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RESEARCH ARTICLE

Correlation of vitamin D deficiency and anti-mullerian hormone levels in infertile females

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ABSTRACT

Objectives: 1. To analyse the levels of vitamin D in infertile females, 2. To analyse the levels of Anti-Mullerian Hormone (AMH) in infertile females, 3. To correlate the vitamin D deficiency levels and AMH levels in infertile females. **Methods**: It was a hospital based cross-sectional study among 100 infertile females of the age group 18-40 years presenting at the Gynae OPD of Gauhati Medical College and Hospital, conducted between 1st June, 2019 and 31st May, 2020. **Results**: Of the infertile females, 46% were vitamin D deficient, 36% had insufficient vitamin D levels while 18% were sufficient in vitamin D. Majority of the study population (66%) belonged to the age group of 21-30 years. In the study group, 35% patients were in the normal weight range, while 39% patients were overweight and 26% females were obese I category. Of the infertile females, 81% had normal AMH values, while 7% had low AMH values and 12% had raised AMH levels. The mean AMH levels were not statistically significant between the vitamin D deficient females and those without deficiency. **Conclusion**: The existence of vitamin D responsive elements on the AMH gene promoter provides a scientific basis for vitamin D to exert its effects on AMH gene expression levels. However, our study could not find any correlation between vitamin D and AMH levels in the infertile females.

Keywords: Infertility, vitamin D, anti-mullerian hormone.

Infertility is a worldwide problem affecting 8-12 percent couples (50-80 million) during their reproductive lives (WHO, 1991). Census of 1981 estimates infertility in India at around 4-6 percent and according to NFHS-1 childlessness is around 2.4 percent of currently married women over 40 years in India (cited in Jejeebhoy, 1998). Causes of infertility vary according to the age of the couples and duration of marriage. Although PCOS remains the main cause, infections are a major cause of tubal factor infertility, and tobacco and alcohol worsen the male factor. One-third of the cases still remain unexplained [1]. Diminished ovarian reserve (DOR) is one of the leading causes of infertility, characterised by a low number of eggs in the woman's ovaries and/or poor quality of the remaining eggs. Ovarian reserve is used to describe a woman's reproductive potential by means of the quality and quantity of the oocytes her ovaries possess [2]. Ovarian reserve tests include biochemical and ultrasonographic tests like basal day 3 FSH, estradiol, Inhibin B, anti mullerian hormone (AMH) and antral follicle count (AFC) and ovarian volume.

Anti-Mullerian Hormone is a peptide growth factor of the transforming growth factor-β family, secreted by the granulosa cells of the ovarian follicles and appears to regulate early follicle development, which is used as a marker of ovarian reserve.

Vitamin D is a lipid soluble vitamin which is synthesized by the skin from cholesterol upon exposure to UV light, mainly assisting in maintaining calcium homeostasis and preserving bone density. The existence of vitamin D-responsive elements on the AMH gene promoter provides a

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clear scientific basis for vitamin D to exert its effects on AMH gene expression levels, which is supported by in vitro animal and human studies [3].

Finding a correlation between vitamin D deficiency levels and AMH levels in infertile females can provide a better perspective and insight on infertility management. Vitamin D deficiency has often been studied as a factor influencing fertility. It's influence on AMH levels is therefore, a matter of concern, provided the wide prevalence of vitamin D deficiency in the general population. Making advances in infertility management thus necessitates relevant studies to be made in this regard.

Objectives

1. To analyse the levels of vitamin D in infertile females.
2. To analyse the levels of Anti-Mullerian Hormone (AMH) in infertile females
3. To correlate the vitamin D deficiency levels and AMH levels in infertile females.

Materials and methods

The study was a hospital based cross sectional study, with a sample size of 100 patients. It was carried out among the patients attending GOPD (Gynae OPD) of Gauhati Medical College and Hospital with complaints of infertility between 1st June, 2019 to 31st May, 2020 based on the following inclusion and exclusion criteria.

Inclusion criteria: Females presenting with infertility, both primary and secondary, in the age group of 18-40 years.

Exclusion criteria:

1. Females in the perimenopausal age group
2. Females on vitamin D supplements
3. Females with history of ovarian surgery and chemotherapy or radiation
4. Females on contraceptive use

Statistical analysis: Data is compiled in Microsoft Excel 2010 & data depicted using tables and diagrams. Statistical analysis was done using SPSS Software. Correlations were observed by using Spearman's rho calculation. Chi-square test was used for calculation of p value. Results were considered significant when the probability (p value) was less than 0.05.

