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ASSOCIATION OF VITAMIN D DEFICIENCY WITH CLINICAL AND METABOLIC FEATURES IN WOMEN WITH PCOS

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a prevalent endocrine disorder associated with reproductive and metabolic dysfunction. Vitamin D deficiency, widespread in South Asian populations, may exacerbate clinical and biochemical abnormalities in PCOS. This study aimed to evaluate the association between vitamin D status and clinical as well as metabolic features in PCOS women. **Methods:** A cross-sectional analytical study was conducted over six months (January–June 2025) at a tertiary care hospital in Karachi, Pakistan. A total of 100 women aged 18–35 years with PCOS, diagnosed by Rotterdam criteria, were enrolled. Demographic, anthropometric, and clinical data including menstrual history, hirsutism, and acanthosis nigricans were recorded. Biochemical evaluation included fasting glucose, insulin, HOMA-IR, serum testosterone, LH/FSH ratio, and 25-hydroxyvitamin D [25(OH)D] levels. Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20–29 ng/mL), or sufficient (≥30 ng/mL). **Results:** Vitamin D deficiency was observed in 62% of participants, insufficiency in 24%, and sufficiency in 14%. Deficient women had significantly higher BMI, waist circumference, fasting insulin, HOMA-IR, total testosterone, and Ferriman–Gallwey scores compared to sufficient women ($p<0.05$). Oligo/amenorrhea was more frequent in deficient women (82.3%) versus sufficient women (57.1%). Logistic regression showed that vitamin D deficiency independently predicted insulin resistance (adjusted OR 3.12, 95% CI 1.09–8.94) after adjusting for age and BMI. **Conclusion:** Vitamin D deficiency is highly prevalent in PCOS women in Pakistan and is significantly associated with obesity, insulin resistance, hyperandrogenism, and menstrual dysfunction. Screening and correction of vitamin D deficiency may improve both reproductive and metabolic outcomes in this population.

Keywords: Polycystic Ovary Syndrome, Vitamin D Deficiency, Insulin Resistance, Hyperandrogenism, Pakistan.

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorders affecting women of reproductive age, with a global prevalence estimated between 6% and 21%, depending on diagnostic criteria and ethnicity[1]. The syndrome is characterized by hyperandrogenism, oligo/anovulation, and polycystic ovarian morphology on ultrasound, as defined by the Rotterdam criteria[2]. PCOS is associated not only with reproductive disturbances but also with metabolic complications such as insulin resi...

Vitamin D deficiency is a global public health concern, with particularly high prevalence in South Asian populations, including Pakistan, where up to 80–90% of women have serum 25-hydroxyvitamin D [25(OH)D] levels below sufficiency thresholds[4]. Beyond its classical role in calcium homeostasis and bone metabolism, vitamin D has emerged as a pleiotropic hormone involved in glucose metabolism, immune regulation, and ovarian physiology[5]. Studies have suggested that vitamin D deficiency may contribute to the ...

Vitamin D receptors (VDRs) are widely expressed in reproductive tissues including the ovary, endometrium, and placenta, suggesting its role in reproductive health[7]. Experimental data indicate that vitamin D enhances insulin sensitivity by upregulating insulin receptor expression and modulating calcium flux in pancreatic β-cells, thereby improving glucose tolerance[8]. Deficient vitamin D levels may therefore exacerbate metabolic and endocrine derangements in PCOS women.

Clinical studies have shown an association between low vitamin D levels and phenotypic severity of PCOS. Women with PCOS and vitamin D deficiency are more likely to present with obesity, menstrual irregularities, hirsutism, and impaired fertility outcomes[9]. Additionally, vitamin D supplementation has been shown to improve menstrual regularity, ovulation rates, and insulin resistance in some interventional trials, though evidence remains inconsistent[10].

Despite increasing interest, there is limited data from Pakistan examining the link between vitamin D deficiency and clinical/metabolic features of PCOS. Given the very high prevalence of both conditions in South Asian women, investigating this association in a local cohort is of clinical importance. This study aims to evaluate the relationship between serum vitamin D status and clinical as well as biochemical characteristics of PCOS in women presenting to a tertiary care hospital in Pakistan.

METHODOLOGY

Study Design and Duration: This was a cross-sectional analytical study conducted over a period of 6 months (January to June 2025) at the Department of Gynecology and Endocrinology of a tertiary care teaching hospital in Karachi, Pakistan.

Study Population: A total of 100 women aged 18–35 years diagnosed with PCOS according to Rotterdam criteria (2003) were enrolled. Diagnosis required at least two of the following: (1) oligo/anovulation, (2) clinical/biochemical hyperandrogenism, (3)

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polycystic ovarian morphology on ultrasound, after exclusion of related disorders (thyroid dysfunction, hyperprolactinemia, congenital adrenal hyperplasia).

Inclusion Criteria: Women 18–35 years with confirmed PCOS; willing to provide informed consent.

