ORIGINAL RESEARCH

Assessment of Relationship Between Vitamin D Level and Polycystic OVARY Syndrome

[1]Dr Neelam Sharma, [2]Dr Devinder Kumar, [3]Dr Shahana

[1]Ante Natal Medical Officer Cum Assistant Professor, Department of Obstetrics and Gynecology GMC Rajouri, Jammu & Kashmir India.
[2]Associate Professor, Department of Obstetrics and Gynecology GMC Rajouri, Jammu & Kashmir India.
[3]PG, Department of Obstetrics and Gynecology GMC Rajouri, Jammu & Kashmir India..

Corresponding Author
Dr. Neelam Sharma
Ante Natal Medical Officer Cum Assistant Professor, Department of Obstetrics and Gynecology GMC Rajouri, Jammu & Kashmir India
Email: neelamyogesh19211@gmail.com

Received: 10April, 2023 Accepted: 15May, 2023

ABSTRACT
Aim: To assess the relationship between vitamin D level and polycystic ovary syndrome. **Methods:** Fifty- eight women of reproductive age 18- 40 years were divided into two groups. Group I with 25(OH)D3 deficiency, and group II with normal 25(OH)D3. Biochemical and hormonal parameters (androgen hormones, gonadotropins, and thyroid function tests) was assessed. Weight, height, Body mass index (BMI) and waist circumference (WC) measurements were recorded. **Result:** The mean age in group I patients was 28.4 years and in group II was 29 years. The mean waist circumference (WC) was 92.4 cm in group I and 83.7 cm in group II. The mean BMI was 29.1 kg/m2 in group I and 31.4 kg/m2 in group II. The difference was significant (P< 0.05). The mean fasting glucose level was 93.2 mg/dl in group I and 81.4 mg/dl in group II. HOMA- IR was 3.8 in group I and 3.2 in group II. Serum calcium was 8.4 mg/dl in group I and 9.1 mg/dl in group II. Triglyceride was 143.5 mg/dl in group I and 137.4 mg/dl in group II. LDL-C was 145.2 mg/dl in group I and 144.9 mg/dl in group II. HDL-C was 40.1 mg/dl in group I and 49.2 mg/dl in group II. The difference was significant (P< 0.05). The mean FSH (mlU/mL) was 6.8 and 6.4 in group I and group II respectively. The mean LH (mlU/mL) was 8.4 and 9.6, serum testosterone (ng/ml) was 7.5 and 5.2, PRL (ng/ml) was 23.1 and 15.4, DHEA-S (ng/ml) was 712.4 and 532.6, TSH (µIU/L) was 2.7 and 2.5 and sT4, pmol/L was 11.2 and 12.4 in group I and group II respectively. A significant difference was observed (P< 0.05). There was correlation between 25(OH)D3 levels and WC, BMI, fasting glucose, HOMA- IR, LH, serum testosterone and DHEA-S (P< 0.05). **Conclusion:** There was correlation between polycystic ovary syndrome and vitamin D deficiency. We suggest that vitamin D deficiency exacerbates the risk of polycystic ovary syndrome.
Key words: vitamin D, Polycystic ovary syndrome, FSH

INTRODUCTION

Polycystic ovary syndrome (PCOS) is an endocrine disease frequently seen in women of reproductive age. PCOS is characterized by polycystic ovarian morphology, hyperandrogenism, and ovulatory impairment.[1] The etiology of PCOS is still unclear. However, evidence suggests a multi-factorial origin, with expression being seen in women with a genetic disposition. The basic finding in the pathophysiology of PCOS is insulin resistance.[2] This develops in association with weight gain and an increase in waist circumference and is powerfully associated with hyperandrogenemia and ovarian dysfunction. Obesity and insulin resistance aggravate hyperandrogenemia. The incidence of cardiovascular diseases, type 2 diabetes mellitus, hypertension, endometrial cancer, and inflammation-related conditions increases in association with increased adipose tissue and hyperandrogenemia in women with PCOS.[3]

