

Original Article

Status and Association of Vitamin D Deficiency with Metabolic Risk Factors in Women with Polycystic Ovary Syndrome

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Abstract

Objectives: To investigate the status and association of vitamin D insufficiency and its relationship to metabolic risk factors in polycystic ovarian syndrome patients.

Methodology: This cross sectional comparative study consisted of 140 women having 70 diagnosed patients of PCOS and 70 controls. By using non-probability consecutive sampling, patients who met the inclusion and exclusion criteria were enrolled. This study was conducted in the department of Obstetrics & Gynecology, Nishtar Medical University, Multan, in a period of one year from January 2022 to January 2023. All research participants' biochemical markers, including testosterone, FSH, LH, blood lipids, glucose, insulin, and serum 25(OH)D were evaluated, along with their demographic data.

Results: The mean age (27.25 ± 3.86 vs. 25.85 ± 4.94) was similar in both groups, mean BMI (26.5 ± 5.83 vs. 23.37 ± 5.28) was significantly (p -value < 0.05) higher in PCOS women higher rate of over weight females (47.14% vs. 32.86%) and obese females (25.71% vs. 7.14%) as compare to normal controls. The mean value of vitamin D level (38.75 ± 20.54 nmol/L) was significantly (p -value < 0.05) lower in PCOS females in contrast to (69.46 ± 23.85 nmol/L) normal healthy controls. The mean values of Fasting plasma glucose level, Insulin and HOMA-IR were significantly (P -value < 0.05) higher in PCOS females. The lipid parameters, LDL-C, and TGs were also found to be significantly (P -value < 0.05) different between PCOS and Controls. body mass index (BMI), FPG, Insuline, HOMA-IR, LDL, TGs, LH and Testosterone level showed a significant (P -value < 0.05) and negative correlation with vitamin D level among females having PCOS.

Conclusion: Vitamin D insufficiency affects PCOS women, particularly those who are obese and have insulin resistance. A strong and negative correlation was observed between the serum 25(OH)D levels and metabolic risk variables including BMI, FPG, Insuline, HOMA-IR, LDL, TGs, LH, and Testosterone level.

Key Words: Polycystic Ovary Syndrome, Vitamin D Insufficiency, Metabolic risk factors.

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Introduction

The most common endocrine metabolic disorder in women is polycystic ovarian syndrome (PCOS), which is an issue with the endocrine system. Numerous studies and investigations have revealed that 5–10% of people worldwide have PCOS. These women are more likely to experience polycystic ovaries, excessive androgenism, and irregular menstrual periods.¹ Anovulation, increased insulin secretion, and central

obesity are all linked to polycystic ovarian syndrome, which can result in chronic issues such diabetes mellitus (DM), endocrine gland cancer, and cardiovascular disorders.²

PCOS, which affects 18% of women in this age group, is the most common endocrine condition that affects women throughout their period of reproduction. Infertility, high androgen levels, polycystic ovaries on

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ultrasound, hirsutism, menstrual disorder, and hyperandrogenism are all symptoms of PCOS.³

According to recent studies, PCOS patients typically have vitamin D deficiency, which has been linked to metabolic issues. When compared to the general population, women with polycystic ovarian syndrome had a higher prevalence of vitamin D deficiency.^{4,5} Vitamin D levels and a number of PCOS symptoms, including infertility, insulin resistance, and hirsutism, have been found to be linked in numerous studies.⁶

The rate of vitamin D deficiency is quite higher among the women having PCOS as compared to normal healthy females of general population and this insufficiency is correlated with PCOS-related comorbidities. The main contributors to the clinical picture of PCOS appear to be hormonal anomalies brought on by inconsistencies in steroidogenesis. According to some data, abnormalities in the steroidogenesis pathway, which are brought on by high levels of androgen or insulin resistance (IR) in PCOS women, are a significant contributor to ovarian dysfunction and aberrant folliculogenesis.^{7,8} Studies conducted in vitro and in vivo showed that ovulatory failure, endocrine changes, and IR, among other PCOS-related symptoms, may be regulated by the vitamin D along the way. In human ovarian cells, vitamin D promotes the formation of estradiol, estrone, and progesterone both independently and, in the case of estradiol, concurrently with insulin.⁹

