

ASSOCIATION OF VITAMIN D DEFICIENCY WITH HYPERANDROGENISM IN FEMALES WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Objective: This study designed to assess the relationship of vitamin D status with clinical features of hyperandrogenism in the young unmarried females **Study design:** A case control study. The study was carried out in Gynecology and Obstetrics unit of Railway Hospital, Rawalpindi from Oct, 2014 to April, 2015. **Materials and Methods:** A sample of 100 diagnosed PCOS patients, age range 16-25 years with clinical features of hyperandrogenism were included in this study with their written consent. 25OH Vitamin D Total Elisa Kit was used to assess the levels of Vitamin D. The Data was analyzed by using SPSS version 21 and ANOVA test was used to assess the relationship. P value < 0.05 was considered significant. **Results:** Vitamin D levels were tested in PCOS patients presenting clinical features of hyperandrogenism and it is found that there is insignificant relationship present between severity of hypovitaminosis D and hirsutism (P=0.669), acne (P=0.480) and alopecia (P=0.317) among PCOS patients. **Conclusion:** Although hirsutism presents itself as the most common feature in PCOS patients (51%), but no significant relationship is found between Hypovitaminosis D and clinical features of hyperandrogenism suggesting insignificant role of vitamin D in the pathogenesis of hyperandrogenism in PCOS patients.

KEYWORDS: Polycystic Ovarian Syndrome; Hyperandrogenism; Vitamin D.

INTRODUCTION

The Polycystic Ovarian Syndrome manifests itself in 6-10% women in their reproductive age and is recognized as the most common reproductive disorder characterized by menstrual irregularity, clinical/biochemical hyperandrogenism and polycystic ovaries causing infertility and affecting females both physically and psychologically [1].

Hyperandrogenism is the important biochemical parameter of PCOS describing the raised levels of androgen in blood of 80-90% of PCOS patients presenting with oligomenorrhea [2-3]. It is thought that elevated level of free circulatory testosterone is resulted by the increased production of androgen from ovaries due to the hyper-secretion of luteinizing hormone (LH) that stimulates the ovarian cytochrome p450c17a and ultimately reduces the Sex Hormone Binding Globulin (SHBG) synthesized in the liver thus developing the

clinical symptoms of hyperandrogenism including hirsutism or excess hair growth, acne and frontal baldness. It has been observed that hirsutism is the most common presentation of hyperandrogenism occurring in 60% of PCOS patients contributing severe depression and anxiety in women. Acne is another presenting complaint in 15-30% of females diagnosed with PCOS but less specific than hirsutism [4].

The popularity of Vitamin D nowadays is undoubtedly due to its involvement in the regulation of many physiological processes including immune system, insulin secretion, cancer, cell differentiation and reproduction through vitamin D receptor (VDR) [5].

Hypovitaminosis D has shown a disastrous impact on public health worldwide in all age groups. Increased prevalence of vitamin D deficiency has been observed in South Asian Countries which include India, Pakistan, Bangladesh, and Sri Lanka [6]. Two different studies from Pakistan have reported the prevalence of vitamin D deficiency about 70-90% in healthy population [7]. Several studies have strongly suggested the role of vitamin D in female reproduction by regulating the gene expression of aromatase and also found the low levels of aromatase in follicles of PCOS females as aromatase being an enzyme of granulosa cell converts the androgen into estrogen demonstrating that de-



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creased level of vitamin D is responsible for the manifestation of hyperandrogenism in PCOS [8].

The aim of our study is to find out any association between severity of hypovitaminosis D and the clinical presentation of hyperandrogenism among PCOS patients.

MATERIALS AND METHODS

Study design: Case-control study.

Ethical Consideration: Written consent was taken after explaining the purpose of study.

Study setting: Study was conducted in Gynecology and Obstetrics department of Railway Hospital, Rawalpindi in collaboration with Department of Biochemistry IIMC, Rawalpindi.

Duration of study: 6 months (June 2014 to November 2014).

Sample size: Two hundred

Grouping: Group 1: Females were divided into two groups, 100 apparently healthy females had normal weight and normal menstrual cycles. None of them had clinical symptoms of hyper-androgenism. Group2: 100 newly diagnosed patient of polycystic ovarian

Sampling technique: Non-probability purposive sampling technique was done.

