DOI - 10.21276/obgyn.2020.7.4 *ISSN Print – 2454-2334; ISSN Online – 2454-2342*

RESEARCH ARTICLE

A comparative study of vitamin D levels between infertile and fertile women in India

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ABSTRACT

Objective: The objective of the study was to compare the levels of vitamin D in infertile and fertile women. **Material and methods**: A total of 150 women coming for treatment for infertility at a semi urban clinic were assessed for vitamin D deficiency. An equal number of women with spontaneous conception served as controls. T test was done to find the difference between the two groups. **Result:** The mean level of vitamin D in fertile women was 20.37ng/ml (±0.66) and in the infertile group was 16.58 ng/ml(± 0.46) but this difference was not statistically significant (P=0.06). **Conclusion:** Significant difference in serum vitamin D levels in fertile and infertile women could not be established.

Keywords: Vitamin D, infertile, fertile.

The role of vitamin D in bone health and calcium homeostasis has been long recognised. However, in the past decade, the focus is gradually shifting to the non skeletal benefits of vitamin D. There is increasing evidence that in addition to sex steroid hormones, the classic regulators of human reproduction, vitamin D also plays a role in modulating the reproductive processes in women and men[1].

Vitamin D is a steroid hormone, mainly produced in the skin after sunlight exposure. Diet and dietary supplements constitute alternative sources of vitamin D for humans [2]. There are 2 distinct forms of vitamin D - ergocalciferol (D_2) and cholecalciferol (D_3). Cholecalciferol is formed in the human skin from 7- dehydrocholesterol (7DHC). UV radiation converts 7-DHC to previtamin D_3 which is rapidly converted to D_3. Green plants, mushroom, fish fat and Cod liver oil are rich sources of ergocalciferol [3, 4].

Vitamin D_3 is provided either by UV radiation of the skin or from diet and is biologically inactive and requires hydroxylation in the liver and kidneys to produce its active form- 1,25,dihydroxy vitamin D or calcitriol [2]. Vitamin D status of the body is best indicated by the circulating levels of 25(OH) vitamin D due to its longer half life and higher serum concentration as compared to 1,25,DHCC [2]. Calcitriol acts through binding to specific nuclear receptor VDR, which acts in concert with the retinoid X receptor (RXR), forming a heterodimer [5]. The VDR-RXR heterodimer binds to vitamin D responsive elements (VDRE) located in the promoter region of the target genes, thus regulating transcription [6].

Although the main role of vitamin D is considered to be the absorption of calcium and phosphorus from the gut, the wide distribution of VDR in almost all human tissues and the fact that 3% of the human genome is regulated by the vitamin D endocrine system points to a extra skeletal role of vitamin D in various systems and organs, reproduction being a very important one amongst them [2,7].

Received: 22nd March 2020. **Accepted:** 4th May 2020.

Saran S. A comparative study of vitamin D levels between infertile and fertile women in India. The New Indian Journal of OBGYN. 2020; 7(1): 16-9.

Calcitriol is produced by the decidua in response to IL-B secreted by the blastocyst. Calcitriol regulates the decidual expression of the genes involved in embryo implantation. The presence of blastocyst up regulates the production of the active form of vitamin D in the endometrium [8]. All these facts point towards a crucial role of vitamin D in reproduction. A study also found that women with higher 25(OH) vitamin D levels in the serum and follicular fluid were significantly more likely to achieve pregnancy as compared to women with lower levels of vitamin D [9].

Both infertility and vitamin D deficiency are burning health issues in today's world. Infertility is defined as failure to conceive for more than 1 year and affects about 48.5 million couples worldwide with significant psychological, medical and economic consequences [10]. Similarly, an epidemic of vitamin D deficiency has been emerging worldwide, with the prevalence of vitamin D insufficiency nearly doubling from 1994 to 2004[11]. In this study we aimed to evaluate the vitamin D levels of women coming for infertility treatment and comparing them with the Vitamin D levels of fertile women.

Materials and methods

This study was a cross sectional study conducted on 150 women attending the infertility clinic at Government Medical College, Badaun and Magadh Maternity and infertility clinic, Badaun from February 2018 to January 2019. Informed consent was taken from all patients participating in the study. The study was conducted in accordance with the ethical standards of our institution and the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Serum Vitamin D levels of a total of 150 women coming for infertility treatments were assessed. A similar group size of patients coming with spontaneous conception served as controls. Vitamin D levels were measured by Enzyme Immunoassay Competition Method with a Final Fluorescent Assay (ELFA). T test was done for comparison of results of both the groups.

Inclusion criteria: All infertile women in the age group of 20-40 years were included and healthy fertile women in the same age group served as controls.

Exclusion criteria: History of smoking or tobacco use, use of any hormones or steroids, known vitamin D deficiency, patients with thyroid disorders and autoimmune disorders were excluded from the study.

