

Vitamin D3 Deficiency in Women Experiencing Infertility: A Comparative StudySatyajit Jena¹, Manamohan Biswal², Sujit Kumar Mohanty³, Tapas Kumar Panda⁴,
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Abstract**Background:** There can be multiple reasons for infertility, making it a complex disease to cure. Infertility leads to emotional trauma among the patients. Low levels of vitamin D3 during childbearing age of a women can lead to infertility. This condition is common among undernourished women.**Objective:** To conduct a comparative study and analyze the serum vitamin D3 level among women of childbearing age, divided into two groups: fertile and infertile.**Methods:** A case-control observational study was conducted in the Department of Obstetrics and Gynecology, SCB Medical College, Cuttack, Odisha, India from July 2021 to July 2022. 122 women participated in the study; they were divided into two groups. 61 women were in the control group and 61 in the infertile group under study. The infertile group was thoroughly examined to rule out other factors of infertility. The blood was collected to measure the serum D3 levels. The data obtained was subjected to statistical analysis.**Results:** There was a substantial difference in the serum D3 levels of both groups. The average serum D3 level for the control group was 26.87 ng/mL, and for the infertile group, it was 7.86 ng/mL. The p-value was less than 0.05. Also, the serum level of vitamin D3 decreases with advancing age.**Conclusion:** Serum vitamin D3 levels decreased significantly in infertile women. The level decreased with advancing age, and so the infertility increased with age. The correlation between body weight and vitamin D3 levels was not significant. Similarly, the sociodemographic factors did not affect the serum vitamin D3 level.**Keywords:** Serum vitamin D3, infertility.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

Infertility, as described by the World Health Organization, is the condition of not achieving spontaneous clinical pregnancy after 12 months of unprotected intercourse. Infertility has many physical, emotional, and social effects, which can lead to mental trauma [1]. As many economic, social, and emotional aspects are related to having a progeny with spontaneous pregnancy, infertility can be a greater issue than other physiological disorders. 10-15% of the females in developed countries are infertile [2]. Whereas around 50% of both males and females are infertile in the many developing region [2].

Physiologically, vitamin D3 is known for calcium and phosphorous metabolism. Several animal and human studies conducted to determine the functions of vitamin D3 found that vitamin D3 plays a significant role in reproductive health [3-5]. Studies have also demonstrated that vitamin D3 levels are related to infertility [4, 5]. The receptors of vitamin D3 play a significant role in the expression of various genes in the female reproductive system, it is present in different tissues of the reproductive system, such as myometrium, endometrium and cervix. It is also found in various studies that the deficiency of vitamin D3 leads to various disorders of the ovary and endometrium, such as PCOS and fibroids [6,

7]. The aim of this study is to comparatively analyze the role of serum vitamin D3 levels in fertility of women. The vitamin D3 levels here are correlated with various socio-demographic factors, body mass index, and infertility.

Methods

Study design: This study was carried out at SCB Medical College & Hospital, a tertiary health institution in Cuttack, Odisha, India, patients were selected for the study from the Gynaecology Department and Post-natal clinic. The blood samples of the women were collected, and they were analysed for levels of vitamin D3 by the Department of Biochemistry, SCB MCH, Cuttack, India.

Participants:

Inclusion criteria for Group 1:

- Infertile females
- Females who consented to the study

Exclusion criteria for group 1:

- Female with preexisting endocrine disorders
- Female using medication which could affect the absorption of vitamin D3
- Female taking vitamin D3 supplements

Criteria for group 2 women who had delivered 6 weeks ago

Inclusion Criteria:

- Spontaneous pregnancy
- Female who consented

Exclusion Criteria:

- Female who had preexisting endocrine disorders
- Female using medication which could affect the absorption of vitamin D3
- Female taking vitamin D3 supplements

A questionnaire was prepared, and the interviewer interviewed the participant according to the preset questionnaire. The questionnaire was set up in such a manner as to collect information regarding the participant's socio-demographic background, gynaecologist, obstetrician, history of reproductive

health, and other health issues. Height was measured on a stadiometer, and weight was measured on a weighing scale.

The level of vitamin D3 was determined using monoclonal antibodies for vitamin D3 from the ELISA kit. The monoclonal antibodies competitively bind to the vitamin D3 available in the serum. The serum samples in which vitamin D was less than 20 ng/ml, the female was considered deficient, 21-29 ng/ml was considered insufficient, and more than 30 ng/ml was considered optimum.