Inclusion criteria: The females having, the presence of two features out of three i.e. polycystic ovarian (PCO) morphology on ultrasound scan (presence of 12 or more follicles measuring 2-9 mm in diameter per ovary or ovarian volume above 10cc), clinical/biochemical hyperandrogenism (hirsutism, acne or alopecia and /or elevated androgens levels) and ovulatory dysfunction (oligomenorrhea or amenorrhea) were existed.

Exclusion criteria: The females taking drugs (oral contraceptive, hypoglycemic drugs, vitamin D supplementation) and with other medical causes including Cushing syndrome, androgen secreting tumor, thyroid disorders, and prolectinemia were excluded from the research.

Sampling tools: Ferriman-Gallwey scoring system was used to evaluate the hair growth at seven sites: upper lip, chin/face, chest, back, abdomen, arms and thighs [9]. A score above 8 was indicative of hirsutism. Body weight in kilogram and height in meters was measured and BMI was calculated as weight (kg) divided by the square of the height (m) [10].

Biochemical analysis: Three ml venous blood was drawn in vacuum clot activator tubes from both groups and centrifuged at 2500-3000rpm for 15 minutes for

serum separation. Serum samples werestored at -20°C until further analysis at Biochemistry Research Laboratory IIMC [11]. The vitamin D assay was measured by Enzyme Linked Immunosorbent Assay by using 25OH Vitamin D Total Elisa Kit: Cat#KAP1917; LOT#131106 (DIA source, SA, Belgium). Hypovitaminosis was defined as plasma level of 25(OH) D less than 30ng/ml, graded as severe vitamin D deficiency for plasma level of 25(OH) D.

Statistical analysis: was done in SPSS version 21.0. Results were compared by applying independent T test and Chi-square. The level of significance was set as P<0.05.

RESULTS

In this case control study a total of 150 participants were included in which there were 100 diagnosed patients of PCOS selected according to Rotterdam criteria and 50 were healthy normal controls of same age group. Vitamin D levels were tested in PCOS patients presenting clinical features of hyperandrogenism and it is found that there is insignificant relationship present between severity of hypovitaminosis D and hirsutism (P=0.669), acne (P=0.480) and alopecia (P=0.317) among PCOS patients.

Vitamin D levels were tested in both the groups and its values were noted and it was found that the mean vitamin D level in control group was 11.846±7.898 ng/ml and in PCOS group patients the mean value of vitamin D level was noted to be 10.618 ±5.296 ng/ml.

The comparison of vitamin D levels in controls and PCOS patients showed that the mean vitamin D level was higher in controls (11.846±7.898ng/ml) as compared to PCOS patients (10.618±5.296ng/ml) but this was not statistically significantly (P-value > 0.05) different in both groups.

Table 1. Comparison of mean Vitamin D level in controls and PCOS patients

Vitamin D level (ng/ml)	Group	N	Mean	P-Value
	Control	50	11.846±7.9	0.324
	PCOS	100	10.618±5.3	

The results of comparison of vit D levels between control group and PCOS group on the basis of different weight categories. There was no significant (p-value > 0.05) difference in mean vitamin D levels when compared in between control and PCOS groups among normal weight (12.056±7.742 vs. 11.098±5.318, p-value = 0.577), over weight (13.024±9.798 vs. 11.032±6.527, p-value = 0.526) and obese subjects (6.307±4.474 vs. 10.354±4.993, p-value = 0.133).

Table 2: Comparison of Vitamin D levels between Control and PCOS group on the basis of different weight categories

BMI	Vit D		PCOS Group		P-value
	N	Mean	N	Mean Vit D	
Normal weight	40	12.06±7.74	20	11.10±5.32	0.577
Over weight	7	13.02±9.8	17	11.03±6.527	0.526
Obese	3	6.31±4.47	63	10.35±4.99	0.133

56% controls and 56% PCOS patients had severe vitamin D deficiency, 30% controls and 38% PCOS women had vitamin D deficiency. Only 1 (2%) woman in control group had sufficient level of vitamin D.