A growing body of evidence has linked higher prevalence of PCOS to vitamin D deficiency. Vitamin D is a steroid hormone that is endogenously synthesized through skin exposure to solar ultraviolet light; however, <10–20% is derived from diet.[4] The active form 1,25-dihydroxyvitamin D acts on its respective receptor (vitamin D receptor), which is present at multiple locations throughout the body (intestine, breast, bones, pancreas, kidney, and immune cells), to modulate the organ metabolism and function. In addition, vitamin D upregulates insulin

synthesis and secretion by pancreatic cells.[5] In women affected by PCOS, a suboptimal vitamin D level (<20 ng/mL) was found to be linked with several risk factors associated with PCOS, including hyperglycemia; increased scores on the homeostatic model assessment for insulin resistance (HOMA-IR); increases in levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and fasting plasma glucose levels; and a decrease in high-density lipoprotein cholesterol (HDL-C) level.[6] We performed this study to assess the relationship between vitamin D level and polycystic ovary syndrome.

MATERIALS AND METHODS

After considering the utility of the study and obtaining approval from ethical review committee, we selected fifty- eight women of reproductive age 18- 40 years. Patients' consent was obtained before starting the study.

Data such as name, age etc. was recorded. A careful physical examination was carried. Weight, height, and waist circumference (WC) measurements were recorded. Body mass index (BMI) was calculated by dividing weight (in kilograms) by height (in meters) squared. WC measurements were performed at the level of the iliac processes and umbilicus. Patients were divided into two groups. Group I with 25(OH)D3 deficiency, and group II with normal 25(OH)D3. Biochemical and hormonal parameters (androgen hormones, gonadotropins, and thyroid function tests) was assessed. The results were compiled and subjected for statistical analysis using Mann Whitney U test. P value less than 0.05 was set significant.

RESULT

Table I Patients distribution

Parameters	Group I	Group II	P value
Age (years, mean)	28.4	29.0	0.17
WC (cm)	92.4	83.7	0.04
BMI (kg/m2)	29.1	31.4	0.02

The mean age in group I patients was 28.4 years and in group II was 29 years. The mean waist circumference (WC) was 92.4 cm in group I and 83.7 cm in group II. The mean BMI was 29.1 kg/m2 in group I and 31.4 kg/m2 in group II. The difference was significant (P< 0.05) (Table I).

Table II Comparison of parameters

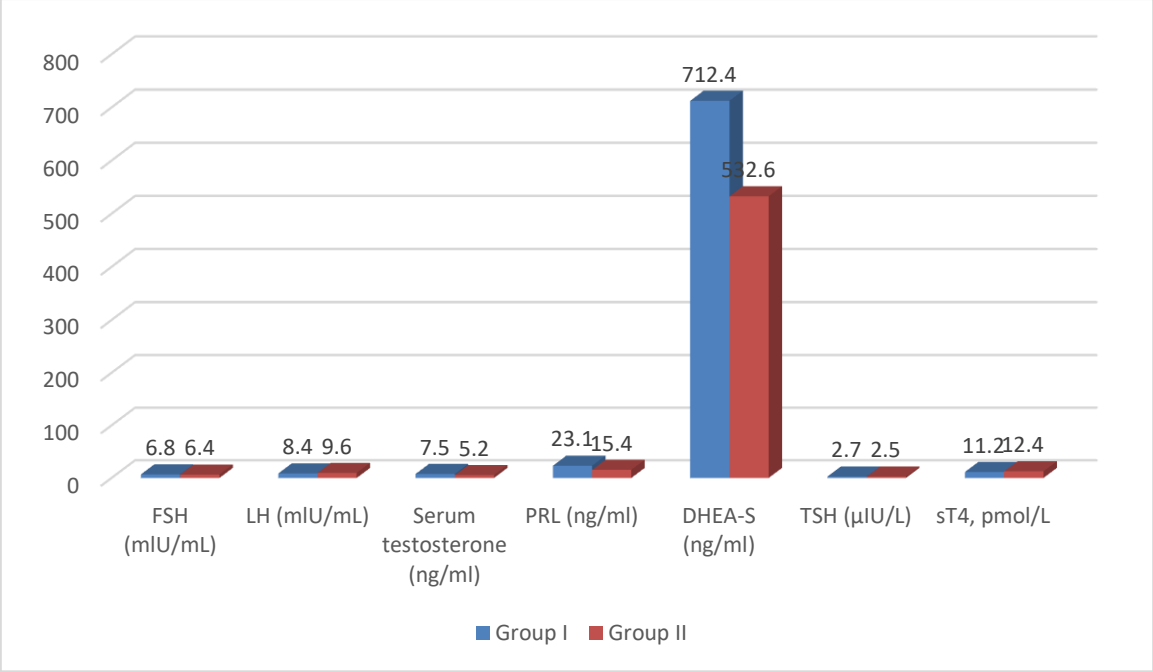
Parameters	Group I	Group II	P value
Fasting glucose (mg/dl)	93.2	81.4	0.17
HOMA- IR	3.8	3.2	0.04
Serum calcium (mg/dl)	8.4	9.1	0.02
Triglyceride (mg/dl)	143.5	137.4	0.05
LDL-C (mg/dl)	145.2	144.9	0.92
HDL-C (mg/dl)	40.1	49.2	0.02

