Original Article

Role of vitamin D and leptin levels in PCOS in young women: A family medicine perspective

Merajul Haque Siddiqui[1], Aisha Beg[2], Ritvija Dixit[3], Shailza Verma[4], Gagan Gunjan[5], Sonu Kumari Agrawal[6]

[1]Department of Biochemistry, Saraswati Medical Institute, Hapur, Uttar Pradesh, India, [2]Department of Biochemistry, Sharda University, Greater Noida, Uttar Pradesh, India, [3]Department of Physiology, Santosh Medical College, Ghaziabad, Uttar Pradesh, [4]Department of Biochemistry, Nagaland Institute of Medical Sciences and Research, Kohima, Nagaland, [5]Department General Medicine, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, India, [6]Consultant Microbiologist, Max Hospital, Saket, India

Abstract

Introduction: Adolescent girls and young women of childbearing age are the main populations affected by endocrinopathy known as polycystic ovarian syndrome (PCOS). It is especially important to take into account whether clinical and biochemical signs of hyperandrogenism are present in female patients. In maintaining metabolic homeostasis, leptin is crucial. According to research, vitamin D deficiency may play a role in the pathophysiology of PCOS by contributing to insulin resistance, inflammation, dyslipidaemia, and obesity, which are all conditions linked to the syndrome. In this study, leptin and vitamin D3 levels will be measured in order to determine how each relates to the aetiology of PCOS. **Materials and Methods:** Hundred young women were allocated into two groups, 50 women with PCOS (diagnosed on the basis of revised Rotterdam criteria for PCOS), taken as a study group, and 50 healthy women with no PCOS as control group. Blood samples were collected and tested for hormonal parameters. **Results:** Between the two groups, there were no appreciable variations in demographic traits. Study groups were found to have considerably higher serum leptin levels than control groups. The study group's vitamin D3 levels were found to be lower than those of the control group. **Conclusion:** Patients with PCOS are a special population with distinctive hormonal profiles that differ from typical profiles in healthy populations. Comparing PCOS to healthy individuals, leptin levels were higher while vitamin D3 levels were lower. It is necessary to conduct more extensive research on the involvement of leptin and vitamin D3 in the aetiology of PCOS.

Keywords: Leptin, PCOS, vitamin D

Introduction

Young women of childbearing age and adolescent girls are the main populations affected by the endocrinopathy known as polycystic ovarian syndrome (PCOS).[1] The majority of reproductive disorders, including PCOS, afflict 15–18% of women in the reproductive age range.[2] It is characterised by hyperandrogenism, ovulatory dysfunction, and polycystic ovaries and is linked to type 2 diabetes risk, obesity/central adiposity, dyslipidaemia, and insulin resistance (IR).[3,4] Obesity, IR, and metabolic syndrome are frequent manifestations of PCOS, a complicated heterogeneous condition.[5,6] The appearance of polycystic ovaries on ultrasonography is a morphological marker.[7] The three main criteria for diagnosing PCOS patients on ultrasound are hyperandrogenism, persistent anovulation, and polycystic ovaries, according to the Rotterdam criteria and National Institute of Health standards.[8] Hyperandrogenaemia, particularly testosterone, is linked to polycystic ovaries

Address for correspondence: Dr. Shailza Verma, Associate Professor, Biochemistry, Nagaland Institute of Medical Sciences and Research, Kohima, Nagaland, India.
E-mail: drshailzaverma@yahoo.co.in

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and is either brought on by elevated levels of luteinizing hormone (LH), which is produced by the anterior pituitary gland or by hyperinsulinaemia.[9] Excessive androgens, which cause hirsutism and virilization, and hyperestrogenemia, which blocks follicle-stimulating hormone (FSH) through negative feedback, are produced by obese women's extra adipose tissue.[10]

It has been demonstrated that vitamin D functions in the uterus, ovary, vagina, and placenta. It has an impact on how the embryo implants, how the pregnancy progresses, and how the offspring fare. It must be acknowledged that there is conflicting evidence, primarily from observational research, that supports its significance to human reproductive health. Hypovitaminosis D's significance in the aetiology of metabolic diseases like IR and diabetes mellitus has been the subject of recent investigations. The investigation of hypovitaminosis D in PCOS patients led to findings that point to a role of vitamin D insufficiency in the pathophysiology of PCOS.[11] Patients with PCOS who are obese had lower serum levels of 25-hydroxyvitamin D than nonobese PCOS patients, according to tests done on their vitamin D levels. The development of IR and decreased glucose tolerance in PCOS patients has been proposed as the mechanism by which vitamin D deficiency causes PCOS. Studies have shown inconsistent results about whether IR in PCOS individuals is caused by vitamin D deficiency or is a result of fat.[12,13]

The hormone leptin, which is generated from adipocytes, measures how much body fat a person has. It also plays a role in IR and energy homeostasis.[14] Obesity, which is usually connected to PCOS, and circulating leptin levels are intimately interrelated. Leptin and its receptors are frequently connected to IR and hyperinsulinaemia. However, it is still unclear how leptin, gonadotropins, and insulin interact in PCOS.[15]

The aim of the present study was to assess Leptin and vitamin D3 levels in young women with PCOS and compared to normal controls.

