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Association of Vitamin D Deficiency with Metabolic and Reproductive Outcomes in PCOS Patients

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Abstract

Background: *Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder in women of reproductive age, often associated with metabolic and reproductive disturbances. Vitamin D deficiency has been increasingly recognized as a potential contributor to the pathophysiology of PCOS, though its clinical impact remains under investigation. This study aimed to assess the association of vitamin D deficiency with metabolic and reproductive outcomes in women with PCOS.*

Methods: *This cross-sectional analytical study was conducted in the Department of Obstetrics and Gynecology, Shaheed Syed Nazrul Islam Medical College, Kishoreganj, Bangladesh, from July 2023 to June 2024. A total of 120 women with PCOS, diagnosed by Rotterdam criteria, were included. Data were analyzed using SPSS version 25.*

Results: *More than half of the women were vitamin D deficient (55.8%), while 25.8% had insufficient and 18.4% had sufficient levels. Deficiency was significantly associated with higher BMI (28.9 ± 4.6 kg/m²), waist circumference (89.4 ± 9.7 cm), fasting glucose (97.2 ± 11.5 mg/dL), fasting insulin (16.7 ± 5.4 µIU/mL), and HOMA-IR (4.0 ± 1.5) ($p < 0.05$ for all). Reproductive disturbances were also more common, with oligo/amenorrhea in 83.6% and ovulation confirmed in only 13.4% of deficient women compared to 59.1% in sufficient women ($p < 0.001$).*

Conclusion: *Vitamin D deficiency is highly prevalent among Bangladeshi women with PCOS and is strongly associated with adverse metabolic and reproductive outcomes. Screening and correction of vitamin D deficiency may improve clinical management.*

Keywords: *Polycystic ovary syndrome, Vitamin D deficiency, Metabolic outcomes, Reproductive outcomes.*

1. INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, characterized by chronic anovulation, hyperandrogenism, and polycystic ovarian morphology [1]. It is a complex condition with significant reproductive, metabolic, and psychological implications. Globally, the prevalence of PCOS varies from 6% to 20%, depending on diagnostic criteria and population characteristics, and it is increasingly recognized as a major contributor to infertility [2].

In Bangladesh and other South Asian countries, the burden of PCOS is rising, likely due to changes in lifestyle, diet, and obesity patterns [3, 4].

Vitamin D, a fat-soluble secosteroid hormone, plays a crucial role in calcium-phosphate homeostasis and skeletal health. In recent years, its role in extra-skeletal functions has received growing attention, particularly in metabolic and reproductive health [5]. Vitamin D receptors are widely distributed in ovarian tissue, endometrium, pancreas, and adipose tissue, suggesting a potential influence on both reproductive and metabolic pathways. Deficiency of vitamin D has been linked to insulin resistance, impaired folliculogenesis [6], menstrual irregularities, and adverse pregnancy outcomes. Considering that PCOS itself is strongly associated with insulin resistance, obesity, and subfertility, vitamin D deficiency may further worsen the clinical presentation and long-term prognosis of affected women [3].

Several studies have reported a high prevalence of vitamin D deficiency among women with PCOS, regardless of geographical location or ethnicity. Low vitamin D levels have been correlated with higher BMI, impaired glucose tolerance, dyslipidemia, and hormonal imbalance in these patients [7].

Furthermore, vitamin D supplementation has been shown in some interventional studies to improve menstrual regularity, ovulation, insulin sensitivity, and even fertility outcomes. However, the available evidence remains inconsistent and population-specific variations are common [8]. In South Asian women, who are at higher risk of both PCOS and vitamin D deficiency due to cultural practices, limited sun exposure, and dietary factors, the relationship between vitamin D and PCOS outcomes requires further investigation [9].

Understanding the association between vitamin D deficiency and metabolic as well as reproductive outcomes in women with PCOS has important clinical implications [10]. It can guide preventive strategies, improve management approaches, and potentially reduce the long-term burden of infertility, metabolic syndrome, and cardiovascular disease in this population. Despite growing evidence globally, there remains a paucity of data from Bangladesh, where both PCOS and vitamin D deficiency are highly prevalent but under-researched [11].

Therefore, this study was designed to evaluate the association of vitamin D deficiency with metabolic and reproductive outcomes in patients with PCOS attending the Department of Obstetrics and Gynecology at Shaheed Syed Nazrul Islam Medical College, Kishoreganj.

