The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 7, 2025

EFFECT OF VITAMIN D ON FERTILITY IN POLYCYSTIC OVARIAN SYNDROME

Dr. Zareen Sattar[*1], Dr. Urooj Lalrehman[2], Dr. Usama Ahmed Ansari[3], Dr. Naveen Manzoor[4], Dr. Rukhshanda Jabeen[5], Dr. Wajid Sheikh[6], Dr. Manoj Kumar[7], Dr. Syed Naseebullah[8], Dr. Erum Sohail[9], Dr. Wasifa Aijaz[10]

*[*1,3,4,7,8]Jinnah Postgraduate Medical Centre (JPMC) Fellow MBBS, FCPS*
[2,9,10]Jinnah Postgraduate Medical Centre (JPMC) Associate Professor MBBS, FCPS
[5]Jinnah Postgraduate Medical Centre (JPMC) Professor MBBS, FCPS
[6]Jinnah Postgraduate Medical Centre (JPMC) Senior Registrar MBBS, FCPS

[*1]zareensattar27@gmail.com, [2]drbaloch79@yahoo.com, [3]uansari12358@gmail.com, [4]naveen_m25@yahoo.com, [5]jabeenrukhshanda@gmail.com, [6]wajidshaikh@gmail.com, [7]manojmoolchandani638@gmail.com, [8]drnaseeb44@gmail.com, [9]erum_nathani@yahoo.com, [10]wasfa.dwa@gmail.com

DOI: https://doi.org/10.5281/zenodo.15828378

Keywords
Fertility, Hormonal Regulation, Ovulation, Polycystic Ovary Syndrome, Reproductive Health, Vitamin D.

Article History
Received on 01 June 2025
Accepted on 01 July 2025
Published on 07 July 2025

Corresponding Author: *
Dr. Zareen Sattar

Abstract

OBJECTIVE: *To determine the association of vitamin D status and fertility outcomes in women with polycystic ovarian syndrome.*

METHODOLOGY: *In this cross-sectional study conducted at the Jinnah Postgraduate Medical Centre, Karachi a total of 275 female patients with polycystic ovary syndrome (PCOS) were included to study the effect of vitamin D on reproductive function. Participants were carefully recruited according to the Rotterdam criteria with a rationale of excluding subjects presenting with other endocrine disorders or had treatment of fertility in the past. Detailed analyses were performed on serum concentrations of vitamin D and ovulatory function, as well as metabolic indices. The data was analyzed using version 26 of SPSS, and $p \leq 0.05$ was considered statistically significant.*

RESULTS: *The investigation encompassed a cohort of 275 females diagnosed with Polycystic Ovary Syndrome (mean age 26.19 ± 5.21 years). Infertile participants exhibited markedly diminished levels of vitamin D (11.95 ± 5.86 ng/mL) in comparison to their fertile counterparts (16.71 ± 5.25 ng/mL, p=0.0001). The incidence of vitamin D deficiency was significantly higher among infertile women (85.3% vs. 74.4%, p=0.033). Elevated testosterone concentrations, insulin resistance (HOMA-IR: 3.42 vs. 3.01, p=0.008), as well as waist-to-hip ratio, were also correlated with infertility.*

CONCLUSION: *The findings reveal a strong correlation of vitamin D deficiency with reproductive problems in women with polycystic ovary syndrome (PCOS). Women with infertility had vitamin D levels that were significantly lower than others and those levels were associated with insulin sensitivity, hormonal disorders and ovulatory problems. However, more research is needed to determine the best treatment methods. Furthermore, supplementation of vitamin D should be incorporated within the management of PCOS, especially in those*

women with challenges in achieving pregnancy, and the vitamin D levels need to be monitored on regular basis.

INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of most common endocrine disorders affecting women of reproductive age with a prevalence of approximately 5%-20%, depending on the specific criteria used to diagnose it [1]. Polycystic ovary syndrome (PCOS) is described as an endocrinological disorder characterized by ovarian dysfunction and clinical or paraclinical indications of hyperandrogenism, as well as the most widespread reproductive disorder to be associated with pathologies of fertility systems [2]. Moreover, apart from the reproductive complications, the diagnosis of PCOS is also associated with a wide range of metabolic disorders such as insulin resistance, obesity, and dyslipidemia [3, 4]. Vitamin D is well known for its important function in bone health and calcium homeostasis but has recently been a focus of much scientific research due to its wider role in reproductive and metabolic health [5, 6]. Various studies have shown that 67% – 85% of the women with PCOS are diagnosed with Vitamin D insufficiency, which may aggravate both metabolic and reproductive abnormalities [7,8]. Digression in serum vitamin D status has been related to anovulation, deviant formation of menstrual cycles, and abnormal folliculogenesis [9,10], all of which may impact reproduction in a negative way [9,10]. Such causative pathways could be through hormone modulation, or alternatively, epigenetic changes. Vitamin D is believed to affect the FSH/LH ratio, the level of androgen, and the follicle maturation, thus exerting its influence on the ovarian function [11-12]. Besides, it has crosstalk with reproduction related genes and changes the gene expression with epigenetic regulation [13-14]. Due to the elevated incidence of vitamin D insufficiency among females diagnosed with polycystic ovary syndrome (PCOS) and the hypothesized implications of vitamin D on infertility, the objective of the current investigation was to examine the correlation between vitamin D concentrations and reproductive outcomes in women afflicted by PCOS [16]. We assessed the impact on ovulation, menstrual cycle regularity, and delays in conception. Achieving a comprehensive understanding of this association could facilitate the development of targeted clinical strategies aimed at enhancing fertility in patients, particularly in women experiencing the challenges associated with PCOS.

METHODOLOGY

This investigation analyzed the influence of vitamin D concentrations on fertility among women diagnosed with polycystic ovarian syndrome (PCOS). The research was conducted within the Endocrinology Department of Jinnah Postgraduate Medical Centre, Karachi, encompassing a sample of 275 women aged between 18 and 40, all of whom were diagnosed with PCOS according to the Rotterdam criteria. Participants were selected utilizing non-probability consecutive sampling, exclusively including those who were actively attempting to conceive and not currently utilizing vitamin D supplements. Exclusion criteria comprised women with other endocrine disorders, ovarian or endometrial malignancies, previous ovarian surgeries, or a documented history of unsuccessful fertility treatments. Blood examinations were performed to quantify vitamin D levels (specifically serum 25-hydroxyvitamin D), while fertility assessments were conducted based on the duration to conception, ovulatory function, and menstrual cycle regularity. Ultrasound imaging was employed to evaluate ovarian health, and hormone levels—including testosterone, LH, FSH, and AMH—were systematically analyzed. Additionally, indicators of insulin resistance such as fasting blood glucose, fasting insulin, and HOMA-IR were documented. The data were processed utilizing SPSS version 26, and various statistical analyses were executed to investigate the relationship between vitamin D and fertility. A p-value of ≤ 0.05 was deemed statistically significant.

RESULTS

The mean age of the study participants is recorded at 26.19 years, accompanied by a standard deviation of 5.21 years, which signifies a relatively youthful demographic. The 95% confidence interval (CI) for age spans from 25.57 to 26.81 years, indicating a limited range of variability in age among the subjects.