A strong relationship has been found between low vitamin D levels and a worse metabolic risk profile in PCOS-affected women, which includes factors including the HOMA-IR score, hyperinsulinemia, and dyslipidemia.¹⁰ Therefore, it is critical to check for hypovitaminosis D in all PCOS patients. Recent interventional trials showing that proper vitamin D supplements improved the sensitivity of insulin and unusual metabolic profiles in Vitamin-D-deficient PCOS patients further underline the necessity of using vitamin D in the treatment of PCOS.¹¹

Metabolic diseases and vitamin D deficiency are linked; however little research has been done on vitamin D status in PCOS-affected women in our country. Therefore, this present study was planned to investigate the status of vitamin D and its association with metabolic risk factors among females having PCOS in comparison to normal healthy controls.

Methodology

In this Cross Sectional Comparative Study, diagnosed patients of polycystic ovarian syndrome and healthy controls visiting to the department of Obstetrics & Gynecology, Nishtar Medical University, Multan, were included. The study period was one year from January 2022 to January 2023. The data gathering process for this study began after gaining approval from the hospital ethical review committee. A nonprobability sequential sampling approach was used to register patients who met our criteria. All of the individuals who were selected for the study received an explanation of the study methodology, and the researcher got their informed written consent. Their non-medical and medical information's confidentiality was upheld. A total of 140 women consisting on 70 diagnosed patients of PCOS and 70 controls were included in the study. WHO sample size calculator was utilized for sample size calculation by using level of significance of 5%, power of test 80% and vitamin D deficiency rate of 54.4% among PCOS and 37.7% in controls.¹⁰

The study group was consisted on women having PCOS in reproductive age (18 to 40 years). While the control group had healthy women in the same age range. Rotterdam criteria were amended and utilized as the diagnostic standards for PCOS. Women with autoimmune disorders, congenital adrenal hyperplasia, or thyroid dysfunction were not allowed to participate in the study.

Demographic data including waist to hip ratio, body mass index and blood pressure were recorded from all women in the study. Obesity was characterized as a BMI > 30 kg/m². All biochemical markers, including serum 25(OH)D, blood sugar, insulin, blood lipids, FSH, LH, and testosterone, were examined. Using the following formulas, HOMA-IR was calculated to assess insulin resistance (IR).

$$\text{HOMAIR} = [(\text{fasting glucose}) \times (\text{fasting insulin})] / 22.5.$$

The level of HOMA IR (> 2.5) was taken as insulin resistance. A level less than (50 nmol/L) of serum 25(OH)D concentrations was defined as vitamin D deficiency, a level of between (50-75 nmol/L) was taken as vitamin D insufficiency and normal level of vitamin D was defined as serum 25(OH)D concentration of more than (75 nmol/L).

The entire set of collected information was entered into SPSS version 25 for analysis. Frequencies along with percentages were calculated for qualitative data and

mean along with SD was calculated for presentation of quantitative data. For qualitative data, the Chi-square test was utilized, and for quantitative data, the independent sample t-test. Significance level was set at P-values ≤ 0.05.

Results

In this cross sectional comparative study 140 women consisting on 70 PCOS patients and 70 normal healthy women were enrolled. The mean age (27.25 ± 3.86 vs. 25.85 ± 4.94) of both the groups was not significantly (p-value > 0.05) different in both groups. The mean BMI value of PCOS group (26.5 ± 5.83 vs. 23.37 ± 5.28) was significantly (p-value < 0.05) higher in PCOS women in comparison to healthy controls. Among

was found that total cholesterol and HDL-C were not significantly (P-value > 0.05) different between both groups but mean values of LDL-C (2.85 ± 0.92 vs. 2.15 ± 0.71) and TGs (1.74 ± 1.46 vs. 1.14 ± 0.58) were found to be significantly (P-value < 0.05) different between PCOS and Controls. The mean value of FSH levels were seen similar in both groups without any significant (P-value > 0.05) difference between both groups on the basis of FSH but mean values of LH (11.78 ± 2.96 vs. 9.58 ± 2.49) and Testosterone (2.78 ± 0.84 vs. 1.52 ± 0.63) were found to be significantly (P-value < 0.05) higher among PCOS group as elaborated in table II.