2. Methodology & Materials

This cross-sectional analytical study was conducted in the Department of Obstetrics and Gynecology, Shaheed Syed Nazrul Islam Medical College, Kishoreganj, Bangladesh, over a period of one year from July 2023 to June 2024, and included a total of 120 women diagnosed with polycystic ovary syndrome (PCOS) according to the Rotterdam criteria, which requires at least two of the following features: oligo or anovulation, clinical or biochemical hyperandrogenism, and polycystic ovarian morphology on ultrasound. Women aged 18 to 40 years, not pregnant or lactating, and willing to participate were included, while those who had received vitamin D or calcium supplementation within the previous three months, were on hormonal therapy, metformin, glucocorticoids, or anti-epileptic drugs, or had a history of diabetes mellitus, thyroid disease, Cushing's syndrome, hepatic or renal dysfunction, or any recent acute illness or surgery were excluded. After obtaining informed consent, sociodemographic and clinical data were recorded and anthropometric measurements such as weight, height, and waist circumference were taken to calculate body mass index (BMI). Menstrual history and family history of PCOS were documented. Fasting venous blood samples were collected for estimation of serum 25-hydroxyvitamin D [25(OH) D], fasting glucose, fasting insulin, lipid profile, and anti-Müllerian hormone (AMH). Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). Insulin resistance was assessed using the homeostasis model assessment index (HOMA-IR). Transvaginal ultrasound was performed in the early follicular phase to evaluate ovarian volume and antral follicle count. All data were entered and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables were expressed as mean ± standard deviation and categorical variables as frequencies and percentages. Comparisons between vitamin D groups were made using chi-square or Fisher's exact test for categorical variables. Correlation between serum 25(OH) D and metabolic or reproductive parameters was assessed using Pearson or Spearman correlation, and multivariable regression analysis was performed to control for confounding variables, with a p-value of less than 0.05 considered statistically significant.

3. RESULTS

Table 1. *Baseline Characteristics of the Study Population (n = 120)*

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean ± SD	26.8 ± 4.5	
Age groups	18–24	39	32.5
	25–29	47	39.2
	30–34	26	21.7
	≥35	8	6.6
BMI (kg/m²)	Mean ± SD	27.6 ± 4.2	
BMI categories	Normal (<25)	31	25.8
	Overweight (25–29.9)	53	44.2
	Obese (≥30)	36	30
Menstrual pattern	Oligomenorrhea	71	59.2
	Amenorrhea	27	22.5
	Regular cycles	22	18.3
Family history of PCOS	Present	19	15.8
	Absent	101	84.2

Table 1 shows the baseline characteristics of the 120 women with PCOS included in the study. The mean age of the participants was 26.8 ± 4.5 years. Most women were in the 25–29 year age group (39.2%), followed by 18–24 years (32.5%), 30–34 years (21.7%), and only 6.6% were ≥35 years. The mean BMI was 27.6 ± 4.2 kg/m², with nearly half of the women classified as overweight (44.2%), while 30.0% were obese and 25.8% had normal BMI. Regarding menstrual patterns, oligomenorrhea was the most common (59.2%), followed by amenorrhea (22.5%), while 18.3% reported regular cycles. A positive family history of PCOS was present in 15.8% of women, whereas the majority (84.2%) reported no such history.

Table 2. *Distribution of Vitamin D Status among Study Participants (n = 120)*

Vitamin D Status	Definition (ng/mL)	Frequency (n)	Percentage (%)
Deficient	<20	67	55.8
Insufficient	20–29	31	25.8
Sufficient	≥30	22	18.4
Mean 25(OH)D (ng/mL)		18.7 ± 7.2	

Table 2 demonstrates the distribution of vitamin D status among the study participants. The mean serum 25(OH)D level was 18.7 ± 7.2 ng/mL. More than half of the women (55.8%) were vitamin D deficient (<20 ng/mL), while 25.8% had insufficient levels (20–29 ng/mL), and only 18.4% had sufficient vitamin D levels (≥30 ng/mL).

