ORIGINAL ARTICLE

THE ASSOCIATION OF VITAMIN D DEFICIENCY IN POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Objective: To determine the association of vitamin D deficiency in patients with polycystic ovarian syndrome (PCOS).

Material & Methods: A case-control study was conducted on forty-eight patients, twenty-four cases and twenty-four controls, at the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, Pakistan, from June 2024 to November 2024. Vitamin D deficiency was assessed in patients with PCOS and in controls. Pregnant patients and those already diagnosed with vitamin D deficiency were excluded from the study. 25 OH D3 levels were measured in both groups, and patients with vitamin D deficiency were classified as positive if vitamin D levels were < 20 ng/mL. A Chi-square test and Pearson Correlation Coefficient were used to assess the association between the two categories.

Results: The mean age of cases was 29.88±6.58 years, while the mean age of controls was 30.54±6.13 years (P=0.71). The mean BMI of cases was 27.16±2.60 kg/m^{2,} while that of controls was 25.40±2.70 kg/m^2; cases had a notably higher BMI than controls (P=0.02). Cases had a higher frequency of vitamin D deficiency (54.2%) than controls (20.8%; p=0.01). The mean vitamin D concentrations were lower in cases than in controls (24.82±8.59 ng/mL vs 29.54±7.91 ng/mL), with a trend toward significance (p=0.054). However, the frequency of vitamin D deficiency was significantly higher in cases than in controls (54.2% vs 20.8%; p=0.017). Vitamin D concentrations were negatively associated with age and BMI in both cases and controls.

Conclusion: Mean vitamin D levels trended lower in PCOS patients; vitamin D deficiency was significantly higher in the PCOS group, and levels were negatively associated with age and BMI in both groups.

Keywords: Vitamin D Deficiency, Obesity, Polycystic ovarian syndrome

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INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a multifaceted condition characterized by hormonal imbalances that result in irregular menstrual cycles and the presence of cysts on one or both ovaries. [1, 2] PCOS affects women throughout their reproductive years. [3] This syndrome is associated with several health complications, including cardiovascular conditions, infertility, obesity, and insulin resistance. [4, 5]

A study conducted in Pakistan on 153 participants found PCOS in 33.3% of cases. [6] Another study conducted in Pakistan showed that obesity, abdominal hair development, irregular periods, cramps, and hormonal acne are related to PCOS. [7] Approximately 50% of the participants were found to have symptoms associated with PCOS. This study reported that 46.5% of the participants indicated their awareness of the hereditary nature of PCOS, and overall, 28.5% of females were found to have a familial predisposition to PCOS.

Insufficient levels of vitamin D lead to calcium instability among women affected with PCOS, which is related to irregular cycles of menstruation and fertility problems. [8, 9] Research has established a link between metabolic changes in PCOS and variations in VDR genes. [10] Insulin resistance and vitamin D are tightly associated, representing a prominent feature of the PCOS phenotype. [11] In conjunction with insulin resistance, Women with PCOS who suffer from deficient vitamin D levels also experience cardiovascular issues. [12]

There exists a multidimensional and delicate relationship between Vitamin D3 and PCOS. Vitamin D significantly enhances glucose metabolism by augmenting

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insulin secretion, promoting insulin receptor expression, and mitigating the effects of Cytokines that promote inflammation. Vitamin D's effect on insulin resistance may explain how it helps with PCOS-related metabolic and reproductive problems. [12] A complete analysis, including many elements, is necessary to comprehend the levels of Vitamin D among women affected with and without having PCOS. At the very start, it is necessary to clarify the processes that govern Vitamin D metabolism and its interactions with hormonal pathways in the context of PCOS. Furthermore, examining the impact of vitamin D concentrations on key metabolic markers, lipid profiles, insulin resistance, and inflammatory markers can yield significant insights into the clinical importance of Vitamin D in the treatment of PCOS.