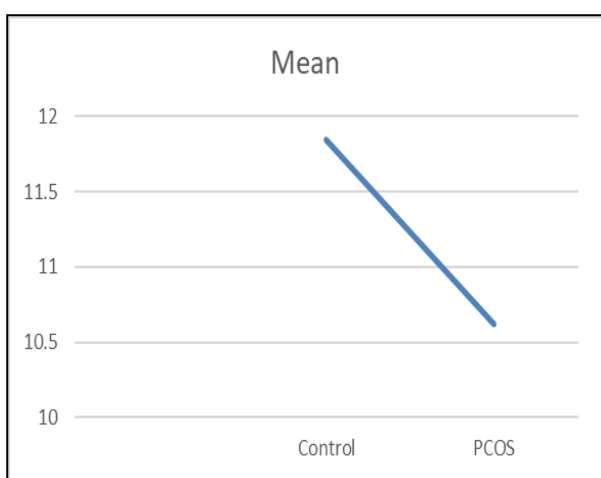


Figure 1. Vitamin D association with PCOS

DISCUSSION

PCOS is one of the most common female endocrine disorders with the prevalence of 5-10% in females of reproductive age causing infertility, metabolic and psychological disturbances leading to decrease quality of life [12]. The present study was designed to find out the relationship between PCOS and vitamin D and to know whether a low vitamin D status is observed in unmarried young female of 16-25 years of age with PCOS.

According to the result of our study 56% controls and 56% PCOS patients had severe vitamin D deficiency and the mean value of vitamin D was higher in controls (11.846 ± 7.898 ng/ml) as compared to PCOS patients (10.618±5.296 ng/ml) but the difference was not statistically significant. So our study could not find any association between serum vitamin D and PCOS. Our findings are similar to the findings observed by Kim et al. who found no differences in the absolute level of serum vitamin D between PCOS patients (19.6±6.6 ng/ml) and matched controls (20.1±7.4 ng/ml) and p= 0.696 and the prevalence of vitamin D deficiency in

controls and patients was 57.9% and 56.5% respectively [11].

Panidis at el. reported that vitamin D levels were similar in women with and without PCOS. These results are also in line with our study [11]. Similar findings were also found in observational study conducted by the Li and colleagues in Scotland in 2011 [13]. The results of our study were similar to the study carried out by Sahn at el. and Figueroa et al. in 2014 and 2015 respectively [14, 15]. Nine of the reviewed studies did not find significant difference between PCOS women and control groups (overall mean 61.2 nmol/l=19.24ng/ml in PCOS women vs 67.1nmol/l=21.10ng/ml in controls) [10].

Sirmans et al. reported lower serum vitamin D level in women with PCOS (n=545) compared to control (n=145) (25.7 vs 32.0 ng/ml, respectively) [4]. Observational study conducted in Italy reported lower serum vitamin D level in 90 PCOS women (32.4nmol/l=10.18ng/ml) than in 40 controls (73.7nmol/l=23.17ng/ml) [16]. Other two observational studies also found significantly lower serum vitamin D level in PCOS women compared to control women [17, 18].

The study carried out by Poel et al. even found a significantly higher serum vitamin D level in PCOS women (29.3ng/ml) than in controls (19.4ng/ml) with similar age and BMI [10]. Although there is discrepancy in the literature about the vitamin D levels between women with and without PCOS but it is clear that vitamin D deficiency is a common finding among controls and PCOS patients.

CONCLUSIONS

This study found no difference in the vitamin D level among PCOS and control subjects. Our results are in agreement with the previous data supporting an association of BMI with PCOS but don't support the significant association of BMI with severity of hypovitaminosis D.

The limitations in our study are due to small sample size, the lack of adjustments of confounding factors that may play a role in causing vitamin D deficiency and secondly the metabolic features of PCOS were not evaluated for comparison with vitamin D level.

Recommendations: To the best of our knowledge we are the first investigating the relationship between vitamin D deficiency and PCOS in Pakistan. To prove our findings new therapeutic approaches and large intervention trials are required.

Conflict of interest: Nil

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