Results

In our study, the prevalence of vitamin D deficiency (<20 ng/mL) was found to be 46%, vitamin D insufficiency (20-30 ng/mL) was 36% and vitamin D sufficiency (>30 ng/mL) was 18%. The mean vitamin D level in the study was 22.37 ± 6.496 ng/mL. Maximum patients were in the age group of 21-30 years and only 2% patients were below 20 years. The

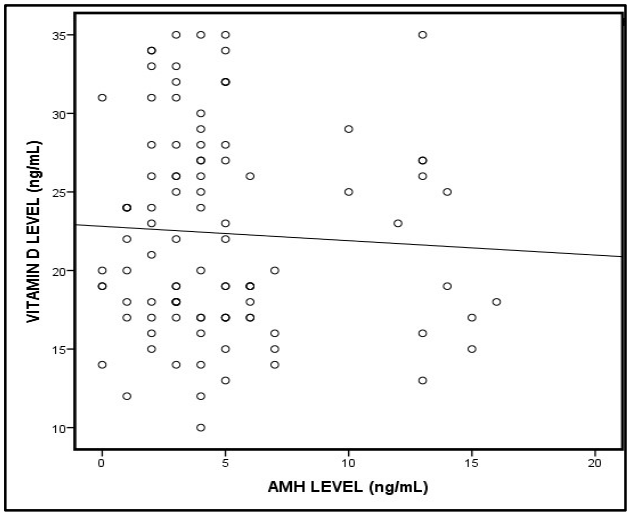

Figure 1: Scatter plot between vitamin D and AMH level in the study group

mean age in the vitamin D deficient (<20 ng/mL) group was 28.39 ± 5.93 years. While in the vitamin D non-deficient (≥20 ng/mL) group, the mean age was 28.39 ± 5.21 years. The difference is not significant (p=0.909> 0.05). The mean BMI in the study group was 23.56 ± 1.58 kg/m^2. 35 females

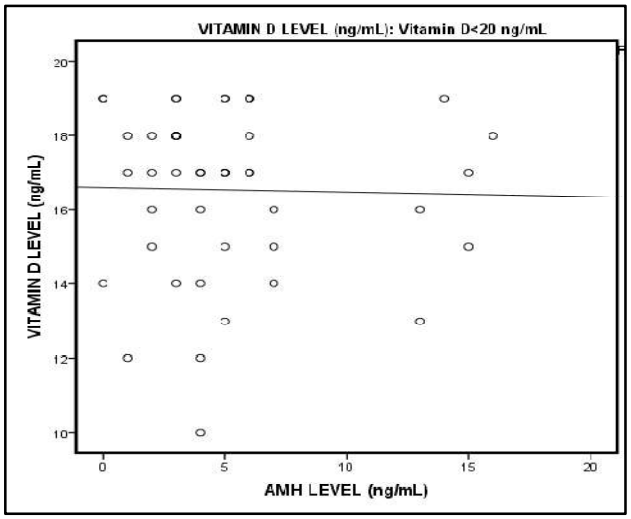

Figure 2: Scatter plot between vitamin D deficiency and AMH levels in the vitamin D deficient group

had normal BMI while 39 females were overweight and 26 females were obese I category. The mean AMH level in the study group was 4.83 ± 3.81 ng/mL. Seven patients had low AMH and 12 patients had raised AMH levels. In the study

group, 81 patients had normal AMH levels. The minimum recorded value was 0.14 ng/mL while highest was 15.88 ng/mL. Out of the 100 females who were in the study group, 79 females belonged to the urban areas and 21 females

