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Original Research Article

Relationship between Vitamin D3 Deficiency and Polycystic Ovarian Syndrome: A Case-Control Study

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Abstract:

Background: The role of vitamin D3 (VD3), a seco-steroid generated in human skin and processed in the liver and kidneys in a sequential manner, in preserving calcium and phosphorus homeostasis and fostering bone mineralization, has long been established. One major cause of ovarian dysfunction in women who anovulate is polycystic ovary syndrome, or PCOS. The purpose of this research is to determine the VD3 level in women with polycystic ovarian syndrome.

Methods: 100 women were included in this study: 50 infertile women with PCOS comprised group A (study group), and 50 patients with other causes of infertility (control group) were chosen. To assess the association between VD3 deficiency and PCOS patients, each patient underwent a US examination, a laboratory analysis of their serum VD3 level (postmenstrual), and a hormonal profile (FSH, LH, AMH, TSH, and prolactin level).

Results: In terms of the LH/FSH ratio, AMH, clinical hyperandrogenism, and irregular menstrual cycle, there was a substantial difference between group A and group B. Regarding TSH, prolactin, and VD3 levels, there was no discernible difference between the two groups. Given that it was below normal in both groups, VD was insufficient. The level of VD3 was significantly correlated negatively with hyperandrogenism and AMH.

Conclusion: Infertility cases and PCO patients had a shortage in vitamin D3, and there was a strong negative association found between the levels of vitamin D3 and clinical hyperandrogenism, LH/FSH ratio, menstrual cycle, and AMH.

Keywords: Vitamin D3 deficiency, PCOS, Infertility

Introduction

The human skin produces vitamin D3, or secosteroid, which is then processed by the liver and kidneys. It is widely recognized for its function in maintaining calcium and phosphorus balance as well as bone mineralization. [1]

Ovarian impairment in females with anovulation is frequently caused by PCOS. Chronic anovulation, hyperandrogenism, and/or the existence of polycystic ovary (PCO) morphology from ultrasound investigation are the key signs. [2]

The disorder's clinical manifestation is linked to varying degrees of metabolic and gonadotropic abnormalities, which are caused by a combination of environmental and hereditary variables.[2] The relationship between a VD deficit and infertility has drawn more attention in recent years. It has been suggested that vitamin D receptors (VDR) are present in human tissues, including the reproductive organs of both sexes, and that they are crucial in promoting the biological activity of vitamin D. Infertility may be caused by a vitamin D deficit, according to a number of research carried out in the last few years. [3]

Low levels of 25(OH) vitamin D may make PCOS symptoms worse, including insulin resistance, irregular menstruation, ovulation, infertility, hyperandrogenism, obesity, and an increased risk of cardiovascular disease. [4]

This study set out to determine and assess the VD3 level in women with polycystic ovarian syndrome.

Material and Methods

100 women who attended the obstetrics and gynecology outpatient and inpatient departments of Sri Krishna Medical College and Hospital, Muzaffarpur, Bihar, were the subjects of this case

control study. The study was carried out between July 2022 and June of 2023.

Before recruiting them for the study and after fully disclosing the purpose and methods, each participant gave their informed written consent.

Two equal groups were formed out of the patients: group A: fifty infertile women with PCOS (diagnosed in accordance with the Rotterdam criteria 2017) made up the study group. (Control group): Group B Fifty patients who had reasons other than PCOS for infertility were selected.

Patients with metabolic bone disease, abnormal liver function, impaired kidney function, patients on medications known to impact the metabolism of calcium and vitamin D (antiepileptic agents, glucocorticoids, antiestrogens, weight loss pills, antiretroviral medications), and patients refusing to engage in the study were the exclusion criteria.

Every case underwent the following tests: a thorough history with a focus on obstetric, menstrual, and past medical history; a general examination that included calculating body mass index (BMI); an assessment of hyperandrogenism (measured using the modified Ferriman-Gallwey scale, where a score of 8 to 15 indicates mild hirsutism and a score greater than 15 indicates moderate or severe hirsutism); a clinical examination; an ultrasound examination; the patients' hormonal profile, including FSH, LH, AMH, TSH, and prolactin on the third day of the menstrual cycle; Every patient had a serum VD3 level tested in a laboratory following the cessation of menstrual blood, and a diagnostic laparoscopy was performed to confirm the diagnosis.