The average Body Mass Index (BMI) is noted to be 26.11 kg/m², with a standard deviation of 3.46 kg/m². The 95% CI for BMI is delineated between 25.70 and 26.52 kg/m², suggesting that the majority of participants possess similar BMI values. Systolic blood pressure is observed to average 110.70 mmHg, with a standard deviation of 9.65 mmHg, and a 95% CI ranging from 109.56 to 111.85 mmHg, which implies normal blood pressure levels within the cohort. Diastolic blood pressure exhibits a mean of 71.22 mmHg, with a standard deviation of 5.22 mmHg, and a 95% CI from 70.60 to 71.84 mmHg, further indicating normal physiological levels. Fasting blood glucose levels are reported to average 91.31 mg/dl, with a standard deviation of 6.28 mg/dl, and a 95% CI extending from 90.56 to 92.06 mg/dl, suggesting normative glucose homeostasis. The Ferriman–Gallwey score, utilized for the evaluation of hirsutism, averages at 8.70, with a standard deviation of 2.01, and a 95% CI between 8.46 and 8.94, indicating mild hirsutism among participants. Total cholesterol levels average 176.11 mg/dl, with a standard deviation of 15.28 mg/dl, and a 95% CI ranging from 174.29 to 177.92 mg/dl, suggesting that the cohort maintains normal cholesterol levels. High-density lipoprotein (HDL) averages 54.06 mg/dl, with a standard deviation of 6.79 mg/dl, and a 95% CI from 53.26 to 54.87 mg/dl, indicating healthful HDL levels. Luteinizing hormone levels are reported to average 9.03 IU/L, with a standard deviation of 2.60 IU/L, and a 95% CI from 8.72 to 9.34 IU/L, suggesting normative reproductive hormone levels. Total testosterone levels average at 1.43 ng/ml, with a standard deviation of 0.34 ng/ml, and a 95% CI from 1.39 to 1.47 ng/ml, indicating standard testosterone levels. Anti-Mullerian hormone levels average 7.77 ng/ml, with a standard deviation of 2.69 ng/ml, and a 95% CI between 7.45 and 8.09 ng/ml, suggesting a normal ovarian reserve. The average concentration of 25(OH)D3, which serves as a biomarker for vitamin D status, is 13.30 ng/ml, with a standard deviation of 6.08 ng/ml, and a 95% CI from 12.58 to 14.03 ng/ml, indicating a potential deficiency in vitamin D. Thyroid-stimulating hormone levels are noted to average 2.16 mIU/L, with a standard deviation of 1.06 mIU/L, and a 95% CI from 2.03 to 2.29 mIU/L, suggesting normal thyroid function as illustrated in Table I.

There exists no statistically significant disparity in age between women with polycystic ovary syndrome (PCOS) who are infertile compared to their fertile counterparts, as evidenced by a p-value of 0.282, which denotes a comparable age distribution across both cohorts. The Body Mass Index (BMI) also does not exhibit a significant difference between the two populations (p-value = 0.599), thereby suggesting that BMI does not serve as a distinguishing criterion for fertility status within this sample. A statistically significant difference is discerned in the waist-to-hip ratio, wherein infertile women present with a higher ratio (p-value = 0.0001), potentially indicating an increased central adiposity among the infertile group. No statistically significant disparities are identified in systolic and diastolic blood pressure between the two cohorts (p-values = 0.569 and 0.220, respectively). Fasting blood glucose levels display a trend towards statistical significance (p-value = 0.053), with fertile women exhibiting marginally elevated levels. Infertile women demonstrate a significantly elevated Ferriman–Gallwey score (p-value = 0.003), which denotes a more pronounced severity of hirsutism. High-density lipoprotein (HDL) levels are markedly diminished in fertile women (p-value = 0.010), whereas low-density lipoprotein (LDL) and triglycerides are observed to be elevated (p-values = 0.034 and 0.027, respectively). Total testosterone levels are significantly higher in women experiencing infertility (p-value = 0.010), thereby suggesting a possible correlation with fertility challenges. A significant difference in 25(OH)D3 levels is noted, with infertile women exhibiting lower concentrations (p-value = 0.0001), indicating an increased occurrence of vitamin D deficiency within this demographic. The prevalence of vitamin D deficiency is significantly greater among infertile women (85.3%) in comparison to fertile women (74.4%), with a p-value of 0.033 as delineated in Table II.

