558 |
| LH/FSH ratio                   | 1.87 ± 0.25      | 1.47 ± 0.55     | 0.168 |
| Estradiol (pg/ml)              | 46.10 ± 12.65    | 40.27 ± 15.21   | 0.117 |
| Total testosterone (ng/ml)     | 1.43 ± 0.57      | 1.38 ± 0.41     | 0.447 |
| Free testosterone (pg/ml)      | 2.10 ± 0.77      | 2.03 ± 0.81     | 0.420 |
| Dehydroepiandrosterone sulfate (mg/ml) | 287.71 ± 123.68 | 271.60 ± 115.92 | 0.263 |
| Sex hormone-binding globulin (nmol/l) | 51.79 ± 23.79  | 49.24 ± 29.66  | 0.609 |
| Free androgen index            | 6.36 ± 2.92      | 5.68 ± 2.73     | 0.160 |
| Prolactin (µg/L)               | 17.59 ± 7.70     | 18.00 ± 8.60    | 0.465 |
| Thyroid-stimulating hormone (mIU/L) | 2.08 ± 1.12   | 2.20 ± 0.96     | 0.342 |
| Anti-Mullerian hormone (ng/ml) | 7.92 ± 4.39      | 7.54 ± 4.59     | 0.561 |
| 25(OH)D₃ (ng/ml)               | 11.63 ± 5.61     | 15.45 ± 6.89    | < 0.001 |
| Vitamin D deficiency           | 236 (86.1)       | 86 (77.5)       | 0.038 |

Variables are listed as mean ± standard deviation and as a percentage (%). BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance. p < 0.05 was considered statistically significant.
menstrual cycle. Thus, it is accepted as the best indicator of vita-
mim D levels [13]. Serum levels of 25(OH)D3 were measured with
an ELISA kit (Immunodiagnostic AG, Germany). The intra- and in-
ter-assay coefficients of variation were 8.9 and 10.6%, respective-
ly, for serum 25(OH)D3. In order to eliminate the effects of time
(seasons) on vitamin D levels, women who gave blood samples at
similar times were included. All samples were collected in spring
when sunlight levels were relatively low in Ankara (longitude: 40°
40’ N, latitude: 32°34’ E, altitude: 891 m, average temperature:
6.1–16.2°C) [14]. Serum 25(OH)D3 levels of less than 20 ng/ml were
classified as vitamin D deficiency [15].

Statistical analysis
Statistical analysis was performed with SPSS software, version
18.0 (IBM, USA). The Kolmogorov–Smirnov method was used to
estimate data distribution. Depending on the data distribution,
Student’s t test for continuous independent variables was used
to test differences between groups. χ² test was used for categori-
cal variables. Correlations between the level of 25(OH)D3 and oth-
er variables were analysed with Pearson’s correlation test. Multi-
variate logistic regression analysis was performed to evaluate the
relationship between serum 25(OH)D3 and specific subgroups
classified according to BMI and HOMA-IR levels. Variables were ex-
pressed as mean ± standard deviation or as a number (percent-
age), and statistical significance was defined as a p value of less
than 0.05.

Results

Anthropometric, clinical and laboratory characteristics of the study groups
Based on the exclusion criteria, 128 women were excluded and
385 women with PCOS were selected as the study population.
Comparisons of the anthropometric, clinical and laboratory pa-
rameters of the fertile and infertile women with PCOS are shown in ▶ Table 1. A total of 274 women were in the infertile group and
111 women were in the fertile group. As the groups were
matched for age, BMI and HOMA-IR levels, the parameters of the
groups were similar except for serum 25(OH)D3 levels and the in-
idence of vitamin D deficiency. Infertile PCOS women had lower
25(OH)D3 levels (11.63 ± 5.61 ng/ml) and a higher incidence of vi-
tamin D deficiency (86.1%) compared to fertile PCOS women
(15.45 ± 6.89 ng/ml and 77.5%, respectively).