This study aims to investigate the association between vitamin D deficiency and PCOS among patients, raise awareness among health workers, and provide local-level data on this topic, thereby improving the management of PCOS-related symptoms.

MATERIAL AND METHODS

A comparative cross- sectional study was conducted with two groups, in which women with PCOS were assigned to the case group and healthy women to the control group. Subjects were recruited from the Department of Obstetrics and Gynecology at Lady Reading Hospital, Peshawar, Pakistan, from June 2024 to November 2024, after obtaining ethical approval from the hospital and patient consent. In both cases and controls, subjects were aged 18 to 40 years. Sample size was determined using OpenEPI, with a previous frequency of vitamin D deficiency of 56. 3% in cases and 56.3. 7% in controls, a test power of 80%, and a 95% confidence interval.

Twenty- four patients in each group were allocated. [13] We used a nonprobability sampling technique. Patients with 12 or more follicles on ultrasonography, measuring 4-9 mm, were labeled as cases. Pregnant patients and those already on vitamin D were not included. We collected blood samples from all subjects and sent them to the hospital laboratory to determine vitamin D concentrations using the CLIA (Chemiluminescent Immunoassay) method.

Vitamin D deficiency was labeled positive if vitamin D levels were < 20 ng/mL. PCOS was diagnosed in all patients using the Rotterdam Criteria, which require at least two of the following three features: irregular or absent ovulation, clinical or biochemical evidence of high androgens, and polycystic morphology on ultrasound. Diabetes was labeled yes if HbA 1 c was > 6. 6.5%; hypertension was labeled yes if systolic BP was ≥ 140 mmHg and diastolic BP was ≥ 90 mmHg. Hirsutism was assessed according to the Ferriman- Gallwey scoring system; a score of less than 8 was considered normal, mild to moderate if 8 to 15, and severe if greater than 15. [14]

All data were recorded on a pre- designed proforma. Data analysis was performed using SPSS 23. For qualitative associations, the Chi- square test was used; for associations between qualitative and quantitative variables, the t- test was used; and Pearson' s correlation coefficient was used to assess correlations between quantitative variables. We considered P significant at 0. 0.05.

RESULTS

Forty-eight women were selected for this study; twenty-four were allocated to the case group (PCOS), and twenty-four to the control group. The mean age of cases was 29.88±6.58 years, while the mean age of controls was 30.54±6.13 years (P = 0.71).

Table 1 presents the categorical demographic details of cases and controls. HbA1c levels were above 6.5% in 16 (66.7%) cases, compared with 7 (29.2%) controls (P = 0.009). Hypertension was more prevalent in cases (11; 45.8%) than in controls (4; P=0.02). Figure 1 compares vitamin D levels between cases and controls. Cases had lower mean vitamin D levels than controls; however, this difference did not reach statistical significance (p=0.054), though it showed a trend toward significance.

Figure 2 compares BMI between cases and controls using an independent t-test; cases had a significantly higher BMI than controls (p=0.026). The comparison of vitamin D deficiency between cases and controls using the Chi-Square test is shown in Table 2. Cases had a significantly higher frequency of vitamin D deficiency than controls (P=0.01). Pearson's correlation coefficient was used to examine the relationship between vitamin D levels and continuous variables (age and BMI).

As shown in Table 3, vitamin D levels demonstrated a significant negative correlation with age in both cases and controls. Similarly, a significant negative association was found between vitamin D levels and BMI in both cases and controls. Table 4 presents the distribution of vitamin D levels between cases and controls.