The mean fasting glucose level was 93.2 mg/dl in group I and 81.4 mg/dl in group II. HOMA- IR was 3.8 in group I and 3.2 in group II. Serum calcium was 8.4 mg/dl in group I and 9.1 mg/dl in group II. Triglyceride was 143.5 mg/dl in group I and 137.4 mg/dl in group II. LDL-C was 145.2 mg/dl in group I and 144.9 mg/dl in group II. HDL-C was 40.1 mg/dl in group I and 49.2 mg/dl in group II. The difference was significant (P< 0.05) (Table II).

Table III Assessment of hormonal parameters

Parameters	Group I	Group II	P value
FSH (mlU/mL)	6.8	6.4	0.94
LH (mlU/mL)	8.4	9.6	0.05
Serum testosterone (ng/ml)	7.5	5.2	0.03
PRL (ng/ml)	23.1	15.4	0.05
DHEA-S (ng/ml)	712.4	532.6	0.01
TSH (µIU/L)	2.7	2.5	0.92
sT4, pmol/L	11.2	12.4	0.82

The mean FSH (mlU/mL) was 6.8 and 6.4 in group I and group II respectively. The mean LH (mlU/mL) was 8.4 and 9.6, serum testosterone (ng/ml) was 7.5 and 5.2, PRL (ng/ml) was 23.1 and 15.4, DHEA-S (ng/ml) was 712.4 and 532.6, TSH (µIU/L) was 2.7 and 2.5 and sT4, pmol/L was 11.2 and 12.4 in group I and group II respectively. A significant difference was observed (P< 0.05) (Table III, graph I).



Graph I Assessment of hormonal parameters

Table IV Correlation of 25(OH)D3 levels and various parameters

Parameters	R value	P value
Age (years, mean)	0.014	0.59
WC (cm)	-0.321	0.02
BMI (kg/m2)	-0.437	0.03
Fasting glucose (mg/dl)	-0.394	0.01
HOMA- IR	-0.382	0.05
FSH (mlU/mL)	-0.183	0.12
LH (mlU/mL)	-0.384	0.02
Serum testosterone (ng/ml)	-0.357	0.04
DHEA-S (ng/ml)	-0.412	0.03
TSH (µIU/L)	0.023	0.63
sT4, pmol/L	0.018	0.52

There was correlation between 25(OH)D3 levels and WC, BMI, fasting glucose, HOMA- IR, LH, serum testosterone and DHEA-S (P< 0.05) (Table IV).

