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THE IMPACT OF VITAMIN D3 LEVELS ON INFERTILITY.

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ABSTRACT

BACKGROUND: Infertility is the fifth most serious global physical or mental health condition. It may have detrimental effects on both partners' social, psychological, physical, and financial well-being. The literature reveals positive relationship between infertility and vitamin D3 level but data on their complex interaction is relatively scarce in Pakistan, highlighting the need for further research. **OBJECTIVE:** To examine the impact of vitamin D3 levels on infertility. **METHODOLOGY:** A cross-sectional investigation was conducted on 132 infertile and 132 fertile women selected through convenience sampling at the Gynecology and Obstetrics ward of the PMC hospital, Nawabshah, Pakistan. Data were collected through a questionnaire and entered and analyzed in computer software Statistical Package for Social Sciences (SPSS) version 25.0. The link between infertility and qualitative variables was examined using the chi-square test, and the mean difference in vitamin D3 across research groups was evaluated using the independent sample t test. A confidence interval of 95% was used for the study. **RESULTS:** Vitamin D3 deficiency and insufficiency were significantly higher in infertile women (53%, 18.9%) compared to fertile women (22%, 11.3%). Infertility significantly increases with the age of participants increased ranging from 3.8% in 20-25 years to 34.8% in 36-40 years. Infertility was higher in the middle class (81.1%) compared to the poor class (18.9%) and significantly higher in illiterates 43.2% followed by primary (30.3%) and low in graduation (3.8%). **CONCLUSION:** Infertile women had significantly greater levels of vitamin D3 inadequacy and insufficiency than fertile women. Besides Vitamin D3, Infertility was found to be associated with age and education of women. Initiatives such as vitamin D3 supplementation, improving women's education and social status and health interventions should be implemented to address this issue.

KEYWORDS: Infertility, Vitamin D, Nawabshah.

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INTRODUCTION

Infertility refers to a condition in which a man and woman are unable to conceive even after one year or more of unprotected intercourse. It presents a major health concern, impacting both the physical and mental well-being of men and women¹. In 2010 Infertility impacted an estimated 48.5 million couples globally. About 10% to 15% of couple's experience infertility globally, while in Pakistan, the number of cases are significantly higher at 21.9%.².

In Pakistan, infertility affects 21.9% of couples, of which primary infertility comprising 3.5% and 18.4% have secondary infertility³. Infertility is the fifth most significant physical or mental condition in the world that restricts a person's abilities, senses, or actions. Sometimes, the underlying cause of infertility is unidentified⁴. Major factors leading to female infertility involve inadequate egg production, scarring or adhesions in the fallopian tubes, and hormonal imbalance that impact the implantation process. Other underlying conditions can also play a role⁵.

Vitamin D has been linked with increased fertility and improved outcomes during pregnancies⁶. It enhances the synthesis of estradiol, progesterone and estrone, which are vital hormones for the reproductive system of women⁷. Research has demonstrated that sufficient quantities of vitamin D enhances the effectiveness of ART (Assisted Reproductive Technology)⁴. Research has also demonstrated that greater rates of pregnancy are linked to vitamin D3 of minimum 30 ng/mL or higher.⁸. A study revealed that women who received donor eggs and had adequate levels of vitamin D experienced increased rates of pregnancy in comparison to those who did not. Females with D3 levels higher than 30 ng/mL demonstrated better rates of successful live births compared to those with lower levels⁹.

Insufficient serum vitamin D3 have not only been associated with negative gestational outcomes such as recurrent miscarriages,

preeclampsia, gestational DM and infertility but have also been associated with implantation failure after IVF and embryo transfer¹⁰. Both vitamin D deficiency and infertility are major public health issues in Pakistan. The literature reveals a positive relationship between infertility and vitamin D3 level but data regarding their complex interaction is relatively scarce in Pakistan so there is great deal of work to be done in this area.

MATERIALS AND METHODS

This Cross-sectional study was conducted at Gynaecology & obstetrics OPD of Peoples University of Medical Health & Sciences Nawabshah (SBA) from March 2022 to March 2023.

The formula $n = z^2 \times p(1-p) / c^2$ is used to calculate the study's sample size. Considering a z-score of 1.96 a 5% margin of error and a 95% confidence interval, the prevalence of infertility is 21%⁴. Total of 132 infertile women and 132 fertile females between the age of 20 and 45 years and with a minimum of three years of married life, were recruited in the study through convenience sampling. Participants who did not consent and those with any of the following conditions were excluded: anemia, PCOS, endometriosis, infections, or kidney and liver diseases.

Data were collected after obtaining written consent from the participants using the structured questionnaire. The questionnaire included inquiries about demographic details, and vitamin D3 levels, among other factors. Blood samples were collected from all selected participants to measure serum vitamin D3. Infertility is defined as the inability to become pregnant following a year or more of sexual intercourse without protection. Normal > 30 ng/ml, Insufficiency > 20 and < 30 ng/ml, and Deficiency < 20 ng/ml were the cutoff values for vitamin D that were taken from the U.S. reference range.

SPSS (Statistical Package for Social Science) version 25.0 was used to analyze the data. The correlation between vitamin D3

levels and infertility was assessed using a chi-square test.

The mean D3 levels in the fertile and infertile groups were compared using an independent sample t test. A p value of less than 0.05 was considered statistically significant, and all analyses were conducted at a 95% confidence interval.