Table 3. *Association of Vitamin D Status with Metabolic Outcomes*

Parameter	Deficient (n=67)	Insufficient (n=31)	Sufficient (n=22)	p-value
BMI (kg/m²)	28.9 ± 4.6	27.2 ± 3.8	25.1 ± 3.5	0.012*
Waist circumference (cm)	89.4 ± 9.7	85.8 ± 8.5	82.3 ± 7.2	0.019*
Fasting glucose (mg/dL)	97.2 ± 11.5	94.1 ± 10.2	90.5 ± 9.4	0.041*
Fasting insulin (µIU/mL)	16.7 ± 5.4	14.2 ± 4.7	12.1 ± 4.1	0.008*
HOMA-IR	4.0 ± 1.5	3.3 ± 1.2	2.7 ± 0.9	0.002**
Dyslipidemia present	41 (61.2%)	15 (48.4%)	7 (31.8%)	0.037*

Table 3 presents the association of vitamin D status with metabolic outcomes among the study participants. Women with vitamin D deficiency had significantly higher BMI (28.9 ± 4.6 kg/m²) compared to those with insufficient (27.2 ± 3.8 kg/m²) and sufficient levels (25.1 ± 3.5 kg/m²) (p = 0.012). Similarly, waist circumference was greater in the deficient group (89.4 ± 9.7 cm) than in the insufficient (85.8 ± 8.5 cm) and sufficient groups (82.3 ± 7.2 cm) (p = 0.019). Mean fasting glucose levels were also highest among vitamin D–deficient women (97.2 ± 11.5 mg/dL) and lowest among sufficient women (90.5 ± 9.4 mg/dL) (p = 0.041). Fasting insulin and HOMA-

IR values were significantly elevated in the deficient group (16.7 ± 5.4 µIU/mL and 4.0 ± 1.5, respectively) compared to the insufficient (14.2 ± 4.7 µIU/mL; 3.3 ± 1.2) and sufficient groups (12.1 ± 4.1 µIU/mL; 2.7 ± 0.9) (p = 0.008 and p = 0.002, respectively).

Furthermore, the prevalence of dyslipidemia was highest in vitamin D–deficient women (61.2%) compared to those with insufficient (48.4%) and sufficient vitamin D levels (31.8%), showing a statistically significant association (p = 0.037).

Table 4. *Association of Vitamin D Status with Reproductive Outcomes*

Parameter	Deficient (n=67)	Insufficient (n=31)	Sufficient (n=22)	p-value
Oligo/amenorrhea	56 (83.6%)	20 (64.5%)	11 (50.0%)	0.006**
Ovulation confirmed (mid-luteal progesterone >3 ng/mL)	9 (13.4%)	11 (35.5%)	13 (59.1%)	<0.001**
Mean AMH (ng/mL)	7.8 ± 2.6	6.4 ± 2.3	5.1 ± 2.0	0.014*
Antral follicle count (AFC)	22.3 ± 6.1	19.5 ± 5.8	16.2 ± 5.2	0.021*
Clinical pregnancy (n=40)	4/24 (16.7%)	3/9 (33.3%)	3/7 (42.9%)	0.098

Table 4 illustrates the relationship between vitamin D status and reproductive outcomes in women with PCOS. The prevalence of oligo/amenorrhea was significantly higher among vitamin D–deficient women (83.6%) compared to those with insufficient (64.5%) and sufficient levels (50.0%) (p = 0.006). Conversely, ovulation, as confirmed by mid-luteal serum progesterone >3 ng/mL, was markedly more frequent in women with sufficient vitamin D (59.1%) than in the insufficient (35.5%) and deficient groups (13.4%) (p < 0.001). Mean serum AMH levels were highest in the deficient group (7.8 ± 2.6 ng/mL), followed by the insufficient (6.4 ± 2.3 ng/mL) and sufficient groups (5.1 ± 2.0 ng/mL), showing a significant decreasing trend with increasing vitamin D levels (p = 0.014).

Similarly, mean antral follicle count was greater among deficient women (22.3 ± 6.1) compared to insufficient (19.5 ± 5.8) and sufficient participants (16.2 ± 5.2) (p = 0.021). Although clinical pregnancy rates among the subgroup of treated women (n = 40) appeared higher in sufficient (42.9%) and insufficient (33.3%) groups compared to deficient women (16.7%), the difference did not reach statistical significance (p = 0.098).

