

ORIGINAL RESEARCH

Serum levels of vitamin d and lipid profile in patients with polycystic ovary syndrome: A comparative study

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is one of the most frequent endocrine illnesses in women of reproductive age. It affects around 5-10% of the world's population. Irregular menstrual cycles, prolonged anovulation and hyperandrogenism are all symptoms of the disease. Hyperinsulinemia, insulin resistance, gestational diabetes, type 2 diabetes, dyslipidemia and cardiovascular disease may develop over time.

Aim: To compare the lipid profile and vitamin D levels in women with and without PCOS in relation to obesity and to determine the Luteinizing hormone[LH], Follicle Stimulating Hormone[FSH], prolactin[prl] levels in women with PCOS in relation to obesity

Method: A total of 152 subjects were taken for the study. 76 PCOS patients were identified ultrasonographically and clinically from November 2015 to July 2017, and 76 normal menstruating women served as controls in the study conducted at Deccan Medical College and Princess Esra Hospital, Hyderabad. All the subjects were categorized as obese or lean based on their BMI.

Results: In comparison to obese participants without PCOS, PCOS obese subjects had higher TG and TC levels and lower HDL levels, according to the study. When compared to lean subjects without PCOS, PCOS lean subjects had higher TG, TC, and LDL values. The HDL levels of PCOS lean patients were observed to be lower than those of lean subjects without PCOS. Vitamin D levels were also shown to be considerably lower in PCOS patients (both obese and non-obese) than in healthy controls.

Conclusion: Supplementary retrospective data-based revisions and randomized meticulous tests with recurrent Vitamin D estimations are required to determine whether Vitamin D deficiency is a co-determinant of hormonal and metabolic

irregularities in PCOS, a byproduct of hormonal and metabolic un-evenness in PCOS, or both.**Keywords: Polycystic ovary syndrome (PCOS), Vitamin D, lipid profile.****INTRODUCTION**

According to the World Health Organization (WHO), PCOS affected 116 million women (3.4 percent) globally in 2012. ⁽¹⁾ PCOS prevalence estimates vary widely over the world, ranging from 2.2 percent to as high as 26 percent. PCOS affects 10% of women in India, yet there is little data on the subject. PCOS is characterized by irregular menstrual cycle, chronic anovulation and hyperandrogenism ⁽¹⁾. Polycystic ovarian syndrome (PCOS) is a genetically complex endocrine condition with a complicated pathophysiology and unknown aetiology. The National Institutes of Health/National Institute of Child Health and Human Disease (NIH/NICHD) ⁽²⁾, the European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine (ESHRE/ASRM) or the 'Rotterdam Criteria' ⁽³⁾, and the Androgen Excess and PCOS Society have published diagnostic criteria for PCOS ⁽⁴⁾. PCOS is a multisystem syndrome that has been associated with reproductive and metabolic abnormalities, as well as cardiovascular illness ^(5,6). The majority of women with PCOS have dyslipidemia, which is characterized by elevated levels of various blood lipids but low HDL-cholesterol (HDL-C) levels ⁽⁶⁾. Changes in cholesterol levels have a significant impact on atherosclerosis, the primary cause of cardiovascular disease (CVD). Women with PCOS are also at a higher risk of cardiovascular disease and stroke ^(7,8). As a result, measures to decrease cholesterol and prevent cardiovascular disease should be prioritised in females with PCOS.

Reduced vitamin D levels in the blood have been linked to an increased risk of a variety of chronic diseases, including common malignancies, autoimmune or infectious disorders and cardiovascular issues, as well as impaired bone metabolism (like rickets, osteoporosis and osteomalacia). Vitamin D deficiency is frequent in women with PCOS, with serum values of 25-hydroxy vitamin D (25OHD) less than 20 ng/ml found in 67–85 percent of women with PCOS. According to certain research, vitamin D insufficiency might increase symptoms of PCOS such as insulin resistance, ovulatory and menstrual abnormalities, reduced pregnancy success, hirsutism, hyperandrogenism, and obesity. Vitamin D insufficiency has been linked to an increased risk of cardiovascular disease (CVD) and lipid imbalances. The binding of vitamin D to its receptor regulates several genes, suggesting that vitamin D may have a role in the genesis of dyslipidemia linked with PCOS ⁽⁹⁻¹⁵⁾. However, there is no evidence that Vitamin D supplementation will affect lipid profiles. Vitamin D supplementation has been proven to alter lipid profiles in some studies ⁽¹⁶⁻²⁰⁾, while other investigations have found no benefit ⁽²¹⁻²³⁾. There have been studies on the effects of vitamin D supplementation on lipid levels in PCOS patients, but no conclusive results have been found ⁽²⁴⁻³³⁾. More research is being done and more data is being provided on Vitamin D's impact on PCOS patients' serum cholesterol, but the results are yet unknown. The present data from the study was used to analyze the association of vitamin D with the blood lipid levels in PCOS patients in relation to BMI.

