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ASSOCIATION OF VITAMIN D AND INFERTILITY AMONG WOMEN

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Abstract:
Objectives: To evaluate the association of Vitamin D and infertility among women.
Materials and Methods: This cross sectional study was conducted at the Gynaecology Department of the Lady Reading Hospital Peshawar from November 2023 to May 2024, following approval from the hospital's ethical committee. A total of 196 patients were enrolled, with informed consent obtained from each patient or guardian. All patients were diagnosed with primary infertility. The assessment of infertility relied on self-reported duration of attempts to conceive. Blood samples (5 ml) were collected from all patients and centrifuged to obtain serum for vitamin D testing. Serum samples were sent to a standard laboratory and analyzed using the Cobas 6000 system. A predefined questionnaire was used to collect data such as sun exposure, as well as demographic information including age and BMI.
Results: The mean age of all patients were 32.63±6.47 years, with mean vitamin D level of 19.09±7.22, and a mean BMI of 20.60 kg/m² (SD 4.79). The mean monthly income was Rs 71,887.75 (SD Rs 22,925.02). Vitamin D levels were mild in 111 patients (56.6%), moderate in 65 patients (33.2%), and severe in 20 patients (10.2%). Infertility was diagnosed in 158 patients (80.6%), while 38 patients (19.4%) were fertile. The binary logistic regression model for the association between vitamin D levels and infertility found that higher vitamin D levels were linked to lower odds of infertility.
Conclusion: Female infertility and reproductive health are impacted by vitamin D deficiency. In order to improve reproductive outcomes through better vitamin D management in fertility assessments, further study is required to elucidate pathways and optimal therapies.

Key words: Infertility, Vitamin D deficiency, women,

INTRODUCTION:

A number of human conditions, including diabetes, autoimmune illnesses, cardiovascular diseases, and cancer, have been related to vitamin D deficiency.(1) Studies underscore its substantial influence, highlighting Vitamin D insufficiency as a global health concern, despite the lack of clear data on its function in infertility.(2-5) Vitamin D is increasingly being considered as a potential factor that could influence female fertility, with numerous studies examining the role of vitamin D supply in reproductive health aspects. There are several studies in that provide valuable insights on the association of Vitamin D level and infertility among women.
A study found that many women with infertility have low vitamin D levels (less than 20 ng/mL). It also found that having low vitamin D is linked to lower signs of ovarian reserve.(6) Similarly, Schmidt

et al. found in a study that women undergoing fertility treatment who had sufficient vitamin D levels (over 30 ng/mL) had higher pregnancy rates compared to those with lower levels. In addition, the mechanisms by which vitamin D might influence fertility have been investigated. Vitamin D receptors are present in reproductive tissues, indicating direct regulatory functions in ovarian function and steroidogenesis.(7) This is supported by another study, which showed an involvement of vitamin D in follicular development and endometrial receptivity, which are crucial for successful conception.(8) In contrast, the study by Wagner et al. found no significant association between vitamin D status and fertility outcomes in a cohort of women with unexplained infertility. These differences show the importance of doing more future studies with larger groups of people and consistent methods to better understand how vitamin D affects fertility.

Vitamin D might affect female fertility, but the exact mechanisms and relationships are still complex and require further investigation. Future research should aim to clarify the causal mechanisms, establish optimal vitamin D thresholds for fertility optimization, and develop interventional strategies to improve reproductive outcomes in women

Objective:
To evaluate the association of Vitamin D and infertility among women.

MATERIALS AND METHODS:
This study was carried out at the Gynaecology Department of the Lady Reading Hospital Peshawar from November 2023 to May 2024.. Women between the ages of 18 and 45 who had not used fertility treatments within the previous six months but had been trying to conceive for at least a year were included in the study. Those with established infertility causes, such as tubal obstruction and male factor infertility, those taking vitamin D supplements, and those with chronic illnesses, such as diabetes mellitus (DM), hyperparathyroidism, and chronic kidney disease (CKD), were excluded.

Once we received approval from the ethics committee, 196 patients who met the selection criteria were enrolled in the study. All the patients were diagnose as primary infertility. After at least a year of consistent, unprotected sexual activity without resulting in a successful pregnancy, a couple is said to be primary infertile. For patients, the self-reported length of time spent trying to conceive was used to determine the infertility assessment. An inform consent were obtained which was duly signed by the patient/guardian. 5 ml blood was taken from all the patients and centrifuge 3000 RPM for 10 minutes at 4°C to obtained serum for testing Vitamin D level. The serum were send to standard laboratory and Vitamin D level were tested by Cobas 6000. Vitamin D levels can be categorized as mild, moderate, and severe based on their concentration in the blood. Mild deficiency is characterized by levels ranging from 20-29 ng/mL, moderate deficiency is indicated by levels between 10-19 ng/mL, and severe deficiency is identified by levels below 10 ng/mL. A predesign questionere were used to collect data such as sun exposure, in addition to demographic information about age and BMI. For statistical analysis SPSS version 26 was used.