Results

Table 1 shows the age profile of the study and control group of women. In this study, the maximum patients of study group were of age 26-30 years (56.6%) followed by 34% of patients in the age bracket of 31-35 years. In comparison, in the control group, which consisted of fertile women, the maximum number of patients were again in the age bracket of 26-30 years but 32% of women were <25 years of age. Women more than 35 years were 4.6% in the infertile group and 3.3% in the control group. Table 2 shows the comparison of age and vitamin D levels in both the groups. As seen, the mean age in the fertile group was 26.07 yrs (± 0.34) whereas it was 31.28(± 0.34) in the infertile group. The mean Vitamin D level in the fertile group was 20.37ng/ml (± 0.66) and 16.58ng/ml (± 0.46) in the infertile group. As is seen, the mean vitamin D level was lower in the infertile group; but this difference was not found to be statistically significant (P=0.06). Table 3 shows the subgroup analysis of vitamin D levels of the women in the infertile group. The women were divided into 3 subgroups on the basis of factors contributing to their infertile status - tubal factors, polycystic ovarian disease (PCOS) and those with no explainable cause. In the tubal group, the mean age was 30.02(± 0.4) and mean vitamin D level was 17.19 ng/ml (± 0.96). Women with PCOS had a mean age of 28.18 years (± 0.41) and vitamin D levels of 15.3 ng/ml (± 1.02). Those in the unexplained group had a mean age of 30.52 years (± 0.24) and mean vitamin D levels of 16.41ng/ml (± 0.15).

Table 1: Age analysis

Age group	Study group Number (%) (N=150)	Control group Number (%) (N=150)
<25 yrs	9(6%)	48(32%)
26-30 yrs	85(56.6%)	65(43.3%)
31-35 yrs	51(34%)	32(21.3%)
>35 yrs	5(3.3%)	5(3.3%)

Table 2: Mean Age and vitamin D levels of both groups

Categories	Mean vit D levels (ng/ml)	Mean age in yrs
Fertile group of women	20.37(SEM 0.66)	26.07(SEM 0.34)
Infertile group of women	16.58(SEM 0.46)	31.28(SEM 0.34)

Table 3: Subgroup analysis of infertile women

Categories	Vit D levels(ng/ml)	Age in years
Tubal factors	17.19(±0.96)	30.02(±0.4)
PCOS	15.3(± 1.02)	28.18(±0.41)
Unexplained	16.41(±0.15)	30.52(±0.24)

Discussion

Vitamin D levels are classified in 3 categories - deficiency, insufficiency and sufficiency as per Institute of

Medicine and Euronut Seneca study [12], Suvimax study [13], and Goswami et al [14]. The reference levels for serum vitamin D are – deficiency <10 ng/ml, insufficiency 10-20 ng/ml and adequate levels > 20 ng/ml.

Although accumulating evidence from animal and human studies suggests that vitamin D is involved in many functions of the human reproductive system, no comprehensive analysis of the potential relationship between vitamin D status and fertility rates is currently available. On this basis, the purpose of this study was to compare vitamin D levels in fertile and infertile or sub fertile women. This issue is of interest considering that vitamin D deficiency is easily amenable to correction and oral vitamin D supplementation is cheap and without significant side effects. In a study by Rudrick et al [15], it was found that vitamin D deficiency was associated in lower pregnancy rates in Non Hispanic whites but not in Asians. Also, vitamin D deficiency was not correlated with ovarian stimulation parameters or with markers of embryo quality, suggesting that its effects may be mediated through the endometrium. Similarly, Fung et al [16] demonstrated an association between vitamin D intake and biomarker levels on conception. Those with intake at or above the estimated average requirement (intake 10µg/ml) and serum levels indicating sufficiency were more likely to achieve a clinical pregnancy.On the other hand, a study by Franasiak JM et al, demonstrated that vitamin D levels had no effect on IVF outcomes following transfer of euploid blastocysts [17]. Similarly, in a study conducted by Fabris et al, no correlation could be found between bio available vitamin D levels and pregnancy rates [18].

Conclusion

The statistical significance of the difference in the vitamin D levels in the infertile and the fertile group of women could not be established. So, in our study, we have not been to reach a conclusive relationship between serum vitamin D levels and infertility. As of now, routine assessment of vitamin D levels in women coming for infertility treatment cannot be recommended. Though its role in maintaining bone health is universally accepted, further studies are required to find out subgroup of women in whom its deficiency and its treatment can lead to a better reproductive outcome. Also, since the cut off levels for vitamin D deficiency have been deduced from the effect of vitamin D on bone health, we may not extrapolate the same levels to define the cut off for deficiency as far as reproductive health is concerned. So, further studies are needed to identify the exact levels and therapeutic supplementation of vitamin D for reproductive health.

Conflict of interest: None. **Disclaimer:** Nil.

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