Collection and management of the specimen: a whole blood specimen was obtained by puncturing the antecubital vein, 2 ml of blood was extracted using a standard plastic syringe, and the blood sample was stored in a simple test tube. The serum was separated using a 4000 rpm centrifugation speed. After that, every serum sample was chilled to -20°C until the entire specimen was gathered for chemiluminescent immunoassay (CLIA). Rejected hemolyzed samples.

The association between VD3 deficiency and PCOS patients was the main finding, and the relationships between VD3 level and menstrual abnormalities, hyperandrogenic manifestations/FSH ratio, and ovarian reserve (AMH) in PCOS patients were the secondary findings.

Statistical analysis was done by SPSS v25 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean, standard deviation (SD) and range and were compared between the two groups utilizing unpaired Student's t-test. Categorical variables were presented as frequency and percentage and were analysed utilizing the Chi-square test or Fisher's exact test when appropriate. Pearson or Spearman coefficient correlation (r) was used to estimate the degree of correlation between two variables. $P<0.05$ was considered statistically significant.

Results

When it came to the patient characteristics in the two study groups, there were significant differences in terms of clinical hyperandrogenism and menstrual cycle irregularity between the two groups, but there were also non-significant relationships in terms of age, BMI, gravidity, and length of infertility between the groups (Table 1).

Table 1 : Patients characteristics in both studied groups (n=50)

Characteristics		Group A	Group B	Test	p-value
Age (in years)	Mean±SD Range	25.1±2.56 20-30	25.65±4.15 19-32	T=1.128	0.260
BMI (kg/m^2)	Mean±SD Range	29.91±5.11 23.7-45.9	29.24±3.54 22.2-37.1	T=1.091	0.277
Gravidity	0 1 2	15(30%) 15(30%) 20(40%)	18(36%) 15(30%) 17(34%)	X^2=0.7613	0.755
Duration of infertility (in years)	Mean±SD Range	2.21±0.89 1-4	2.1±0.61 1-3	T=1.038	0.301
Menstrual cycle	Regular Irregular	10(20%) 40(80%)	48(96%) 2(4%)	X^2=16.977	<0.001
Clinical hyperandrogenism	No cases Mild cases Moderate cases Severe cases	22(44%) 21(42%) 2(4%) 5(10%)	47(94%) 3(6%) 0 0	X^2=0.000	<0.001

According to laboratory tests, group A significantly outperformed group B in terms of the LH/FSH ratio and AMH, although there was no significant difference between the two groups in terms of TSH and prolactin (Table 2).

Table 2: Laboratory investigations in both studied groups (n=50)

Variables		Group A	Group B	Test	p-value
LH/FSH ratio	Mean±SD Range	1.27±0.27 0.6-1.75	0.55±0.10 0.37-0.79	24.941	<0.001
AMH (ng/ml)	Mean±SD Range	6.36±3.01 1.1-11.8	2.89±1.17 1-5.2	10.748	<0.001
TSH (IU/ml)	Mean±SD Range	2.09±0.95 0.88-5.2	1.99±0.77 0.96-3.6	0.957	0.442
Prolactin (ng/ml)	Mean±SD Range	18.81±7.10 0.5-33.4	17.31±7.44 9-35	0.319	0.146

There was no discernible change in the VD3 levels between the two groups (Table 3).

Table 3: VD_3 level in both groups

Variables		Group A	Group B	Test	p-value
VD_3 level (ng/ml)	Mean±SD Range	13.63±3.54 8.13-24.4	14.17±3.72 6.14-24.9	1.052	0.297

When comparing the VD3 level to other parameters, Table 4 shows that there was an insignificant link with the menstrual cycle and the LH/FSH ratio, but a negative significant correlation with hyperandrogenism and AMH.

Table 4: Correlation between VD3 level and other parameters

Variables	R	p-value
Hyperandrogenism	-0.150	0.034
LH/FSH ratio	-0.126	0.075
Menstrual cycle	0.021	0.768
AMH	-0.164	0.021

Discussion

Regarding VD3 level, there was a negligible difference between the two groups (p=0.297). Each group had insufficient levels of vitamin D. [5]

In line with our findings, Rahsepar et al.'s case-control study comprised 90 healthy women and 60 PCOS women (20–40 years old). The PCOS group had a mean serum 25(OH)D of 10.76±4.17), which was lower than the control group's mean of 12.07±6.26), but the difference was not statistically significant (p=0.125). [6]

Additionally, Davis et al. demonstrated that although the difference did not achieve statistical significance (21.2% versus 13.6%, p=0.13), a larger proportion of VD insufficiency was seen among PCO cases. [7]

This was not in line with According to Wehr et al., the serum VD level in PCOS-affected women (n = 545) was 25.7 ng/ml, whereas it was 32 ng/ml in the control group (n = 145). [8] This could have contributed to our control group's lower serum VD level; it could have been brought on by differences in lifestyle, geography, or ethnicity.