Associations between serum 25(OH)D3 levels and other parameters
When all women included in the study were considered, 25(OH)D3
levels correlated negatively with BMI, WHR, HOMA-IR, sex hor-
mone-binding globulin and AMH levels (r = -0.425, p = 0.021;
r = -0.370, p = 0.036; r = -0.477, p = 0.040; r = -0.118, p = 0.025
and r = -0.356, p = 0.016; respectively) and positively with LH lev-
els (r = 0.187, p = 0.047) (▶Table 2).

Serum 25(OH)D3 levels of subgroups
When infertile and fertile PCOS women were stratified into two
subgroups according to their BMI (< 30 kg/m² was classified as
non-obese and ≥ 30 kg/m² as obese), there was no statistically sig-
nificant difference between obese (14.13 ± 11.88 ng/ml) and non-
obese (15.93 ± 14.34 ng/ml) women with regard to 25(OH)D3 lev-
els in the fertile group (p = 0.505). However, serum vitamin D lev-
als were significantly lower in obese women (10.67 ± 5.86 ng/ml)
compared to non-obese (12.62 ± 5.53 ng/ml) women in the infer-
tile PCOS women (p = 0.041). When infertile and fertile PCOS
women were grouped according to their HOMA-IR levels as IR
positive (HOMA-IR ≥ 2.5) or IR negative (HOMA-IR < 2.5), serum
25(OH)D3 levels were similar for IR negative (16.96 ± 6.38 ng/ml)
and IR positive (14.20 ± 5.06 ng/ml) women in the group of fertile
PCOS women (p = 0.311). However, in the group of infertile PCOS
women, 25(OH)D3 levels were significantly lower in women with
IR (10.48 ± 5.30 ng/ml) compared to women without IR
(12.84 ± 5.83 ng/ml) (p = 0.015) (▶Table 3).

When we evaluated the subgroups with regard to vitamin D
deficiency using multivariable logistic regression analysis, we

▶Table 2 Association between clinical parameters and serum
25(OH)D3 levels.

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>p</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.046</td>
<td>0.372</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.425</td>
<td>0.021</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>-0.370</td>
<td>0.036</td>
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<tr>
<td>Systolic blood pressure</td>
<td>-0.048</td>
<td>0.360</td>
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<tr>
<td>Diastolic blood pressure</td>
<td>-0.084</td>
<td>0.204</td>
</tr>
<tr>
<td>Ferriman–Gallwey score</td>
<td>0.066</td>
<td>0.195</td>
</tr>
<tr>
<td>Fasting blood glucose</td>
<td>-0.035</td>
<td>0.491</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>-0.146</td>
<td>0.071</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>-0.477</td>
<td>0.040</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.121</td>
<td>0.119</td>
</tr>
<tr>
<td>High-density lipoprotein</td>
<td>0.088</td>
<td>0.078</td>
</tr>
<tr>
<td>Low-density lipoprotein</td>
<td>0.076</td>
<td>0.145</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.002</td>
<td>0.965</td>
</tr>
<tr>
<td>Luteinizing hormone</td>
<td>0.187</td>
<td>0.047</td>
</tr>
<tr>
<td>Follicle-stimulating hormone</td>
<td>-0.071</td>
<td>0.263</td>
</tr>
<tr>
<td>LH/FSH ratio</td>
<td>0.147</td>
<td>0.099</td>
</tr>
<tr>
<td>Estradiol</td>
<td>-0.029</td>
<td>0.646</td>
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<tr>
<td>Total testosterone</td>
<td>0.211</td>
<td>0.134</td>
</tr>
<tr>
<td>Free testosterone</td>
<td>-0.037</td>
<td>0.478</td>
</tr>
<tr>
<td>Dehydroepiandrosterone sulfate</td>
<td>-0.117</td>
<td>0.131</td>
</tr>
<tr>
<td>Sex hormone-binding globulin</td>
<td>-0.118</td>
<td>0.025</td>
</tr>
<tr>
<td>Free androgen index</td>
<td>0.158</td>
<td>0.093</td>
</tr>
<tr>
<td>Prolactin</td>
<td>-0.092</td>
<td>0.151</td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>-0.036</td>
<td>0.496</td>
</tr>
<tr>
<td>Anti-Mullerian hormone</td>
<td>-0.356</td>
<td>0.016</td>
</tr>
</tbody>
</table>