Table I: Clinical Characteristics of Study Participants (n=275)	
Mean ± SD	**95% CI**
Age in years= 26.19 ± 5.21	25.57-–26.81
Body Mass Index in kg/m^2 = 26.11 ± 3.46	25.70-–26.52

Waist-to-hip ratio = 0.82 ± 0.21	0.82⁓0.83
Systolic Blood Pressure in mmHg = 110.70 ± 9.65	109.56⁓111.85
Diastolic Blood Pressure in mmHg = 71.22 ± 5.22	70.60⁓71.84
Ferriman–Gallwey score= 8.70 ± 2.01	8.46⁓8.94
Fasting Blood Glucose in mg/dl = 91.31 ± 6.28	90.56⁓92.06
Fasting Insulin in µIU/mL = 12.96 ± 4.60	12.41⁓13.51
HOMA-IR = 3.31 ± 1.16	3.17⁓3.44
Total Cholesterol in mg/dl = 176.11 ± 15.28	174.29⁓177.92
High-Density Lipoprotein in mg/dl = 54.06 ± 6.79	53.26⁓54.87
Low-Density Lipoprotein in mg/dl = 98.94 ± 14.61	97.20⁓100.67
Triglycerides in mg/dl = 126.17 ± 18.31	124.00⁓128.35
Luteinizing Hormone in IU/L = 9.03 ± 2.60	8.72⁓9.34
Follicle-stimulating Hormone in mIU/L = 5.26 ± 1.31	5.11⁓5.42
Total Testosterone in ng/ml = 1.43 ± 0.34	1.39⁓1.47
Dehydroepiandrosterone Sulfate in mcg/dL = 283.09 ± 84.66	273.04⁓293.14
Sex Hormone-Binding Globulin in nmol/l = 51.13 ± 15.72	49.27⁓53.00
Thyroid-Stimulating Hormone in mIU/L = 2.16 ± 1.06	2.03⁓2.29
Anti-Mullerian Hormone in ng/ml = 7.77 ± 2.69	7.45⁓8.09
25(OH)D_3 in ng/ml = 13.30 ± 6.08	12.58⁓14.03

Table II: Comparison of Clinical Characteristics of Infertile and Fertile women with PCOS (n=275)

Mean ± SD	**Infertile** (n=197)	**Fertile** (n=78)	**P-Value**
Age in years	25.98 ± 5.18	26.73 ± 5.27	0.282
Body Mass Index in kg/m^2	26.18 ± 3.51	25.94 ± 3.35	0.599
Waist-to-hip ratio	0.83 ± 0.02	0.81 ± 0.01	0.0001
Systolic Blood Pressure in mmHg	110.49 ± 9.60	111.23 ± 9.82	0.569
Diastolic Blood Pressure in mmHg	71.46 ± 5.41	70.60 ± 4.68	0.220
Ferriman–Gallwey score	8.48 ± 1.98	9.27 ± 1.99	0.003
Fasting Blood Glucose in mg/dl	90.85 ± 6.35	92.47 ± 5.99	0.053
Fasting Insulin in µIU/mL	13.08 ± 4.57	12.65 ± 4.70	0.489
HOMA-IR	3.42 ± 1.18	3.01 ± 1.06	0.008
Total Cholesterol in mg/dl	175.89 ± 15.24	176.67 ± 15.49	0.704
High-Density Lipoprotein in mg/dl	54.73 ± 6.70	52.38 ± 6.78	0.010
Low-Density Lipoprotein in mg/dl	97.76 ± 15.31	101.91 ± 12.28	0.034
Triglycerides in mg/dl	124.63 ± 19.34	130.05 ± 14.82	0.027
Luteinizing Hormone in IU/L	9.20 ± 2.63	8.59 ± 2.48	0.079
Follicle-stimulating Hormone in mIU/L	5.33 ± 1.31	5.09 ± 1.31	0.173
Total Testosterone in ng/ml	1.46 ± 0.33	1.34 ± 0.34	0.010
Dehydroepiandrosterone Sulfate in mcg/dL	286.23 ± 84.48	275.15 ± 85.14	0.329
Sex Hormone-Binding Globulin in nmol/l	51.75 ± 15.63	49.59 ± 15.96	0.306

Thyroid-Stimulating Hormone in mIU/L	2.11 ± 1.04	2.28 ± 1.09	0.231
Anti-Mullerian Hormone in ng/ml	7.89 ± 2.70	7.46 ± 2.66	0.238
25(OH)D_3 in ng/ml	11.95 ± 5.86	16.71 ± 5.25	0.0001
Vitamin D deficiency, n (%)	168 (85.3%)	58 (74.4%)	0.033

DISCUSSION

This study highlights a significant association between vitamin D deficiency and reduced fertility in women diagnosed with polycystic ovary syndrome (PCOS). Women experiencing infertility exhibited significantly lower serum 25(OH)D3 concentrations (11.95 ± 5.86 ng/mL) in comparison to their fertile peers (16.71 ± 5.25 ng/mL, p=0.0001), with vitamin D deficiency being notably more prevalent in the infertile cohort (85.3% vs. 74.4%, p=0.033). These findings align with previous research suggesting that women with PCOS who face infertility commonly present with diminished vitamin D levels and a higher incidence of deficiency [15].