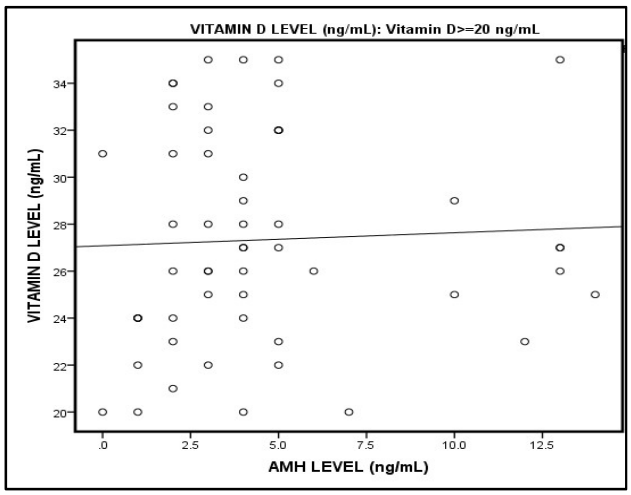

Figure 3: Scatter plot between vitamin D and AMH levels in the vitamin D non-deficient group

hailed from rural areas. Out of the 100 females who were in the study group, 8 females belonged to the upper middle (II) class, 67 females belonged to the lower middle (III) class, 20 females belonged to the upper lower (IV) class and 5 females were from the lower (V) economic class. Primary infertility was found in 64 females while 36 patients presented with secondary infertility. Seventy females were from Hinduism while 30 females belonged to Islam. Education upto 12th class was found in 68 females while 32 females were graduates or above. Eleven females worked at professional set-ups while 89 females were engaged in non-professional work. No correlation was found between vitamin D levels and AMH levels in the study group (r=-0.183; p=0.068) (figure 1). There was no correlation between vitamin D deficiency levels and AMH levels (figure 2) separately in the vitamin D deficient and non-deficient group (figure 3).

Discussion

Vitamin D deficiency and its influence on the AMH levels of infertile females has been subjected to much discussion. In a study conducted by Ruchika Garg et al[4] in 2018 among 1052 women, prevalence of vitamin D deficiency (<20 ng/mL) was found to be 64.06%, vitamin D insufficiency (20-30 ng/mL) was 34.69% and vitamin D sufficiency (>30 ng/mL) was 1.23%. In our study, the prevalence of vitamin D deficiency (<20 ng/mL) was found to be 46%, vitamin D insufficiency (20-30 ng/mL) was 36% and vitamin D sufficiency (>30 ng/mL) was 18%. In a study conducted by Indu Lata et al[5] between 2014 and 2016 at Lucknow, they found the prevalence of vitamin D deficiency to be 64.28% among 70 infertile females. In another study, 81.3 to 98.2 % of women with impaired fertility had deficient or insufficient vitamin D levels [6].

The mean Vitamin D level in our study was 22.37 ± 6.496 ng/mL. It was 9.30 ± 5.59 ng/ml in the study done by InduLata et al[5] while the mean vitamin D level was 29.7±13.3 ng/mL in a study conducted by Bednarska-Czerwińska et al[7] in 2019 at Poland among 53 infertile women.

In the study by InduLata et al[5], the mean AMH values in the cases was 1.94 ± 1.30 ng/mL while it was 3.47 ± 2.59 ng/mL in the control group (p=0.003). They found a significant difference in the AMH values in the vitamin D deficient infertile females and the controls who did not have vitamin D deficiency. In our present study, no correlation was found between the vitamin D levels in the infertile females and the AMH levels, p value being 0.068. Drakopoulos et al[8] also could not find any correlation between vitamin D and AMH (spearman's r=0.02, p value=0.7). Merhi et al [9] in 2012 performed a cross-sectional nested study and could demonstrate a weak significant positive correlation between serum vitamin D and AMH in late reproductive aged women, although no association was found in younger patients. In a systematic review and meta-analysis done by Irene Moridi et al[10] in 2020 regarding the association between vitamin D and Anti Mullerian Hormone, they studied the data from 18 cross-sectional studies and 6 interventional studies to find that the cross-sectional studies demonstrated conflicting results, several studies finding positive results while most studies reported largely negative findings. The studies conducted among infertile females mostly reported negative findings

Conclusion

The study could not establish any correlation between the vitamin D deficiency and AMH levels in women with infertility. The discrepant findings in various cross-sectional studies including the present study are likely due to the heterogeneity in the study populations. Moreover, vitamin D levels are influenced by race, ethnicity, geographic area and seasons. Limited sample size in our study could be one of the causes that has led to this inability to find any correlation, if exists. Cross-sectional studies are limited in nature as it evaluates a single point of time and hence, individual fluctuations of AMH and vitamin D are not accounted

thereof. More insight regarding the relationship between vitamin D and AMH can be gained by prospective interventional studies.

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

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