Additionally, the study by Eftekhar et al. revealed that PCOS patients had lower serum VD levels than control individuals (p<0.001). [9] This could be attributed to differences in lifestyle, geography, or ethnic group.

Furthermore, Li et al. demonstrated that women with PCOS had lower serum VD levels than the control group. [10] This could have contributed to our control group's lower serum VD level; it could have been brought on by differences in lifestyle, geography, or ethnicity.

Mahmoudi et al. also discovered that, although having comparable age and BMI, PCOS-afflicted women had a noticeably lower serum VD level than the control group. [11] This could have contributed to our control group's lower serum VD level; it could have been brought on by differences in lifestyle, geography, or ethnicity. Moreover, healthy women, not infertile ones, were the control group.

This was consistent with the study by Eftekhar et al. [9] They demonstrated that PCO patients had considerably higher AMH levels. Bhide et al. also demonstrated that AMH levels were considerably greater in women with PCO morphology than in the control group. [12] In the groups with low AMH (<4 ng/ml), moderate AMH (4–11 ng/ml), and high AMH (>11 ng/ml), the prevalence of PCOS rose from 21% to 37%.

In line with Hashemi et al., there was no discernible change in TSH between the PCO and control groups. [13] Benetti-Pinto et al. disagree with our findings, finding that 149 women had normal thyroid function and 19 of them had young PCO women with subclinical hypothyroidism. [14] This discrepancy might result from the patients in our study who were

linked to a different cause of infertility than PCOD being excluded.

Tagliaferri et al. discovered that TSH median values were considerably higher in PCOS patients than in controls, which contradicts our findings. [15] 1% of controls and 14% of PCOS participants had subclinical hypothyroidism. This discrepancy might result from the patients in our study who were linked to a different cause of infertility than PCOD being excluded. They contrasted PCO with a healthy control, which is another explanation. Furthermore, Kachoie et al. demonstrated that 50% of women with PCOS who were of reproductive age had elevated TSH levels. [16] This discrepancy might result from the patients in our study who were linked to a different cause of infertility than PCOD being excluded.

Hashemi et al. reported no discernible variation in prolactin levels between the PCO and control groups, which is consistent with our findings. [13] Kachoie et al. descriptive analytical investigation, which involved PCOS patients, contradicted our findings. [16] Prolactin serum levels ranged from 18.56 to 69.81 ng/l, with a mean of 18.56±11.53 ng/l. It differed greatly from the standard level. This discrepancy might result from the patients in our study who were linked to a different cause of infertility than PCOD being excluded. Additionally, prolactin levels were shown to be considerably higher in PCO women with subclinical hypothyroidism by Benetti-Pinto et al. [14] This discrepancy might result from the patients in our study who were linked to a different cause of infertility than PCOD being excluded.

The amount of VD3 and hyperandrogenism had a significant negative connection (r=-0.150, p=0.034). The VD3 level and AMH had a strong negative connection (r=-0.164, p=0.021). The menstrual cycle and the LH/FSH ratio had negligible relationships with the VD3 level (r=-0.126 and 0.021, respectively, p=0.075 and 0.768). Rashad et al. demonstrated a negative correlation between the VD3 level and free testosterone, which is consistent with our findings. [17] Arslan et al. showed, in contrast to our findings, that there was no correlation between the PCO group's AMH levels and 25(OH)D levels. [18] This could be attributed to lifestyle differences, regional conditions, or distinct ethnic groups.

Kozakowski et al. discovered that the LH/FSH ratio (LH/FSH) was connected with VD in PCOS women with abdominal obesity, which contradicts our findings. This could be attributed to lifestyle differences, regional conditions, or distinct ethnic groups. [19] To determine the impact of VD deficit or supplementation on the effectiveness of PCO disease care, more research is required.

Conclusion

Infertility cases and PCO patients had a shortage in vitamin D3, and there was a strong negative association found between the levels of vitamin D3 and clinical hyperandrogenism, LH/FSH ratio, menstrual cycle, and AMH.