METHODS**STUDY SUBJECTS**

The study consisted of 152 subjects. 76 PCOS patients were identified clinically and ultrasonographically and 76 normal menstruating women were taken as controls in our study done at Deccan Medical College, Hyderabad and Princess Esra Hospital Hyderabad from November 2015 to July 2017. Venous blood samples were drawn under aseptic precautions and stored at -20°C after centrifugation at 3000 rpm for 10 min at 20°C . FSH, LH, PRL and

VIT D were estimated on MINI VIDAS by enzyme immunofluorescence assay sandwich method. Triglycerides {TG}, Total cholesterol {TC}, High density lipoproteins {HDL} and low density lipoproteins {LDL} were estimated on COBAS c311-roche by enzymatic colorimetric method.

INCLUSION CRITERIA

- History of irregular cycles
- Hirsutism
- Ultrasonographic finding of polycystic ovaries

EXCLUSION CRITERIA

- Previous history of hypertension
- Diabetes Mellitus
- Renal disease
- Thyroid disorder
- Adrenal hyperplasia
- Dyslipidemia
- Liver disorders and other chronic disorders affecting the parameters under study
- Patients on drugs altering lipid and vitamin D levels.

ANTHROPOMETRIC MEASUREMENTS

Height and weight of the individuals were obtained following standard protocol and instrument. Height was measured using a stadiometer and weight by a weighing scale.

BMI was calculated as per formula: Weight (Kg)/Height (meter²). The measurements were scored to classify their state of obesity.

The study consisted of a total of 152 women who were divided into following groups according to Basal metabolic index (BMI). It is detailed in Table below:-

Group	Number of Subjects N	BMI
PCOS overweight and Obese	38	BMI \geq 25
PCOS Lean	38	BMI<25
Overweight and Obese without PCOS	38	BMI \geq 25
Lean without PCOS	38	BMI <25

STATISTICAL ANALYSIS

The data was entered in MS Office Excel 2011. The Graph Pad prism software 13.0 was used to analyze the data. The results were expressed in terms of mean \pm SD. A p value less than 0.05 was considered statistically significant. Test of significance used was student “ t” test which compared the variables.

RESULTS

VITAMIN D STATUS IN WOMEN WITH PCOS AND WOMEN WITHOUT PCOS

A total of 152 subjects were taken for the study .Among them, 76 were PCOS confirmed women patients and 76 were normal menstruating women who were included in the study. Biochemical and clinical characteristics are presented in the Table 1-4.

Table 1. Biochemical findings of PCOS obese and obese (without PCOS) subjects:

Parameter	PCOS obese BMI \geq 25 (n=38) Mean \pm SD	Obese (without PCOS) BMI \geq 25 (n=38)	p-value

		Mean ± SD	
TG mg/dl	201.7±18.113	174.2±4.038	<0.0001
TC mg/dl	208.33±12.776	211±10.42433	<0.0001
HDL mg/dl	37.8±5.405	49.72±20.04	0.051
LDL mg/dl	104.04±31.02	108.5714±28.07	<0.0001
Vit D ng/ml	6.06±3.29	15.08±1.21	<0.0001

As summarized in the table-1, serum Triglycerides, Total Cholesterol, and LDL values of obese women with PCOS were suggestively higher than those of obese women without PCOS (P=0.0001). These women had lower levels of HDL and Vitamin D compared to their healthy counterparts (P=0.0001).