DISCUSSION

Polycystic ovary syndrome (PCOS) is a common cause of ovarian dysfunction in women with anovulation.[7]The main symptoms are characterized by chronic anovulation, hyperandrogenism, and/or the presence of polycystic ovary morphology from ultrasound examination. The phenotypic manifestation of this disorder is associated with various degrees of gonadotropic and metabolic abnormalities determined by the interaction of multiple genetic and environmental factors.[8]

Vitamin D plays a physiologic role in reproduction including ovarian follicular development and luteinization via altering anti-müllerian hormone (AMH) signalling, follicle-stimulating hormone sensitivity and progesterone production in human granulosa cells. It also affects glucose homeostasis through manifold roles.[9] The potential influences of vitamin D on glucose homeostasis include the presence of specific vitamin D receptor (VDR) in pancreatic β-cells and skeletal muscle, the expression of 1-α-hydroxylase enzyme which can catalyze the conversion of 25-hydroxy vitamin D [25(OH)D] to 1,25-dihydroxyvitamin D, and the presence of a vitamin D response element in the human insulin gene promoter.[10] We performed this study to assess the relationship between vitamin D level and polycystic ovary syndrome.

Our results showed that the mean age in group I patients was 28.4 years and in group II was 29 years. The mean waist circumference (WC) was 92.4 cm in group I and 83.7 cm in group II. The mean BMI was 29.1 kg/m2 in group I and 31.4 kg/m2 in group II. Gokosmanoglu et al[11] in their study two hundred sixty-seven patients with PCOS were divided into two groups Group 1 with 25(OH)D3 deficiency, and Group 2 with normal 25(OH)D3. Biochemical and hormonal parameters (androgen hormones,

gonadotropins, and thyroid function tests) were compared between the two groups. Eighty-six percent of the patients (n=231) were in Group 1 and 14% (n=36) in Group 2. Statistically significantly higher concentrations of serum testosterone, dehydroepiandrosterone-sulfate and LH were determined in Group 1 ($p<0.05$). 25(OH)D3 concentrations were negatively correlated with body mass index ($r=-0.459$), serum testosterone ($r=-0.374$) and dehydroepiandrosterone-sulfate levels ($r=-0.418$); (all; $p< 0.05$).

Our results showed that the mean fasting glucose level was 93.2 mg/dl in group I and 81.4 mg/dl in group II. HOMA- IR was 3.8 in group I and 3.2 in group II. Serum calcium was 8.4 mg/dl in group I and 9.1 mg/dl in group II. Triglyceride was 143.5 mg/dl in group I and 137.4 mg/dl in group II. LDL-C was 145.2 mg/dl in group I and 144.9 mg/dl in group II. HDL-C was 40.1 mg/dl in group I and 49.2 mg/dl in group II. Bindayel et al[12] in their study thirty-one women with PCOS and 75 controls answered a questionnaire on vitamin D. The patients with PCOS had lower vitamin D levels ($p < 0.05$), a significantly higher rate of obesity ($p < 0.05$), and significantly higher serum triglyceride levels than did controls. The number of patients with PCOS consumed milk and dairy products ($p < 0.05$) and exposed to sun ($p < 0.006$) were lower compared to controls. Triglyceride levels were significantly correlated with body mass index (BMI); vitamin D level was not significantly correlated with anthropometrical or biochemical variables. These results affirm that vitamin D levels are lower in women with PCOS; however, despite the significantly higher proportion of obesity among patients with PCOS, hypovitaminosis was not associated with BMI.

Our results showed that the mean FSH (mlU/mL) was 6.8 and 6.4 in group I and group II respectively. The mean LH (mlU/mL) was 8.4 and 9.6, serum testosterone (ng/ml) was 7.5 and 5.2, PRL (ng/ml) was 23.1 and 15.4, DHEA-S (ng/ml) was 712.4 and 532.6, TSH (µIU/L) was 2.7 and 2.5 and sT4, pmol/L was 11.2 and 12.4 in group I and group II respectively. There was correlation between 25(OH)D3 levels and WC, BMI, fasting glucose, HOMA- IR, LH, serum testosterone and DHEA-S ($P< 0.05$). PCOS and vitamin D deficiency have been described as risk factors for atherosclerosis and hypertensive disorders.[13] Previous studies have shown that these increase the morbidity and mortality associated with cardiovascular disease. Vitamin D replacement has also been shown to reduce systolic blood pressure and mortality associated with cardiovascular disease.[14]

CONCLUSION

There was correlation between polycystic ovary syndrome and vitamin D deficiency. We suggest that vitamin D deficiency exacerbates the risk of polycystic ovary syndrome.