Table No 1: Demographics of patients with cases and controls

Demographics		Groups				P value
		Cases		Controls		
		N	%	N	%	
Marital status	Married	17	70.8%	15	62.5%	0.54
	Unmarried	7	29.2%	9	37.5%	
Monthly income (PKR/ Month)	Monthly income < 50000	6	25.0%	4	16.7%	0.73
	Monthly income 50000 to 80000	16	66.7%	17	70.8%	
	Monthly income > 80000	2	8.3%	3	12.5%	
HbA1c	≤ 6.5%	8	33.3%	17	70.8%	0.009
	> 6.5%	16	66.7%	7	29.2%	
Hypertension	Yes	11	45.8%	4	16.7%	0.02
	No	13	54.2%	20	83.3%	
Hirsutism	Normal	4	16.7%	17	70.8%	0.0001
	Mild	15	62.5%	7	29.2%	
	Moderate to severe	5	20.8%	0	0.0%	
BMI distribution	Normal	6	25.0%	14	58.3%	0.05
	Overweight	13	54.2%	8	33.3%	
	Obese	5	20.8%	2	8.3%	

Table No 2: Comparison of Vitamin D Deficiency between cases and controls

		Vitamin D deficiency		Total	p value
		Yes	No		
Groups	Cases	13	11	24	0.017
		54.2%	45.8%	100.0%	
	Controls	5	19	24	
		20.8%	79.2%	100.0%	
Total		18	30	48	
		37.5%	62.5%	100.0%	

Table No 3: Secondary analysis of vitamin D levels with age and BMI

Age (Years)		
Correlation	P value	Pearson'(r)
Cases	0.004	-0.56
Controls	0.01	-0.47
BMI (Kg/m2)		
Cases	0.002	-0.58
Controls	0.01	-0.47

Table No 4: Comparison of different Vitamin levels between cases and controls

		Groups				p value
		Controls		Cases		
		n	%	n	%	0.059
Vitamin D levels	Deficient	5	22.7%	13	56.5%	
	Insufficient	7	31.8%	3	13.0%	
	Sufficient	10	45.5%	7	30.4%	

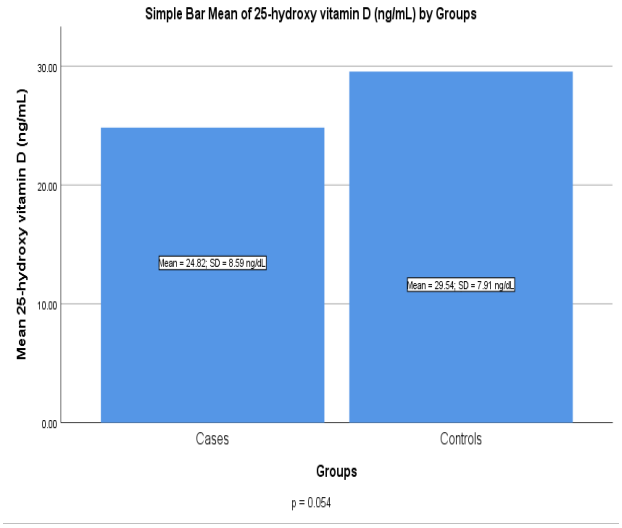

Fig 1: Comparison of Vitamin D levels in cases and controls using an independent-samples t-test

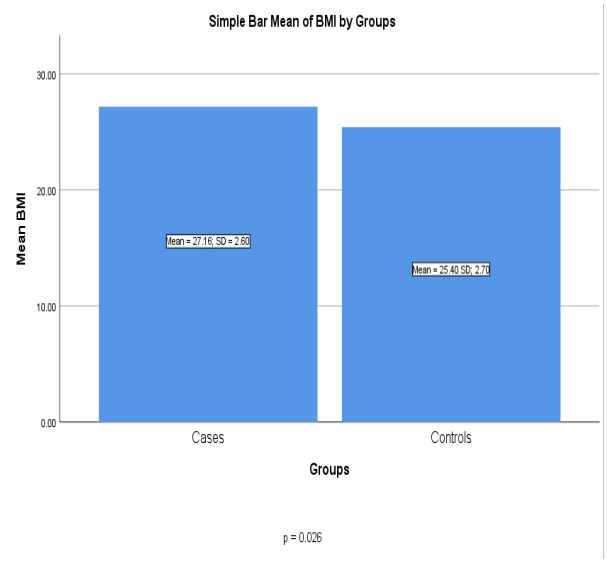

Fig 2: Comparison of BMI in cases and controls using an independent-samples t-test

DISCUSSION

This study was conducted on 48 women, of whom 24 had PCOS, and 24 were healthy controls. Neither group showed a notable difference in mean age, monthly income, or marital status.