4. Discussion

This study highlights a high prevalence of vitamin D deficiency among women with PCOS, with more than half (55.8%) of participants being deficient and only 18.4% achieving sufficient levels. The mean serum 25(OH) D was 18.7 ± 7.2 ng/mL, well below the sufficiency threshold. These findings are consistent with earlier reports showing that vitamin D deficiency is disproportionately common in women with PCOS compared to the general population [12, 13].

We observed that women with vitamin D deficiency had significantly higher BMI (28.9 ± 4.6 kg/m²) and waist circumference (89.4 ± 9.7 cm) compared to sufficient women (25.1 ± 3.5 kg/m² and 82.3 ± 7.2 cm, respectively). This aligns with the work of Wang et al., who reported similar associations between hypovitaminosis D and central adiposity in PCOS, as well as Moini et al., who confirmed a positive correlation between low vitamin D and elevated BMI in this population. These associations may reflect vitamin D's role in regulating adipogenesis and insulin sensitivity [14, 15].

Insulin resistance was also more pronounced in our vitamin D–deficient group, as shown by elevated fasting insulin (16.7 ± 5.4 µIU/mL) and HOMA-IR (4.0 ± 1.5). These results are supported by Williams et al., and Menichini et al., who both noted that vitamin D deficiency worsens glucose-insulin dynamics in PCOS [16, 17]. Gokosmanoglu et al., also emphasized that vitamin D–deficient women had higher rates of insulin resistance and metabolic syndrome [18]. Mechanistically, vitamin D may influence insulin receptor expression and β-cell function, thereby reducing compensatory hyperinsulinemia.

In addition, 61.2% of vitamin D–deficient women in our study had dyslipidemia, compared with 31.8% of those with sufficient levels (p = 0.037). This trend parallels findings by Dastorani et al., who showed that vitamin D supplementation improved lipid metabolism in PCOS candidates for IVF [19]. Figurová et al., also reported that low vitamin D levels were linked to atherogenic lipid profiles, highlighting the cardiovascular risk implications in PCOS patients [20].

Reproductive outcomes were also influenced by vitamin D status. Oligo/amenorrhea was more

prevalent in deficient women (83.6%) compared to sufficient ones (50.0%). Similarly, ovulation rates were lowest in the deficient group (13.4%) and highest in the sufficient group (59.1%), a highly significant finding ($p < 0.001$). These results reinforce evidence from Arslan & Akdevelioğlu, who found that vitamin D sufficiency improved menstrual regularity and ovulation [21]. Vitamin D receptors have been identified in ovarian granulosa and theca cells, supporting its direct role in folliculogenesis and steroidogenesis [22].Interestingly, we found that mean AMH levels (7.8 ± 2.6 ng/mL) and antral follicle counts (22.3 ± 6.1) were significantly higher in vitamin D–deficient women, suggesting more pronounced follicular arrest. This echoes the findings of Eftekhar et al., who reported a similar pattern in PCOS phenotypes with low vitamin D. While higher AMH may reflect increased follicle number, it may also indicate poor follicular maturation, consistent with ovulatory dysfunction [23].

Although clinical pregnancy rates were not significantly different across groups, a trend toward higher rates in vitamin D–sufficient women (42.9%) compared to deficient ones (16.7%) was observed. Randomized trials, such as those by Maktabi et al. and Lerchbaum et al., have shown that vitamin D supplementation can improve reproductive markers and potentially fertility outcomes in PCOS [24, 25].

5. Limitations Of The Study

This study has some limitations. Being a single-center study with a relatively small sample size, the findings may not be generalizable to all populations. The cross-sectional design limits the ability to establish causal relationships between vitamin D deficiency and reproductive/metabolic outcomes. Additionally, potential confounders such as dietary intake, lifestyle factors, and seasonal variation in vitamin D levels were not fully controlled.

6. Conclusion

Our findings strengthen the evidence that vitamin D deficiency adversely affects both metabolic and reproductive aspects of PCOS. Given that 55.8% of our cohort was deficient, screening for and correcting vitamin D insufficiency may represent a simple, cost-effective adjunct in the management of PCOS. Future large-scale randomized controlled trials are needed to determine whether supplementation can translate into meaningful improvements in fertility and long-term metabolic health.

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Conflicts of interest

There are no conflicts of interest.

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