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Research Article

Serum Vitamin D Levels in Different Phenotypes of Polycystic Ovarian Syndrome (PCOS) A Case-Control Study

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Abstract: Polycystic ovarian syndrome (PCOS) is the most common heterogeneous multisystem endocrinopathy in women of reproductive age, with an ovarian manifestation of various metabolic disturbances. Based on Rotterdam criteria, PCOS is further classified into four phenotypes. Vitamin D deficiency affects 65- 75% of PCOS patients. There is very little research on the relationship between vitamin D deficiency and PCOS phenotypes. As a result, we intended to investigate the relationship between vitamin D, PCOS, and various PCOS phenotypes. This is a case-control study where we had been 100 people in the study. A total of 50 PCOS participants were classified into phenotype A, phenotype B, phenotype C, and phenotype D using Rotterdam criteria. There were 50 participants who did not have PCOS. Serum vitamin D levels were measured in the study population. The CIDRF (Central Inter-Disciplinary Research Facility) used an ELISA kit and reader to quantify vitamins. The results obtained were further classified as deficient (20ng/ml), insufficient (21-29ng/ml), and sufficient (30ng/ml). SPSS version 17 was used to analyse the results. The mean vitamin D level among women with PCOS was 15.9±9.3, women without PCOS was 20.5±9.2, the difference between the means was statistically significant(p-0.015). Among the participants with PCOS Phenotype A accounted for 36%, phenotype B 26%, phenotype C 20%, phenotype D 18%. The serum vitamin D levels among different phenotypes of PCOS was not statistically significant (p-0.978). There was no statistically significant difference in the mean vitamin D levels, among the phenotypes of PCOS (p - 0.978). Vitamin D deficiency was found to be more prevalent in women with PCOS in this study. In PCOS, it is recommended to screen for and treat with vitamin D. There is no significant difference between phenotypes.

Keywords: Ovarian Disease, Polycystic, Phenotype, Vitamin D and Correlation

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1. INTRODUCTION

PCOS is the most common heterogeneous multisystem endocrinopathy in women of reproductive age, with an ovarian manifestation of various metabolic disturbances and a wide range of clinical features. The Rotterdam criteria are used to diagnose PCOS. After excluding other androgen excess or related disorders, it includes clinical and/or biochemical hyperandrogenism, ovulatory dysfunction (chronic oligomenorrhea or amenorrhea), and polycystic ovarian morphology. The presence of any 2 of these 3 features is suggestive of PCOS. Contingently, four unique phenotypes are recognized as per the Rotterdam and Androgen Excess -PCOS (AE-PCOS) society criteria. The phenotypes prevailing are PCOS[1] A, B, C, and D in which phenotype A (Hyperandrogenism + Ovulatory disturbances +Polycystic ovarian morphology), phenotype B (Hyperandrogenism + Ovulatory disturbances), Phenotype C (Hyperandrogenism+ Polycystic ovarian morphology), Phenotype D (Ovulatory disturbances+ Polycystic ovarian morphology). Vitamin D deficiency is well known in PCOS. This prevalence ranges between 65-75%. Wehr et al[3] discovered that women with PCOS had low serum vitamin D levels in a study. It also demonstrated that vitamin D deficiency was more likely to be linked to metabolic syndromes. An integrative review, however, concluded that vitamin D deficiency neither contributes to the pathogenesis of PCOS nor causes it. [4] This reflects the fact that there is conflict in this area. There are conflicting reports regarding vitamin D levels and PCOS phenotype. [2,5] Furthermore, there is a scarcity of literature in the Indian population. As a result, we intended to investigate the relationship between vitamin D and various phenotypes of PCOS.

2. METHODOLOGY

2.1 Type of Study

This case control prospective study was conducted in the Department of Obstetrics and Gynaecology at Mahatma Gandhi Medical College and Research Institute after, Institute Human Ethical committee approval (MGMCRI IHEC/2018/OBG-12). from January 2019 to June 2020.

2.2 Inclusion Criteria

Women between 20 to 40 yrs., using Rotterdam criteria, were diagnosed as PCOS and grouped in to various phenotype (A, B, C, D).

2.3 Exclusion Criteria

Women already on vitamin D, received treatment for PCOS and known case of adrenal hyperplasia or any other endocrinopathies were excluded. Women, in the same age group, without PCOS were considered as control.

2.4 Biochemical Measurements

Each participant was enrolled after obtaining the informed consent. Three ml of venous blood was collected from women in both the groups in a EDTA tube. The samples collected were stored and processed in Central Inter- Disciplinary Research Facility (CIDRF). Vitamin D level was estimated using the ELISA kit in the ELISA reader at CIDRF. The results obtained were classified as sufficient(30ng/ml), Insufficient (> 20- 29ng/ml), Deficient(<20ng/ml). Data were collected using pre-validated proforma were entered into an Excel sheet (MS 2010).