The Pearson Correlation coefficient (r) was calculated for all the study variables to find out the relationship of

Table I: Distribution of demographic characteristics and vitamin D levels

Characteristics	PCOS (n=70)		Control (n=70)		P-value
	Frequency	Percentage	Frequency	Percentage	
Age of the participants					
Mean ± SD	27.25 ± 3.86		25.85 ± 4.94		0.126
Body Mass Index (BMI)					
Mean ± SD	26.5 ± 5.83		23.37 ± 5.28		0.001*
Body Mass Index (BMI) Grades					
Under weight (< 19)	5	7.14%	8	11.43%	0.000*
Normal (19-25)	14	20.00%	34	48.57%	
Over weight (25-30)	33	47.14%	23	32.86%	
Obese (≥ 30)	18	25.71%	5	7.14%	
Vitamin D levels among participants (nmol/L)					
Mean ± SD	38.75 ± 20.54		69.46 ± 23.85		0.000*
Vitamin D status among participants (nmol/L)					
Deficiency (<50)	47	67.14%	13	18.57%	0.000*
insufficiency (50-75)	19	27.14%	18	25.71%	
Normal (> 75)	4	5.71%	39	55.71%	

* Significant at 5% level of significance

PCOS females the rate of over weight females (47.14% vs. 32.86%) and obese females (25.71% vs. 7.14%) was significantly (p-value < 0.05) higher as compare to normal controls. The mean value of vitamin D level (38.75 ± 20.54 nmol/L) was significantly (p-value < 0.05) lower in PCOS females in contrast to (69.46 ± 23.85 nmol/L) mean value in normal healthy controls as given table I.

The comparison of metabolic parameters of females with PCOS and healthy controls showed that mean values of Fasting plasma glucose level (mmol/L) (6.28 ± 1.34 vs. 4.38 ± 0.48), Insulin (µU/mL) (13.55 ± 4.26 vs. 7.95 ± 2.45), and HOMA-IR were noted to be higher significantly among PCOS females in contrast to healthy controls. In comparison of lipid parameters, it

Table II: Distribution of Metabolic parameters of PCOS and Controls

Variables	PCOS (n=70)	Control (n=70)	P-value
Fasting plasma glucose level (mmol/L)	6.28 ± 1.34	4.38 ± 0.48	0.000*
Insulin (µU/mL)	13.55 ± 4.26	7.95 ± 2.45	0.000*
HOMA-IR (n)	9.08 ± 2.85	5.27 ± 1.15	0.000*
Total Cholesterol (mmol/L)	5.07 ± 1.98	4.87 ± 1.42	0.493
HDL-C (mmol/L)	1.78 ± 0.85	1.94 ± 1.18	0.359
LDL-C (mmol/L)	2.85 ± 0.92	2.15 ± 0.71	0.000*
TGs (mmol/L)	1.74 ± 1.46	1.14 ± 0.58	0.002*
FSH (mIU/mL)	6.81 ± 1.71	7.65 ± 1.69	0.495
LH (mIU/mL)	11.78 ± 2.96	9.58 ± 2.49	0.000*
Testosterone (nmol/L)	2.78 ± 0.84	1.52 ± 0.63	0.000*

all these variables including metabolic parameters, lipid parameters and thyroid parameters with vitamin D levels of PCOS patients and it was found that body mass index (BMI), FPG, Insuline, HOMA-IR, LDL, TGs, LH and Testosterone level showed a significant (P-value < 0.05) and negative correlation with vitamin D level among females having PCOS as given in detail in table III.

Table III: Correlation of vitamin D with other parameters among PCOS women

Variables	Pearson Correlation "r"	P-value
Age	- 0.138	0.079
BMI	- 0.329	0.019*
Fasting plasma glucose level (mmol/L)	- 0.176	0.041*
Insulin (μ U/mL)	- 0.304	0.001*
HOMA-IR (n)	- 0.309	0.023*
Total Cholesterol (mmol/L)	- 0.287	0.328
HDL - C (mmol/L)	0.174	0.354
LDL - C (mmol/L)	- 0.518	0.008*
TGs (mmol/L)	- 0.627	0.017*
FSH (mIU/mL)	0.169	0.288
LH (mIU/mL)	- 0.448	0.047*
Testosterone (nmol/L)	- 0.380	0.029*