RESULTS: The mean age of the patients is 32.63±6.47 years. The mean vitamin D level is 19.09±7.22 ng/mL. The mean body mass index (BMI) is 20.60 kg/m² with an SD of 4.79 kg/m². The patients have a mean monthly income of Rs 71,887.75 with an SD of Rs 22,925.02. Regarding sun exposure, 37.2% (73 patients) reported having sun exposure, while 62.8% (123 patients) did not. Among the patients, 111 (56.6%) have mild vitamin D levels (20-29 ng/mL), 65 (33.2%) have moderate (10-19 ng/ml), and 20 (10.2%) have severe (<10 ng/ml). Out of all the enrolled patients, 158 (80.6%) were diagnosed with infertility, while 38 (19.4%) were found to be fertile. Table 4 presents the binary logistic regression model showing the association between vitamin D levels and infertility.

Table 1: Characteristics of all the enrolled patients *(n=196)*

Variables	Mean±SD
Age (Years)	32.63±6.47
Vitamin D (ng/mL)	19.09±7.22
BMI (kg/m2)	20.60±4.79
Income Rs (Monthly)	71887.75±22925.02
Sun exposer	
Yes	73(37.2%)
No	123(62.8%)

Table 2: Frequency of vitamin D level of all enrolled patients *(n=196)*

Variables	Frequency	Percentage
Vitamin D level		
Mild (20-29 ng/mL)	111	56.6
Moderate (10-19 ng/mL)	65	33.2
Severe (<10 ng/mL)	20	10.2

Table 3: Frequency of infertility *(n=196)*

Variables	Frequency	Percentage
Infertility	158	80.6
Fertility	38	19.4

Table 4: Binary logistic regression model showing association of vitamin D and infertility *(n=196)*

	B	**SE**	**Wald**	EXP (B)	p-value	95% C.I. for EXP (B)	
						Lower bound	Upper bound
Vitamin D	-0.342	0.216	2.507	0.710	0.113	0.465	1.085
Constant	0.524	0.360	2.12	1.689	0.145		

Discussion:

Over 48 million couples worldwide struggle with infertility, making it a persistent public health concern. There are significant financial, physical, and psychological effects of this disorder. As in many other places, research on the correlation between vitamin D levels and birth outcomes is crucial in Pakistan. Higher levels of vitamin D are linked to improved reproductive health and successful pregnancies. Vitamin D deficiency is common in Pakistan because of a number of variables, such as dietary choices, cultural norms, and insufficient sun exposure. Insufficient levels of vitamin D affect over 90% of Pakistani women who are of reproductive age.(9) The main goal of this study was to examine the link between vitamin D and infertility among women in Pakistan. It is concerning that vitamin D insufficiency is so common, and the results of our study agree with those of earlier studies conducted in Karachi, Pakistan.(10, 11) Pregnant women in Pakistan had a high deficiency rate of 79.7%, which was especially noticeable in metropolitan areas, according to the 2018 National Nutrition Survey (NNS).(12)

A study showed that vitamin D deficiency is common among pregnant women in Pakistan and is associated with poor pregnancy outcomes, which aligns with our findings.(9) In our study the mean vitamin D level is 19.09±7.22 ng/mL and out of all the enrolled patients, 158 (80.6%) were diagnosed with infertility. The exponentiated coefficient (EXP (B)) is 0.710, meaning that for every unit rise in vitamin D levels, the risks of infertility drop by a factor of 0.710. A negative relationship is indicated by an EXP (B) of less than 1, i.e., lower probabilities of infertility are associated with higher levels of vitamin D. The genuine effect, however, may be null or even positive, as indicated by the confidence interval for EXP (B), which spans from 0.465 to 1.085, including 1. This underscores the lack of statistical significance. The findings of the present study support another study (13), which

indicated a strong correlation between low levels of vitamin D and poor reproductive outcomes. However, other studies (14) found conflicting evidence about the role of vitamin D in fertility.
It was stated that the chance of live births was higher in people with vitamin D levels over 30 ng/mL than in those with lower levels.(15) Vitamin D production depends on sunlight exposure, and the insufficiency of this vital mineral in Pakistani women is a complex problem driven by dietary, lifestyle, and cultural variables. Pakistani women tend to cover much of their bodies with clothing, which reduces the amount of sunlight that reaches their skin. Women who wear hijabs or burqas are especially likely to engage in this activity. Pregnancy complications and infertility are associated with hypovitaminosis D.(8, 16) Additionally, pre-pregnancy Vitamin D levels greater than 75 nmol/L (30.05 ng/mL) have been linked to increased chances of conception, decreased rates of miscarriage, and a rise in live births.(17) According to studies, people with PCOS frequently have reduced vitamin D levels. Vitamin D supplementation was reported by Wehr et al.(18) to improve metabolic abnormalities and menstruation frequency in women with PCOS, both of which are important for fertility. Agic et al. (2007) found a correlation between endometriosis, a disorder known to affect fertility, and vitamin D insufficiency. According to their research, vitamin D may have an impact on inflammation and immunological responses, two important processes in the onset and spread of endometriosis.(19)

Conclusion and recommendation:
It was concluded that deficiency of vitamin D affects female infertility and reproductive health. Further research is reommended to determine the exact processes and best treatments. Women may have improved reproductive outcomes if their vitamin D status is taken into consideration as part of thorough fertility examinations. Vitamin D deficient women were advised to take supplements.

Limitation of study: One of the limitations was the small sample size, which limited the findings' applicability to more diverse groups of women. The study's relevance to all women was further impacted by potential selection biases, such as concentrating on particular demographic groups or causes of infertility.

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