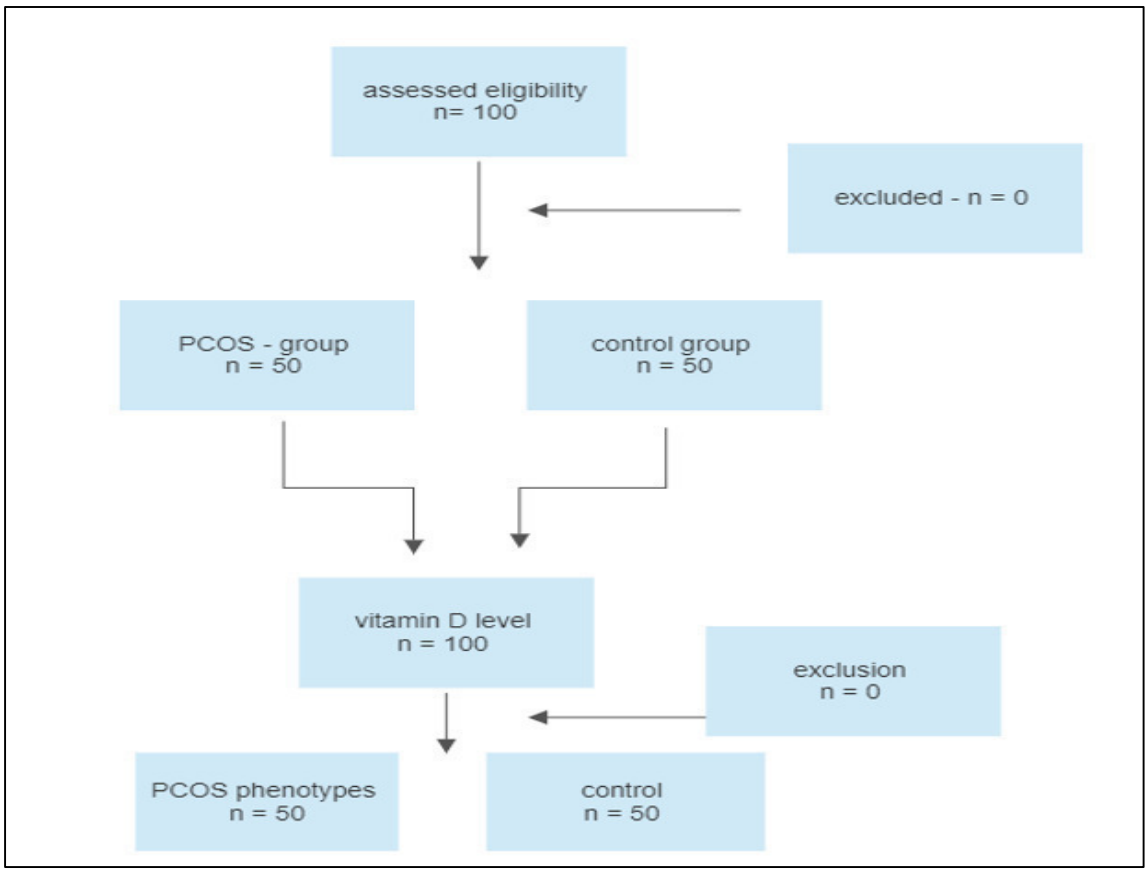
2.5 Phenotype Identification

Type A ovaries have hyperandrogenism, chronic anovulation, and polycystic ovaries; type B ovaries have hyperandrogenism as well as chronic anovulation; type C ovaries have hyperandrogenism but also polycystic ovaries; and type D ovaries have chronic anovulation as well as polycystic ovaries.

3. STATISTICS ANALYSIS

Considering the prevalence of vitamin D deficiency in women with PCOS is about 70%,[6] with CI as 0.05, power as 0.2, a minimum sample size of 96 was obtained. Categorical variables were summarized as percentage. The correlation analyses was used for phenotypic relation with vitamin D level. Comparison of continuous variables between groups were analyzed using independent t-test. To test the hypothesis chi Square test, independent sample t test and ANOVA were used appropriately. p value < 0.05 was considered as statistically significant.

Consort flow diagram



4. RESULT

During the study period total of 2860 women in reproductive age attended the gynecology OPD. Out of them, 256(8.9%) women were diagnosed to have PCOS, of them 50 women who fulfilled the inclusion criteria were considered. The age of both the group were matched. However, difference in BMI was significant**. (**Table 1**)**

Table 1 showing demographics

	Women with PCOS	Women without PCOS	*p* value*
Mean age in yrs., SD	25.9 (4.5)	26.1(4.9)	0.9
Mean BMI(kg/m^2), SD	27.6 (5.5)	24 (3.5)	0.000

Table 2 showing different phenotypes

Phenotype of PCOS	Number of women in each phenotype n (%)
Phenotype A	18 (36)
Phenotype B	13 (26)
Phenotype C	10(20)
Phenotype D	9 (18)