Table 2. Biochemical findings of PCOS lean and lean (without PCOS) subjects

Parameter	PCOS lean BMI ≤25 (n=38) Mean ± SD	Lean (without PCOS) BMI ≤25 (n=38) Mean ± SD	p-value
TG mg/dl	187.765±19.449	158.2±9.148	<0.0001
TC mg/dl	190.871±33.428	140.286±21.85	<0.0001
HDL mg/dl	41.25±2.36	60.14±7.17	<0.0001
LDL mg/dl	110±19.60442	90±10.06	<0.0001
Vit D ng/ml	12.01±1.16	38.25±3.4	<0.0001

As summarized in the Table-2, the PCOS lean participants had statistically considerable increase in the concentrations of the TG, TC, and LDL in comparison to the PCOS lean women. These women had lower levels of HDL and Vitamin D compared to their healthy counterparts (p =0.0001, respectively). In the lean without PCOS TG, TC, HDL, LDL and Vitamin D level are within the normal range which is statically compared.

Table 3. Biochemical findings of PCOS obese and PCOS lean subjects:

Parameter	PCOS obese BMI ≥25 (n=38) Mean ± SD	PCOS lean BMI ≤25 (n=38) Mean ± SD	p-value
TG mg/dl	201.7±18.113	187.765±19.449	<0.0001
TC mg/dl	208.33±12.776	190.871±33.428	<0.0001
HDL mg/dl	37.8±5.405	41.25±2.36	0.644
LDL mg/dl	104.04±31.02	110±19.60442	0.432
Vit D ng/ml	6.06±3.29	12.01±1.16	<0.0001

Also it was observed in the table-3, that PCOS obese women had higher TG and TC levels compared to PCOS lean women. Obese women with PCOS had considerably decreased vitamin D levels (P=0.0001). There was no significant change in HDL and LDL values. In the above table-4, the PCOS patients exhibited considerably higher TC, TG, LDL, and lower HDL values than healthy controls in our study. Obese patients with PCOS had greater TG and lower HDL levels than obese patients without PCOS, according to our findings. The TG, TC, and LDL levels of PCOS lean individuals were greater than those of lean people without PCOS. In this study, women with PCOS who were overweight or normal weight had lower 25-OH D levels than women without PCOS, with a p value of 0.0001. The accumulation of triglycerides could be the cause of the rise in TGs. This buildup could be caused by increased lipogenesis, slower clearance, or impaired fatty acid oxidation. Increased VLDL particle secretion by the liver results in higher plasma triglyceride levels.

Table 4. Hormonal levels of PCOS obese and PCOS lean subjects

Parameter	PCOS obese BMI \geq 25 (n=38) Mean \pm SD	PCOS lean BMI \leq 25 (n=38) Mean \pm SD	p-value
FSH mIU/ml	6.376 \pm 0.48	4.955 \pm 1.48	0.001
LH mIU/ml	10.338 \pm 1.08	15.48 \pm 0.95	<0.0001
PRL ng/ml	12.108 \pm 0.88	14.195 \pm 5.17	0.002

Table-4summarises the hormonal profile of Patients of PCOS .It was found thatFSH, LH and PRL are higher in PCOS obese patients as compared to PCOS Lean pateints (p<0.005).