* Significant at 5% level of significance

Discussion

Most common risk factors of PCOS include types 2 diabetes mellitus, cardiovascular disease and metabolic syndrome and PCOS is considered as most frequent and common cause of anovulatory infertility.¹² Many other diseases like hyperinsulinemia, insulin resistance, dyslipidemia and central obesity has been found to be associated with PCOS. Metabolic abnormalities are frequent in PCOS-affected females, literature shows that till the age of forties, around 10% females with PCOS develop type 2 diabetes mellitus and impaired glucose tolerance, IR and hyperinsulinemia is developed in 30%-40% of PCOS females.¹³ According to a recent meta-analysis, women with PCOS have higher levels of LDL and non-HDL cholesterol than women without the condition, independent of BMI. This indicates that dyslipidemia affects PCOS patients more frequently than control patients. According to the most recent data, IR is thought to play a major role in the pathophysiology of PCOS and contribute to both metabolic and reproductive abnormalities.¹⁴ The mechanism of metabolic abnormalities, particularly IR, in PCOS-affected women has been the subject of numerous investigations.

The findings of the present study were found very much in agreement to these findings. The comparison of metabolic parameters of females with PCOS and healthy controls showed that mean values of Fasting plasma glucose level (6.28 ± 1.34 vs. 4.38 ± 0.48), Insulin (13.55 ± 4.26 vs. 7.95 ± 2.45), and HOMA-IR were found significantly (P-value < 0.05) raised among females having PCOS as compared to healthy controls. In comparison of lipid parameters, it was found mean values of LDL-C (2.85 ± 0.92 vs. 2.15 ± 0.71) and TGs (1.74 ± 1.46 vs. 1.14 ± 0.58) were found to be significantly (P-value < 0.05) different between PCOS and Controls.

Vitamin D deficiency is one of the most common nutritional health issues in the world, affecting 20 to 48% of adults overall and increasing to 58 to 91% of women who are subfertile. Although there is considerable debate over the optimal level of 25(OH)D, 50 nmol/L can be regarded as a marker of vitamin D sufficiency.¹⁵ In this present study it was found that the rate of (>50 nmol/L) was (18.57%) significantly less among females with PCOS as compared to (67.14%) females in normal healthy controls. Many studies have shown that mean vitamin D levels are significantly lower in PCOS females. A study of Bindayel found that mean vitamin D levels (49.20 ± 22.5 nmol/L) were significantly lower in Saudi women with PCOS than (61.01 ± 33.9 nmol/L) in women who do not have PCOS.¹⁶ Similar trend was found in the present study in which it was observed that mean Vitamin D level was very low (38.75 ± 20.54 vs. 69.46 ± 23.85 nmol/L) among females presented with PCOS in comparison to non PCOS females.

The results of the present investigation revealed a strong negative correlation between serum 25(OH)D levels in PCOS women and BMI, FPGL, insulin, HOMAIR, LDL-C, TGs, LH, and testosterone. These findings imply that vitamin D insufficiency is more likely to occur in PCOS individuals with metabolic risk factors. Similar findings have been reported by different studies investigated relationship of Vitamin D and metabolic risk factors among females, who presented with PCOS.^{10, 17}

Recent interventional trials have confirmed the significance of vitamin D grading in nutrition, aetiology, and therapy of PCOS by demonstrating that adequate vitamin D elevation in females with vitamin D insufficiency leads to improvement in their worsened reproductive and metabolic hormone profiles[RR1]. It

has been established that all patients with PCOS require a vitamin D status check. Granulosa and theca cells of developing follicles have normalized hormone release and receptor appearance due to vitamin D. It includes the development, maturity, and fertilization of follicles.^{18,19}

Conclusion

Our findings indicate that vitamin D insufficiency affects many PCOS women, particularly those who are obese and have insulin resistance. In PCOS women, a correlation between the serum 25(OH)D levels and metabolic risk variables was discovered. Women with PCOS frequently lack vitamin D, and this condition is considerably more common in obese and insulin-resistant women. In PCOS-affected women, low serum 25(OH)D has been associated to metabolic abnormalities. Among females with PCOS, vitamin D level demonstrated a significant and negative relationship with BMI, FPG, Insuline, HOMA-IR, LDL, TGs, LH, and Testosterone level. It is important to conduct large-scale, multi-site randomized control trials to better understand how vitamin D supplementation may benefit PCOS women's metabolic health.

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