The most common phenotype found was phenotype A and the least common was D. (Table2)

Table 3 showing Difference in Vitamin D level

Serum Vitamin D Level (ng/ml)	Women with PCOS(N=50) n(%)	Women without PCOS(N=50) n(%)	*p* value*
Sufficient	4(8)	7(14)	0.009
Insufficient	9(18)	21(42)	
Deficient	37(74)	22(44)	

In the qualitative assessment of vitamin D level, it is observed that majority of the study population in both the groups were having deficient vitamin D level. (Table3)

Table 4 showing Vitamin D levels			
	Women with PCOS(N=50)	Women without PCOS(N=50)	*p* value*
Mean Serum Vitamin D (ng/ml), (SD)	15.9(9.3)	20.5(9.2)	0.015

The difference of serum vitamin D levels in the women with and without PCOS was found to be statistically significant (Table4)

4.1 Different Types of PCOS and Vitamin D Levels

There was no statistically significant difference found in the serum vitamin D levels, between different phenotypes of PCOS. It's clear from our study, the so called hyperandrogenism is not corelating with vitamin D levels. There is no correlation between Vitamin D levels and differing phenotypes of PCOS. This is unique for our study. The p value is 0.978. Even though there is significance between the PCOS groups and the control, there is no statistical significance between different phenotypes. (Table 5)

Table 5 showing different phenotypes and vitamin D levels					
Phenotype of PCOS	Phenotype A	Phenotype B	Phenotype C	Phenotype D	*p*-Value*
MeanSerum Vitamin D (ng/ml),(SD)	16.6 (9.6)	16.0 (9.8)	15.0 (11.2)	15.5 (6.7)	0.978

5. DISCUSSION

There exist conflicting reports about level of serum vitamin D in PCOS and its phenotype. This study aimed to compare serum vitamin D level of four phenotype of PCOS. We found significant reduction of serum vitamin D level in PCOS women in comparison to women without PCOS. However, this difference among different phenotype of PCOS is not significant. A wide variation was observed in mean age of women with PCOS among various studies reported. It was 22.0±2.17 years for Shah et al to 34±5 years for Krul et al.[6,7] But in the present study the mean age of women with PCOS nearly matched to that of i.e. 24.8±5.6.[8] Similar trend was observed in the control group also. Mean BMI of women with PCOS varies from 27.7± 5 Kg/m^2 by [8] to 34.25 Kg/m^2 by [2,8]. Present study matched to that with. In spite of this variation, it is clear that, PCOS is associated with high BMI. The distribution of phenotype is not uniform in the available literature. Phenotype A forms the major subgroup i.e. 66%, 58.6% and 31% in studies reported by.[9-11] Present study matches with that of Ma et al. But phenotype C and D forms the major subgroup as reported by i.e. 72.1% and %.[12,13] This discrepancy of phenotype distribution may be due to genetic variation of the population studied. According to the study done by the proportion of vitamin D deficiency was higher in women with PCOS than in women without PCOS i.e.59.9%,44% and39.1%.[2,6,14] The mean vitamin D level in women with PCOS was low compared to women without PCOS as seen in the studies done by 11.9±6.9 and 7.7±3.9[6,15]. Similar trend was observed in the present study. In a study by Eftekhar, et al found the mean serum level of vitamin D in PCOS phenotype A, B, C and D 20.97 ± 8,20.92 ± 9.43, 20.54 ± 9.53 and 19.97 ± 9.33 (ng/ml). Even if, there is a visible difference between mean serum vitamin D level of this and present study, not so among the different phenotypes of the same studies.[16] The strengths of the present study were a single observer study where cases and controls were matched. The estimation of vitamin D was done in CIDRF using proper calibration. However, the limitations associated with this study were small sample size of each phenotype and majority of the study population were indoor workers, which might have influenced the vitamin D levels in the PCOS group. A study [17]found that vitamin D levels were lesser in Chinese women with PCOS, particularly those who have hyperandrogenemia. In PCOS, there was independent negative correlation between 25(OH)D and hyperandrogenemia. Females with elevated body Mass index (BMI at age 26 years may be prioritized for hyperandrogenemia appraisal in PCOS women with vitamin D deficiency.

6. CONCLUSION

From the present study, it may be concluded that there was a statistically significant difference in the mean serum vitamin D levels among the women with PCOS and without PCOS. The most common phenotype was phenotype A and the least common phenotype was phenotype D. That was no significant difference in serum vitamin D levels with respect to different phenotypes of PCOS. Further studies with a larger sample size in each phenotype are recommended to conclusively establish the variation of serum vitamin D levels in PCOS, particularly related to phenotypes. Vitamin D supplementation can be given to all women with PCOS. Variation in vitamin D dosage is not required in different phenotypes of PCOS as the difference in vitamin D level among the phenotypes was not significant.

7. AUTHOR CONTRIBUTION STATEMENT

SG has designed the study and communicating, KLM and MR have done the data collection and statistics

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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