DISCUSSION

This is a first kind of study done in women with PCOS in the Deccan population. One of the most frequent hormonal illnesses among women of reproductive age is polycystic ovarian syndrome (PCOS). PCOS is a prevalent diagnosis among women who are experiencing infertility. Insulin resistance (IR), which is common in PCOS patients, may be linked to a variety of metabolic issues. IR also increases HDL particle catabolism and LDL particle formation. It is possible that this is attributable to a protein known as cholesterol ester transfer protein. Hyperandrogenism alters the lipid profile in addition to insulin resistance. Hepatic lipase activity, which is involved in HDL particle breakdown, has been associated to hyperandrogenism. As a result, the lipid profiles of PCOS patients are more atherogenic than those of controls. Obesity in PCOS women may be exacerbated by elevated triglyceride levels . An altered lipid profile (atherogenic), obesity and IR may all raise the risk of CVD. PCOS sufferers should be evaluated and monitored on a frequent basis to avoid CVD complications. Vitamin D deficiency is common in PCOS patients. According to multiple studies, PCOS patients who are deficient in Vitamin D have a higher risk of metabolic and endocrine issues. There have been no prospective observational studies on the link between Vitamin D deficiency and PCOS. Based on our findings, we conclude that there is no evidence to support the idea that Vitamin D deficiency has a role in the development of PCOS or vice versa. We have established, however, that PCOS is linked to vitamin D deficiency. While PCOS may worsen Vitamin D deficiency in some people, it's also probable that it's an already prevalent concomitant disease. It's difficult to establish a cause-and-effect relationship between vitamin D deficiency and PCOS due to limited sample sizes and a wide range of outcomes in past studies. For a better understanding of the link between vitamin D insufficiency and PCOS, prospective research in a larger, well-defined sample of women with and without PCOS is required. Future revisions should look at women at different phases of the disease's course (if possible) and measure their vitamin D levels to see if vitamin D deficiency is a cause or an implication of PCOS metabolic and hormonal dysregulations. Women with PCOS should have their blood sugar levels checked on a regular basis. LDL and triglyceride levels were higher in the PCOS group, while HDL levels were lower, However the difference was not significant.

Vitamin D deficiency was shown to be more common in women with PCOS in our study. The majority of the study group was found to be vitamin D deficient when compared to the control group, which was similar to the findings of Wehr E et al ³⁷. In this investigation, serum vitamin D levels in the study and control groups were 12.01 1.16+ ng/ml and 38.4 3.4 ng/ml, respectively, with a statistically significant difference. The current study's findings were comparable to those of Figueroa et al ³⁸. Wher et al. found vitamin deficiency in 72.8 percent of PCOS women, whereas Kim et al. ³⁸, found no difference in serum 25-(OH) vitamin D levels in PCOS women compared to controls ³⁹.In contrast, Kumar et al. ³⁴found

that PCOS women had lower levels of serum 25-OH vitamin D than controls. Vitamin D levels in our sample showed declining trends when compared to normal, which is consistent with these findings. Many observational studies have revealed that vitamin D may have a role in PCOS metabolic abnormalities⁴⁰. Vitamin D supplementation had no significant beneficial effect on insulin kinetics or cardiovascular risk variables in a recent research in PCOS⁴¹. Others have found that PCOS patients have considerably lower vitamin D levels than controls⁴². Eftekhari et al. discovered no significant differences in serum vitamin D levels between the different types of PCOS⁴³. A high frequency of vitamin D insufficiency has been linked to metabolic syndrome, which could have serious consequences for public health⁴⁴⁻⁴⁵. These findings imply that screening for vitamin D insufficiency could be helpful in detecting PCOS early and preventing it from progressing to type 2 diabetes. Exploration of vitamin D's role in PCOS pathogenesis on a larger scale could provide a focus for future clinical trials and provide insight into vitamin D's potential role in PCOS pathophysiology and therapy. Glucose homeostasis may be influenced by vitamin D. The human insulin gene promoter has a vitamin D response element, and vitamin D receptors can be found in pancreatic beta cells and skeletal muscles. The discrepancies in vitamin D insufficiency in PCOS seen in this study against those found in other populations could be attributable to varying degrees of gonadotrophic and metabolic abnormalities caused by combinations of many hereditary and environmental variables. As seen by the previously described correlations with blood sugar, lipid profile and BMI in the preceding section, vitamin D has an inverse association with metabolic abnormalities in PCOS⁴⁴⁻⁴⁸.

CONCLUSION

Low vitamin D levels have been linked to PCOS, and genes involved in vitamin D metabolism have been identified as potential genes for PCOS susceptibility. Future studies involving VDR SNPs and PCOS, as well as vitamin D polymorphism and metabolic disturbances in PCOS, are needed to clarify the relationship of vitamin D metabolism with insulin resistance. Polymorphism in the VDR gene has been correlated and reported to play a role in insulin secretion and sensitivity in PCOS women.

AUTHORS CONTRIBUTION

FAN, SA conceptualized, demonstrated, designed, documented and HB, MW drafted in consultation with other co-authors. All the authors approved final draft for publication. SA and HB have equally contributed.

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CONFLICT OF INTEREST

Nil.

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