RESULTS

Approx. 31.1% participants were aged between 26 and 30, and 30.7% were in the ages 36 and 40. (Table no: 1). Most of the participants were illiterate (44.3%) and (21.6%) were primary educated, while only 7.2% had completed their graduation (Table 1)

A majority (83%) of participants were from the middle class, while only 17% were from

the poor class (Table no 1). Cases of vitamin D3 deficiency were more pronounced in the infertile women (53%) compared to the fertile women (22.7%) (P value < 0.05). The mean D3 level was substantially decreased as well in infertile group (24.80) than fertile group (34.23) (P value < 0.05). Infertility significantly increases with age. It ranged from 3.8% in the age group of 20 and 25 to 34.8% in 36-40 years (P value < 0.05) (Table no: 3). Infertility was more prevalent in the middle class (81.1%) compared to the poor class (18.9%) (P value = 0.337) (Table no 4). As degree of education increases, the cases of infertility declined, ranging from 57% in illiterate participants to 3.8% in those with a graduation degree. (P value < 0.05) (Table no: 5).

Table 1. Baseline Demographic Profile of subjects



Age	Frequency	Percentage	Education	Frequency	Percentage
20 – 25 years	18	6.8%	Illiterate	117	44.3%
26 – 30 years	82	31.1%	Primary	57	21.6%
31 – 35 years	65	24.5%	Secondary	36	13.6%
36 – 40 years	81	30.7%	Higher Secondary	35	13.3%
41 – 45 years	18	6.8%	Graduation	19	7.2%
Total	264	100%	Total	264	100%
Socioeconomic Status	Frequency	Percentage			
Poor Class	45	17%			
Middle Class	219	83%			
Total	264	100%			

Table no: 2 Association between infertility and vitamin D3 level

Vitamin D3	Infertile Group		Fertile Group		P Value
	Frequency	Percentage	Frequency	Percentage	
Vitamin D3 Deficiency	70	53	30	22.7	< 0.05
Vitamin D3 Insufficiency	25	18.9	15	11.3	
Normal	37	28.03	87	66	
Total	132	100	132	100	

Table no: 3 Association between infertility and age

Age	Infertile Group		Fertile Group		P value
	Frequency	Percentage	Frequency	Percentage	
20-25 years	5	3.8	13	9.8	< 0.05
26-30 years	31	23.5	51	38.6	
31-35 years	35	26.5	30	22.7	
36-40 years	46	34.8	35	26.5	
41-45 years	15	11.4	3	2.5	
Total	132	100	132	100	

Table no: 4 Association between infertility and socioeconomic status

Socioeconomic status	Infertile Group		Fertile Group		P value
	Frequency	Percentage	Frequency	Percentage	
Poor Class	25	18.9	20	16.2	0.337
Middle Class	107	81.1	112	84.8	
Total	132	100	132	100	
Total	132	100	132	100	

Table no: 5 Association between infertility and education

Education	Infertile Group		Fertile Group		P value
	Frequency	Percentage	Frequency	Percentage	
Graduation	5	3.8	14	40.6	< 0.05
Higher Secondary	12	9.1	23	17.4	
Secondary	18	13.6	18	13.6	
Primary	40	30.3	17	12.9	
Illiterate	57	43.2	60	45.5	
Total	132	100	132	100	

DISCUSSION

Infertility is characterized by the inability to achieve pregnancy after a year or more of unprotected intercourse and it can impact the reproductive health of either the male or female partner³. Low levels of vitamin D3 in breast milk are associated with vitamin D deficiency, which increases the risk of infertility and other adverse gestational outcomes, according to observational studies.¹¹ Vitamin D has been shown to be beneficial for pregnancy outcomes. Although studies on human subjects are limited, particularly prospective studies that establish clear cause and effect relationships, research in developing countries like Pakistan, are even more scarce. According to our research, the prevalence of vitamin D3 insufficiency and inadequacy was slightly higher in infertile women compared to fertile women (Table no: 2), with findings

that are statistically significant (P value < 0.05). Similarly, mean vitamin D3 level was slightly higher in fertile women compared to infertile women and the findings were statistically significant (P value < 0.05). These findings are aligned with research conducted in Lower Saxon Germany where the Vitamin D3 level in infertile women were lower¹². On the other hand, clinical trial in Iran showed that Vitamin D3 has significant effect on fertility¹³. Whereas some systemic reviews have revealed mixed results¹⁴. These variations in the study outcomes could be due to differences in sample distribution and potential confounders. More prospective research with multivariate models is required to establish causal and dose response relationship. As women age, fertility declines significantly, with a woman in her 20s having an 85% chance of

conceiving in the first year, which decreases to 66% at age 35 and possibly 44% at 40. The risk of miscarriage also rises, with a 27% chance at 40 compared to 16% at age 30, reflecting the impact of aging on egg quality and ovarian function¹⁵. Age was found to be a significant predictor of infertility in our study, with women between the ages of 36 and 40 having the greatest rates, (table 3). Similar results were obtained in study conducted in Iran where advancing maternal age was associated with infertility and study conducted in Rawalpindi^{16, 17}.

There was no apparent association between infertility and socioeconomic status (table 4). However the rates of infertility significantly declined as the education level increased, with only 3.8% rates among graduates. (Table 5). Raising women's education and socioeconomic status, can drastically reduce the infertility rates.

CONCLUSION

Infertile women were far more likely than fertile women to have vitamin D3 deficiency and insufficiency. In addition to vitamin D3, Infertility was strongly associated with factors such as age and education level of women. To address this issue, initiatives should focus on promoting vitamin D3 supplementation, enhancing women's education and socioeconomic status, and implementing targeted health interventions to reduce the burden of infertility.

ETHICS APPROVAL: The ERC gave ethical review approval.

CONSENT TO PARTICIPATE: written and verbal consent was taken from subjects and next of kin.

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AUTHORS' CONTRIBUTIONS:

All persons who meet authorship criteria are listed as authors, and all authors certify

that they have participated in the work to take public responsibility of this manuscript. All authors read and approved the final manuscript.

CONFLICT OF INTEREST: No competing interest declared

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