REFERENCES

1. Rashidi B, Haghollahi F, Shariat M, Zayerii F. The effects of calcium-vitamin D and metformin on polycystic ovary syndrome: a pilot study. Taiwan J Obstet Gynecol. 2009;48:142–7.
2. Garg G, Kachhawa G, Ramot R, Khadgawat R, Tandon N, Sreenivas V, et al. Effect of vitamin D supplementation on insulin kinetics and cardiovascular risk factors in polycystic ovarian syndrome: a pilot study. Endocr Connect. 2015;4:108–16.
3. Al-Daghri NM, Al-Attas OS, Alkharfy KM, Khan N, Mohammed AK, Vinodson B, et al. Association of VDR-gene variants with factors related to the metabolic syndrome, type 2 diabetes and vitamin D deficiency. Gene. 2014;542:129–33.
4. Dasgupta S, Dutta J, Annameneni S, Kudugunti N, Mohan Reddy B. Association of vitamin D receptor gene polymorphisms with polycystic ovary syndrome among Indian women. Indian J Med Res. 2015;142:276–85.
5. Wehr E, Trummer O, Giuliani A, Gruber HJ, Pieber TR, Obermayer-Pietsch B. Vitamin D-associated polymorphisms are related to insulin resistance and vitamin D deficiency in polycystic ovary syndrome. Eur J Endocrinol. 2011;164:741–9.
6. Geisthövel F, Rabe T. The ESHRE/ASRM consensus on polycystic ovary syndrome (PCOS)--an extended critical analysis. Reprod Biomed Online. 2007;14(4):522–535.
7. Gupta T, Rawat M, Gupta N, Arora S. Study of Effect of Vitamin D Supplementation on the Clinical, Hormonal and Metabolic Profile of the PCOS Women. Journal of Obstetrics and Gynaecology of India. 2017;67(5):349–355.
8. Rosenfield RL, Ehrmann DA. The Pathogenesis of Polycystic Ovary Syndrome (PCOS): The Hypothesis of PCOS as Functional Ovarian Hyperandrogenism Revisited. Endocrine Reviews. 2016;37(5):467–520.
9. Skowronska P, Pastuszek E, Kuczynski W, Jaszczol M, Kuc P, Jakiel G, et al. The role of vitamin D in reproductive dysfunction in women - a systematic review. Annals of Agricultural and Environmental Medicine. 2016;23(4):671–676.
10. Wang W, Zhang J, Wang H, Wang X, Liu S. Vitamin D deficiency enhances insulin resistance by promoting inflammation in type 2 diabetes. International Journal of Clinical and Experimental Pathology. 2019;12(5):1859–1867.
11. Gokosmanoglu F, Onmez A, Ergenç H. The relationship between Vitamin D deficiency and polycystic ovary syndrome. African Health Sciences. 2020 Dec 16;20(4):1880-6.
12. Bindayel IA. Low vitamin D Level in Saudi women with polycystic ovary syndrome. Frontiers in Nutrition. 2021 Apr 12;8:611351.
13. Van Ballegooijen AJ, Kestenbaum B, Sachs MC, de Boer IH, Siscovick DS, Hoofnagle AN, et al. Association of 25-hydroxyvitamin D and parathyroid hormone with incident hypertension: MESA (Multi-Ethnic Study of Atherosclerosis) Journal of the American College of Cardiology. 2014;63(12):1214–1222.
14. He C, Lin Z, Robb SW, Ezeamama AE. Serum Vitamin D Levels and Polycystic Ovary syndrome: A Systematic Review and Meta-Analysis. Nutrients. 2015;7(6):4555–4577