Results

In total 122 women participated in the study. They were divided into 2 groups. The fertile group had 61 women and the infertile group had 61 women. The infertility and vitamin D3 levels were correlated with age. It was found that with the advancing age the levels of vitamin D3 decreased substantially. In case of fertility it was observed that majority of the women above 35 years were infertile and women below 30 years were fertile. The mean age of the fertile group was 29 years, and the mean age of infertile group was 34 years. Religion, occupation, educational status, and economic background were similar in both groups. The p-value when age was compared with infertility status was less than 0.05, indicating the statistical significance of the correlation. The vitamin D3 levels were analysed in the fertile group and the infertile group. The mean serum vitamin D3 level for infertile group was 8.3 ng/mL, and the mean serum vitamin D3 level for fertile group was 25.4 ng/mL (Table 1).

Table No. 1 illustrates the ratio of vitamin D3 deficiency among fertile and infertile women. It was found that all the women in the infertile group were deficient in vitamin D3 that is all of them had vitamin D3 levels less than 20 ng/ml. In contrast out of 61, 14 women were deficient in vitamin D3 level in the fertile group. 23 women among 61 in the fertile group had vitamin D3 level in the range of 21-29 ng/ml. Numerically, most women in the fertile group had vitamin D3 level above 30 ng/ml. The vitamin D3 levels were correlated with infertility and the p value was 0.001 indicating that the correlation was statistically significant.

Table 1: Proportion of vitamin D3 deficient women under study

| Parameters | Fertile group | Infertile group |
|--------------|---------------|-----------------|
| Mean | 25.4 ng/ml | 8.3 ng/ml |
| Deficient | 23% | 100% |
| Insufficient | 37% | 0 |
| Sufficient | 39% | 0 |

When the BMI and the vitamin D3 deficiency were compared it was found that women with deficiency were either underweight or obese. Women with normal BMI and overweight BMI had optimum levels of vitamin D3. However, when the BMI was

correlated with deficiency it was found that the relation was not statistically significant.

Discussion

It was found in this study that women within the initial childbearing age were fertile compared to the women at the later stage of childbearing age. The mean age of the fertile group was 29 years whereas the infertile women had the mean age of 34 years. The p-value for the difference in the age was 0.0001 indicating the difference was statistically significant. The delay in the age can be due faith-based procedures and unorthodox methods being carried out at the earlier stage to treat infertility which makes it difficult to treat at the advanced age [7].

The average serum vitamin D3 among the fertile group was 25.49 ng/ml and among the infertile group, it was 8.3 ng/ml. Also, 100% of the women in the infertile group were deficient compared to the fertile group only 23% of them were deficient. This finding is contradictory to the study conducted where they found 50% of the fertile women to be deficient [8].

However, the studies conducted in colder regions have a higher proportion of vitamin D3 deficiency this could be attributed to less exposure to sunlight [9, 10]. This study was conducted in Cuttack, India, where sunlight is abundant, but a study reported that dark-skinned individual requires more exposure to the sun for the formation of vitamin D3 than fair-skinned individual [10]. This can explain the existing deficiencies. Also, a sedentary lifestyle contributes to vitamin D3 deficiency [9, 10]. A study found that individuals with vitamin D3 deficiency have a reduced probability of clinical pregnancy with in-vitro fertilization [11]. This also occurs if the oocytes are donated and placed in the mother's uterus. This indicates that infertility with vitamin D3 deficiency is due to its role in the endometrium.

The association of BMI with vitamin D3 deficiency was not found to be statistically significant, but it was found that underweight and obese patients had decreased serum vitamin D3 compared to normal and overweight individuals. As vitamin D3 is soluble in fat it is deposited in the adipose tissue and its serum level decreases. A study reported a similar finding that obese individuals have decreased levels of serum vitamin D3 [12, 13]. Other sociodemographic factors such as occupation, religion, and education did not have any correlation with infertility.

Limitation and Recommendation

The lack of a local reference range for classifying serum vitamin D concentration as sufficient, insufficient and deficient, is another acknowledged limitation of this study. As a result, it may be essential for women who are trying to conceive to have blood vitamin D levels that are optimised.

Conclusion

In the course of our research, we discovered that the levels of vitamin D in patients who were experiencing infertility were 8.31ng/ml, but the levels in the control group were 25.4ng/ml. The majority of women who experienced infertility were more than 35 years old.

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