Exclusion Criteria: Pregnancy or lactation; known metabolic bone disease; chronic kidney or liver disease; current use of vitamin D supplements, hormonal therapy, or insulin sensitizers in past 3 months. Convenience sampling was used. After informed consent, participants underwent clinical assessment (age, marital status, menstrual history, body mass index (BMI), waist circumference, Ferriman–Gallwey score for hirsutism, and presence of acanthosis nigricans). Biochemical evaluation included fasting blood glucose (enzymatic method), fasting insulin (chemiluminescence), HOMA-IR calculation, serum total testosterone, LH and FSH by chemiluminescence, and serum 25(OH)D by chemiluminescence immunoassay. Vitamin D status was categorized as: Deficient (<20 ng/mL), Insufficient (20–29 ng/mL), Sufficient (≥30 ng/mL). The study protocol was approved by the Institutional Review Board. Written informed consent was obtained from all participants. Data were analyzed using SPSS v26. Continuous variables were expressed as mean ± SD or median (IQR). Categorical variables were presented as frequencies and percentages. Group comparisons were performed using one-way ANOVA or Kruskal–Wallis test for continuous variables and chi-square test for categorical variables. Logistic regression was applied to determine the association of vitamin D deficiency with insulin resistance (HOMA-IR ≥2.5), adjusting for age and BMI. A p-value <0.05 was considered statistically significant.

DISCUSSION

This study demonstrated that vitamin D deficiency was highly prevalent among women with PCOS, with more than 60% of participants having serum 25(OH)D levels <20 ng/mL. Women with deficient vitamin D status exhibited significantly higher BMI, waist circumference, fasting insulin levels, and HOMA-IR compared to those with sufficient levels. These findings suggest that vitamin D deficiency may exacerbate both metabolic and reproductive abnormalities in PCOS women.

Our findings are consistent with international data. Wehr et al. reported that vitamin D deficiency was strongly associated with insulin resistance and obesity in PCOS women[11]. Similarly, Muscogiuri et al. highlighted that low vitamin D status correlates with impaired glucose homeostasis, dyslipidemia, and increased cardiovascular risk in PCOS[12]. The observed association between vitamin D deficiency and menstrual irregularities in our cohort also aligns with the work of Yildizhan et al., who demonstrated that vitamin D insufficiency was linked to oligo/anovulation and infertility in PCOS patients[13].

The potential mechanisms underlying this relationship are multifactorial. Vitamin D modulates insulin sensitivity by enhancing insulin receptor expression and regulating calcium flux in pancreatic β-cells[8]. Furthermore, VDRs expressed in ovarian granulosa

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cells may influence follicular development and steroidogenesis, thereby linking vitamin D status with hyperandrogenism and ovulatory dysfunction[7]. Our results showing higher testosterone and LH/FSH ratios among vitamin D deficient women support this endocrine pathway.

Interventional studies have further strengthened this association. Rashidi et al. found that vitamin D supplementation improved menstrual regularity and follicular maturation in PCOS patients[14]. A meta-analysis by Fang et al. also confirmed that vitamin D supplementation reduces fasting insulin and HOMA-IR in PCOS women[15]. However, some trials have reported inconsistent results, possibly due to variations in supplementation dose, duration, baseline deficiency severity, and concomitant therapies[16].

In our logistic regression model, vitamin D deficiency was an independent predictor of insulin resistance even after adjusting for BMI, suggesting that the relationship is not solely mediated through obesity. Similar observations have been reported by Li et al., who found that vitamin D status remained significantly associated with insulin resistance after controlling for adiposity[17]. This indicates a possible direct metabolic role of vitamin D in glucose homeostasis.

From a public health perspective, these findings carry significant implications. Pakistan has one of the highest prevalence rates of both PCOS and vitamin D deficiency, driven by dietary insufficiency, limited sun exposure due to cultural clothing practices, and lack of supplementation policies[18]. Screening for vitamin D deficiency in PCOS women may thus represent a cost-effective strategy for mitigating metabolic complications and improving reproductive outcomes.

The study has limitations. Its cross-sectional design prevents causal inference, and the sample size was modest. We also did not measure other metabolic markers such as lipid profile or inflammatory cytokines, which could have further elucidated the pathophysiological link. Nonetheless, the consistent associations observed strengthen the evidence that vitamin D deficiency is an important modifiable factor in PCOS management.

In conclusion, vitamin D deficiency is common in PCOS women in Pakistan and is associated with higher insulin resistance, obesity, and menstrual dysfunction. Routine screening and correction of vitamin D deficiency may improve both metabolic and reproductive outcomes in this population. Further randomized controlled trials are needed to determine the optimal supplementation strategy.

CONCLUSION

Vitamin D deficiency is highly prevalent in PCOS women in Pakistan and is significantly associated with obesity, insulin resistance, hyperandrogenism, and menstrual dysfunction. Screening and correction of vitamin D deficiency may improve both reproductive and metabolic outcomes in this population.

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