Despite extensive research on PCOS and vitamin D, a notable gap remains in the literature regarding the independent contributions of PCOS and obesity-related mechanisms to vitamin D deficiency.

Many previous studies have reported an association between PCOS and low vitamin D levels without adequately controlling for BMI, potentially overestimating the direct effect of PCOS.

Furthermore, most existing studies have been conducted in Western populations, with limited data from South Asian settings, where dietary patterns, sunlight exposure, and genetic factors may differ significantly. The role of age as a modifier of the PCOS-vitamin D relationship has also been insufficiently explored.

Various investigations have observed a higher occurrence rate of Vitamin D deficiency among women with PCOS. [9, 10] Our results showed similar findings: 54.2% of PCOS cases had low vitamin D levels, compared with only 20.8% of healthy controls. In the current study, the difference showed a trend toward significance. Supporting our findings, a Pakistani study reported similar observations and concluded that women with PCOS had higher rates of vitamin D deficiency than women without PCOS. [15] A study conducted in India reported that the majority of women with PCOS had vitamin D deficiency or insufficiency when compared to healthy controls; a total of 56.3% of PCOS patients had vitamin D deficiency, while 35.4% had vitamin D insufficiency. [13]

Insulin resistance is common in patients with PCOS and is strongly linked to vitamin D deficiency. [16] In our study, the case group had a higher prevalence of diabetes than the controls. The aforementioned Pakistani study reported similar findings, noting that patients with PCOS had higher glucose levels than controls. [15] Studies suggest that vitamin D supplementation can help control insulin resistance in patients with PCOS. [17, 18]

One of the findings of our study was a negative correlation between vitamin D levels and increasing BMI. It has been hypothesized that being overweight could be associated with insufficient vitamin D intake. [19] Researchers found that serum 25(OH)D levels were lower in people with a higher body fat percentage. This has been attributed to adipose tissue sequestering fat-soluble vitamin D. Research has demonstrated a significant negative association between low vitamin D levels, increased fat mass, and the likelihood of future weight gain. This correlation has been consistently demonstrated. [20, 21] Similar to our findings, the aforementioned Indian study reported a negative correlation between low vitamin D levels and high BMI. [13] A study conducted in Pakistan reported similar findings, showing an association between obesity and vitamin D deficiency. [22] Another important finding of our study was the negative association between low vitamin

D levels and increasing age. The aforementioned Indian study also reported similar findings, showing a negative correlation between low vitamin D levels and advancing age. [13]

Several limitations of this study should be acknowledged. The small sample size limited statistical power and precluded robust multivariable adjustment for confounders such as BMI, sunlight exposure, dietary vitamin D intake, and seasonal variation. With only 18 vitamin D deficiency events, the study violated the recommended events-per-variable ratio for logistic regression. As a single-center study, it limits the generalizability of our findings to other populations. We also did not assess biochemical hyperandrogenism, body fat percentage, or parathyroid hormone levels, which may have provided further insights. Despite these limitations, our findings provide valuable preliminary data on the PCOS-vitamin D relationship in a Pakistani population and highlight the need for larger, multi-center prospective studies with comprehensive covariate adjustment.

CONCLUSION

While mean vitamin D levels showed only a trend toward lower levels in PCOS patients, the proportion of patients with vitamin D deficiency was significantly higher in the PCOS group. Further interventional studies are required to determine whether vitamin D supplementation has a therapeutic role in improving metabolic outcomes in patients with PCOS, particularly those with higher BMI.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Sabir SA	✓	✓	×	×	✓	×
Sultan S	✓	×	✓	✓	✓	×

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

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