BMI: body mass index; HOMA-IR: homeostasis model assessment of insulin resistance.
r: Pearson’s correlation coefficient.
p < 0.05 was considered statistically significant.
found that infertile obese women (OR [95% CI]: 2.69 [1.02–7.11], p = 0.045) and infertile IR (+) women (OR [95% CI]: 3.03 [1.31–7.05], p = 0.010) were the subgroups with significant vitamin D deficiency (Table 4).

Discussion

In this study, we aimed to evaluate serum vitamin D levels in fertile PCOS women compared to infertile PCOS women. We also investigated whether vitamin D levels differ in terms of female fertility when IR and obesity are present. The results revealed that serum vitamin D levels were lower in infertile PCOS women compared to fertile women. When IR or obesity was present, vitamin D levels were reduced even further.

There are currently a number of in vitro and in vivo studies showing that there may be a relationship between vitamin D deficiency and ovarian physiology in both humans and animals [5]. In serum, there is a correlation between circulating vitamin D and AMH levels [6]. AMH is primarily produced by the granulosa cells of small antral and pre-antral ovarian follicles in adult women [17]. Like vitamin D levels, serum AMH levels show seasonal variability, with levels in winter lower than in summer. However, appropriate vitamin D supplements (supplements of vitamin D3, not vitamin D2) may suppress the seasonal changes in AMH levels [18]. This condition strongly indicates that AMH production in adults may be regulated by vitamin D. In the ovary, AMH inhibits primordial follicle recruitment and the sensitivity of growing follicles to follicle-stimulating hormone (FSH), leading to atresia and the death of follicles containing oocytes [17]. Serum AMH levels are two to three times higher in PCOS women than in ovulatory healthy women [19]. The elevated AMH levels in women with PCOS may reduce the sensitivity of antral follicles to FSH and could therefore lead to follicular arrest. Moreover, it has been postulated that in vitamin D-deficient PCOS women, vitamin D supplementation lowers abnormally elevated serum AMH levels, and lower serum AMH levels might potentially improve the ovulatory process by decreasing intrafollicular androgens and increasing follicular sensitivity to FSH in PCOS women [20]. Therefore, serum vitamin D may play an important role in the elimination of ovulatory dysfunction and infertility in PCOS women. Consistent with the literature, the fact that serum vitamin D levels were lower in infertile PCOS women compared to fertile women and the inverse relationship between serum 25(OH)D3 and AMH levels in our study suggests that vitamin D is important for ovulatory function and fertility in PCOS women.

Obesity is associated with female infertility. In obese women, increased estrogen due to peripheral aromatization of androgens, hyperandrogenism due to IR and hyperinsulinemia disturb the neuroregulation of the hypothalamic-pituitary-gonadal axis. This alteration may lead to impaired ovulatory function and female infertility [21,22]. More than half of all women with PCOS are obese [23]. Many PCOS studies in the literature have shown that vitamin D deficiency is more common in obese PCOS women than in non-obese women and that there is a negative correlation between vitamin D levels and BMI [24,25]. This is probably due to the fact that there is more storage of fat-soluble vitamin D in adipose tissue, which is greater in obese PCOS women. Moreover, obese PCOS women may have more sedentary lifestyle than women who are not obese, i.e., they may spend more time indoors with less exposure to sunlight [26,27]. Despite all this available information, it has not been fully proven whether the fertility problems in women with PCOS are the result of obesity, lower vitamin D levels, or both. Nevertheless, in our study, serum vitamin D levels were lower in infertile PCOS women than in fertile ones, irrespective of BMI. In addition, in the infertile group, obese women had the lowest vitamin D levels and the group of infertile obese women had the greatest vitamin D deficiency. These findings suggest that de-
increased vitamin D levels in PCOS women may be associated with fertility problems, and that this correlation is even higher in the presence of obesity.