One plausible explanation for this correlation is the critical role that vitamin D plays in maintaining hormonal equilibrium and facilitating ovulation. It is recognized for its ability to modulate ovarian functionality, affect the luteinizing hormone to follicle-stimulating hormone ratio, and govern follicular maturation [16,17]. Insufficient levels of vitamin D have been associated with anovulation and irregular menstrual cycles, which are characteristic features of infertility in PCOS [18]. In alignment with this, our investigation revealed that infertile women had significantly elevated testosterone levels (1.46 ± 0.33 ng/mL vs. 1.34 ± 0.34 ng/mL, p=0.010), thereby bolstering the hypothesis that vitamin D may mitigate hyperandrogenism, subsequently enhancing ovulatory performance [19].

Another pivotal element affecting fertility in PCOS is insulin resistance, which has been closely associated with vitamin D metabolism. Our study identified that infertile women exhibited significantly higher HOMA-IR values (3.42 ± 1.18) relative to fertile women (3.01 ± 1.06, p=0.008), signifying heightened insulin resistance within the infertile cohort. Previous research indicates that vitamin D can enhance the expression of insulin receptors, optimize pancreatic β-cell functionality, and diminish hyperinsulinemia, all of which are conducive to improved glucose metabolism and favorable reproductive outcomes [20,21]. A study conducted by Kokanalı et al. established an inverse correlation between vitamin D levels and insulin resistance, revealing that infertile women with PCOS presented with lower vitamin D concentrations (10.48 ± 5.30 ng/mL) and more pronounced insulin resistance compared to their fertile peers [15].

Obesity is another well-established factor influencing both vitamin D concentrations and fertility. Although our study did not reveal significant disparities in body mass index (BMI) between fertile and infertile women, the waist-to-hip ratio was significantly elevated in the infertile group (0.83 ± 0.02 vs. 0.81 ± 0.01, p=0.0001), indicating central adiposity as a contributing factor to adverse fertility outcomes. Prior research suggests that obese women with PCOS are at an increased risk for vitamin D deficiency, which may exacerbate both metabolic dysfunction and reproductive irregularities [20-21].

Notwithstanding these findings, our study is not without its limitations. As a cross-sectional study, it does not establish a causal relationship between vitamin D deficiency and infertility. Furthermore, external variables such as exposure to sunlight, seasonal fluctuations, and dietary intake were not considered, which could affect vitamin D status. While the exclusion of participants utilizing vitamin D supplements ensures the integrity of baseline measurements, it concurrently restricts the understanding of how supplementation may influence fertility outcomes.

CONCLUSION

The findings reveal a strong correlation of vitamin D deficiency with reproductive problems in women with polycystic ovary syndrome (PCOS). Women with infertility had vitamin D levels that were significantly lower than others and those levels were associated with insulin sensitivity, hormonal disorders and ovulatory problems. However, more research is

needed to determine the best treatment methods. Furthermore, supplementation of vitamin D should be incorporated within the management of PCOS, especially in those women with challenges in achieving pregnancy, and the vitamin D levels need to be monitored on regular basis.

REFERENCES

Muscogiuri G, Altieri B, de Angelis C, Palomba S, Pivonello R, Colao A, et al. Shedding new light on female fertility: the role of vitamin D. Rev Endocr Metab Disord. 2017;18(3):273-83.

Muscogiuri G, Altieri B, Annweiler C, Balercia G, Pal HB, Boucher BJ, et al. Vitamin D and chronic diseases: The current state of the art. Arch Toxicol. 2017;91(1):97-107.

Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clin Endocrinol (Oxf). 2012;77(3):343-50.

Tannus S, Tan J, Son WY, Dahan M. Prevalence, clinical characteristics, and reproductive outcomes of polycystic ovary syndrome in older women referred for tertiary fertility care. Arch Gynecol Obstet. 2017;297(5):1037-42.

Menichini D, Forte G, Orrù B, Gullo G, Unfer V, Facchinetti F. The role of vitamin D in metabolic and reproductive disturbances of polycystic ovary syndrome: A narrative mini-review. Int J Vitam Nutr Res. 2020;92(3):126-33.

Zhao J, Liu S, Wang Y, Wang P, Qu D, Liu M, et al. Vitamin D improves in-vitro fertilization outcomes in infertile women with polycystic ovary syndrome and insulin resistance. Minerva Med. 2019;110(3):199-208.

Shahrokhi SZ, Ghaffari F, Kazerouni F. Role of vitamin D in female reproduction. Clin Chim Acta. 2016;455:33-8.

Nandi A, Sinha N, Ong E, Sonmez H, Poretsky L. Is there a role for vitamin D in human reproduction? Horm Mol Biol Clin Investig. 2016;25(1):15-28.

Franasiak JM, Lara-Molina EE, Pellicer A. Vitamin D in human reproduction. Curr Opin Obstet Gynecol. 2017;29(3):189-94.

Voulgaris N, Papanastasiou L, Piaditis G, Angelousi A, Kaltsas G, Mastorakos G, et al. Vitamin D and aspects of female fertility. Hormones. 2017;16(1):5-21.

Azziz R. Polycystic Ovary Syndrome. Obstet Gynecol. 2018;132(2):321-36.

Pal L, Zhang H, Williams J, Santoro NF, Diamond MP, Schlaff WD, et al. Vitamin D status relates to reproductive outcome in women with polycystic ovary syndrome: secondary analysis of a multicenter randomized controlled trial. J Clin Endocrinol Metab. 2016;101(8):3027-35.

Mu Y, Cheng D, Yin TL, Yang J. Vitamin D and polycystic ovary syndrome: A narrative review. Reprod Sci. 2021;28(8):2110-7.

Kuyucu Y, Çelik LS, Kendirlinan Ö, Tap Ö, Mete UÖ. Investigation of the uterine structural changes in the experimental model with polycystic ovary syndrome and effects of vitamin D treatment: An ultrastructural and immunohistochemical study. Reprod Biol. 2018;18(1):53-9.

Kokanalı D, Karaca M, Ozakşit G, Elmas B, Üstün YE. Serum vitamin D levels in fertile and infertile women with polycystic ovary syndrome. Geburtshilfe Frauenheilkd. 2019;79(5): 510-6.

Berry S, Seidler K, Neil J. Vitamin D deficiency and female infertility: A mechanism review examining the role of vitamin D in ovulatory dysfunction as a symptom of polycystic ovary syndrome. J Reprod Immunol. 2022;151:103633.

Mu Y, Cheng D, Yin TL, Yang J. Vitamin D and polycystic ovary syndrome: A narrative review. Reprod Sci. 2021;28(8):2110-7.

Menichini D, Forte G, Orrù B, Gullo G, Unfer V, Facchinetti F. The role of vitamin D in metabolic and reproductive disturbances of polycystic ovary syndrome: A narrative mini-review. Int J Vitam Nutr Res. 2020;92(3):126-33.

Sulaiman EA, Dhiaa S, Merkhan MM. Overview of vitamin D role in polycystic ovarian syndrome. MMSL. 2022;91(1):37-43.

Morgante G, Darino I, Spanò A, Luisi S, Luddi A, Piomboni P, et al. PCOS physiopathology and vitamin D deficiency: biological insights and perspectives for treatment. J Clin Med. 2022;11(15):4509.

Várbíró S, Takács I, Tűű L, Nas K, Sziva RE, Hetthéssy JR, et al. Effects of vitamin D on fertility, pregnancy and polycystic ovary syndrome—a review. Nutrients. 2022;14(8):1649