References

1. Perez-Lopez FR. Vitamin D: the secosteroid hormone and human reproduction. Gynecol Endocrinol. 2007;23:13-24.
2. Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2012;77:343-50.
3. Rainer D, Davis E, Peck J, Hansen K, Craig L. Vitamin D Deficiency and Time to Pregnancy in Women With Polycystic Ovary Syndrome. Fertil Steril. 2012;97:22-4.
4. Krul-Poel YH, Snackey C, Louwers Y, Lips P, Lambalk CB, Laven JS et al. The role of vitamin D in metabolic disturbances in polycystic ovary syndrome: a systematic review. Eur J Endocrinol. 2013;169:853-65.
5. Knox S, Harris J, Calton L, Wallace AM. A simple automated solid-phase extraction procedure for measurement of 25-hydroxy VD3 and D2 by liquid chromatography-tandem mass spectrometry. Ann Clin Biochem. 2009; 46:226-30.
6. Rahsepar M, Mahjoub S, Esmaelzadeh S, Kanafchian M, Ghasemi M. Evaluation of vitamin D status and its correlation with oxidative stress markers in women with polycystic ovary syndrome. Int J Reprod Biomed. 2017;15:345-50.
7. Davis EM, Peck JD, Hansen KR, Neas BR, Craig LB. Associations between vitamin D levels and polycystic ovary syndrome phenotypes. Minerva Endocrinol. 2019;44:176-84.
8. Wehr E, Trummer O, Giuliani A, Gruber HJ, Pieber TR, Obermayer-Pietsch B. Vitamin D-associated polymorphisms are related to insulin resistance and vitamin D deficiency in polycystic ovary syndrome. Eur J Endocrinol. 2011;164:741-9.
9. Eftekhar M, Mirhashemi ES, Molaei B, Pourmasumi S. Is there any association between vitamin D levels and polycystic ovary syndrome (PCOS) phenotypes? Arch Endocrinol Metab. 2020;64:11-6.
10. Li HW, Brereton RE, Anderson RA, Wallace AM, Ho CK. Vitamin D deficiency is common and associated with metabolic risk factors in patients with polycystic ovary syndrome. Metabolism. 2011;60:1475-81.
11. Mahmoudi T, Gourabi H, Ashrafi M, Yazdi RS, Ezabadi Z. Calciotropic hormones, insulin resistance, and the polycystic ovary syndrome. Fertil Steril. 2010;93:1208-14.

12. Bhide P, Homburg R. Anti-Müllerian hormone and polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2016;37:38-45.
13. Hashemi AH, Mozdarani H, Naghavi A. Comparison of the Levels of LH and FSH, TSH, Prolactin, Progesterone and Estradiol Hormones between Iranian Infertile Women with Polycystic Ovary Syndrome and Healthy Women. Int J Med Sci Public Health. 2016; 5:370-5.
14. Benetti-Pinto CL, Berini Piccolo VR, Garmes HM, Teatin Juliato CR. Subclinical hypothyroidism in young women with polycystic ovary syndrome: an analysis of clinical, hormonal, and metabolic parameters. Fertil Steril. 2013; 99:588-92.
15. Tagliaferri V, Romualdi D, Guido M, Mancini A, De Cicco S, Di Florio C et al. The link between metabolic features and TSH levels in polycystic ovary syndrome is modulated by the body weight: an euglycaemic-hyperinsuli naemic clamp study. Eur J Endocrinol. 2016; 175:433-41.
16. Kachoie A, Jahanipoor A, Ghahiri A. Evaluation of Serum Prolactin Levels in Patients with Polycystic Ovary Syndrome. Journal of Isfahan Medical School. 2012;30:1-6.
17. Rashad NM, Abd El-Fatah AH, Lashin ME-B, Abomandour HG, Allam RM. Impact of vitamin D supplementation on cardio-metabolic status and androgen profile in women with polycystic ovary syndrome: placebo-controlled clinical trial. Middle East Fertil Soc J. 2019 ;24:5.
18. Arslan E, Gorkem U, Togrul C. Is There a Relationship Between Vitamin D Deficiency Status and PCOS in Infertile Women? Geburtshilfe Frauenheilkd. 2019;79:723-30.
19. Kozakowski J, Kapuścińska R, Zgliczyński W. Associations of vitamin D concentration with metabolic and hormonal indices in women with polycystic ovary syndrome presenting abdominal and gynoidal type of obesity. Ginekol Pol. 2014;85:765-70.