IR is a hormonal abnormality and plays a key role in PCOS. It can be related to obesity or can occur independently of it. Many studies have shown an inverse relationship between vitamin D levels and IR, but it is unclear whether vitamin D deficiency and IR coexist in PCOS women or whether the two are casually related [28]. As mentioned above, we found a negative correlation between vitamin D and HOMA-IR levels. Some studies have suggested that vitamin D affects insulin sensitivity, increasing insulin secretion and release and enhancing insulin receptor expression, and may prevent the overproduction of proinflammatory cytokines that are suggested to mediate IR. Therefore, vitamin D deficiency could be a contributing factor for IR, which is a common feature in PCOS. However, the underlying mechanisms require further exploration [29, 30]. With IR, organs are resistant to insulin and unable to absorb glucose from the bloodstream, leading to high blood sugar levels. Beta cells in the pancreas subsequently increase their production of insulin, further contributing to high blood insulin levels and hyperinsulinemia occurs. Increased insulin promotes ovarian and adrenal androgen biosynthesis and amplifies LH-induced androgen production by theca cells. Insulin also lowers sex hormone-binding globulin levels, thereby increasing bioactive, freely floating androgen levels in the bloodstream. Finally, hyperandrogenization occurs. An excess amount of androgen converts to estrogen. High estrogen levels increase the pituitary gland’s secretion of LH. High estrogen also suppresses FSH, causing follicles to develop poorly. Insulin also acts on the granulosa cells of small follicles and amplifies the early response to increased LH, leading to terminal differentiation of granulosa cells in small follicles and resulting in an early arrest of follicular growth which causes anovulation. In addition, hyperinsulinemia may adversely affect endometrial function and environment and result in implantation failure [31]. Thus, IR, which is inversely related to vitamin D levels in women with PCOS, may lead to reproductive problems causing infertility. In our study, the fact that infertile PCOS women with IR had the lowest vitamin D levels and infertile PCOS women with IR were the only group at risk of vitamin D deficiency supports the proposed relation between vitamin D, IR and infertility in PCOS.

Our study has some limitations. Firstly, a retrospective study design may raise doubts in the reliability of the obtained data. For example, weather conditions or individual properties such as length of time spent outside and clothing habits are likely to affect vitamin D synthesis in the skin. Unfortunately, due to the retrospective design, it was not possible to evaluate such factors. Secondly, measuring serum 25(OH)D3 levels only once at the time of PCOS diagnosis and the lack of follow-up of the women does not necessarily reflect vitamin D status throughout the period of infertility. These factors should be considered and taken into account in future studies. Another limitation of our study was that the study population was limited to women from a single geographic region. More studies are needed with other participants from different geographic regions who have different exposures to sunlight. Finally, as our patients were matched for age, BMI and HOMA-IR, our results can only be interpreted for this cohort of women. Our study also has a number of strengths. The relatively large number of cases and well-matched controls made the results and comparisons reliable, as age, BMI and HOMA-IR levels did not affect findings.

Conclusion

This study shows that vitamin D levels are lower in PCOS women who have a fertility problem, regardless of obesity and IR. Infertile PCOS women who are obese or have IR have even lower vitamin D levels and the likelihood of vitamin D deficiency is greater. Thus, vitamin D deficiency may play a role in the pathogenesis of fertility problems in PCOS women. However, further future longitudinal cohort studies together with prospective randomized trials are needed to better clarify the role of vitamin D in the pathogenesis of female infertility in PCOS women.

Conflict of Interest

The authors declare that they have no conflict of interest.

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