Materials and Methods

The Department of Biochemistry at the tertiary level hospital conducted this retrospective study in cooperation with the Department of Physiology in the period from February 2020 to March 2021.

Study population

Hundred young women were allocated into two groups: 50 women with PCOS (diagnosed on the basis of revised Rotterdam criteria for PCOS) taken as a study group and 50 healthy women with no PCOS as a control group. The following were the inclusion requirements: (i) between the ages of 20 and 36; (ii) PCOS diagnosed in accordance with the Rotterdam criteria,[8] which states that PCOS is present if any two of the following three criteria are satisfied: (1) oligoovulation and/or anovulation, (2) excessive androgen activity (clinically or biochemically), and (3) polycystic ovaries (as determined by ultrasonography); (iii) a body mass index (BMI) of less than 25; and (iv) patients who are infertile due to either primary or secondary infertility. Women who were pregnant, nursing, or who had diabetes, liver disease, Cushing syndrome, who had any other serious medical conditions, as well as those who had taken glucocorticoids, antiandrogens, ovulation-inducing medications, antipsychotics, or hormone replacement therapy within the previous three months were excluded from this study.

Women in both groups had information about medical, personal, family, dietary, and menstrual history. BMI, waist to hip ratio, waist circumference, and blood pressure were recorded along with clinical and anthropometric data.

Sample for hormonal assay

Each subject's morning fasting venous blood sample of 10 ml was taken on the second through seventh day of the menstrual cycle or after progesterone withdrawal. Serum FSH, LH, prolactin, thyroid-stimulating hormone (TSH), oestrogen, prolactin, and total testosterone were measured. Further, vitamin D level and leptin level were measured in serum.

Statistical method

SPSS Software version 21 was used to analyse the data. The mean and standard deviation were used to express the results. Continuous variables were compared using the Student's *t*-test. $P < 0.05$ was considered as statistically significant.

Results

Demographic characteristics of the study and control groups

Participants in the study group had an average age of 20.4 ± 2.7 years, whereas those in the control group had an average age of 21.0 ± 2.5 years. This parameter's difference between the two groups was not statistically significant. The two groups did not differ statistically significantly in terms of body weight, height, or BMI, as shown in Table 1.

Comparison of hormonal parameters in the study and control group

Table 2 presents the hormonal characteristics of the enrolled patients. The study group had higher levels of FSH and LH, as compared to the control group. The levels of testosterone and oestrogen were also measured to be greater in the study group

Table 1: Demographic characteristics of study populations

Parameter	Study group Mean+SD	Control group Mean+SD	*P*
Age (years)	20.4±2.7	21.0±2.5	0.45
Height [cm]	154.1±4.8	155.2±4.7	0.47
Body weight [kg]	65.1±10.7	63.2±9.8	0.34
BMI [kg/m^2]	23.1±3.2	22.6±2.5	0.54

Data analysed by mean±SD

Table 2: Hormonal characteristics of study populations

Parameter	Study group	Control group	*P*
FSH (IU/L)	6.81±1.48	5.55±0.21	0.005
LH (IU/L)	11.78±0.38	5.87±0.49	0.001
Estradiol (pg/mL)	47.17±8.86	45.11±0.05	0.125
Testosterone (ng/mL)	1.03±0.02	0.41±0.02	0.001
Prolactin (ng/ml)	18.67±1.91	18.86±2.49	0.072
TSH (mIU/L)	3.21±1.29	2.67±0.88	0.167
Vitamin D3 (ng/mL)	10.28±0.79	9.1±0.11	0.001
Leptin (ng/mL)	16.97±0.89	15.86±0.12	0.021

Data analysed by mean±SD

compared to the control group. The levels of prolactin and TSH were comparable in both groups. Leptin concentrations were 16.97 ± 0.89 and 15.86 ± 0.12 ng/ml, respectively, in the study and control groups. In comparison to control groups, leptin levels were considerably higher in study patients ($P = 0.021$). In the PCOS and control groups, the levels of vitamin D3 were 10.28 ± 0.79 and 9.1 ± 0.11 ng/ml, respectively. $P = 0.0001$ revealed that the vitamin D3 levels in the PCOS group were lower than those in the control group.

Discussion

The most prevalent endocrine condition affecting women of reproductive age is PCOS. Although obesity and IR are thought to be inherent to PCOS, neither of these disorders is listed among the diagnostic criteria.[8] PCOS is a major contributor to infertility as well as other metabolic diseases. Obese patients with typical IR and hormonal problems make up the majority of PCOS patients.

In the present study, PCOS patients in young women were compared to patients without PCOS where demographic characteristics were not significant, as shown in Table 1. The study group showed typical hormonal profiles in terms of FSH, LH, and testosterone. TSH, oestradiol, and prolactin were the hormones that did not significantly rise in the study group as compared to the control group.

According to previously published studies, women with PCOS syndrome may have serum levels of vitamin D that are higher, lower, or not significantly different from healthy controls. This leads to the conclusion that vitamin D's contribution to PCOS aetiology is uncertain.[16] Vitamin D3 levels examined in this study discovered that the study group had lower levels of Vitamin D3 than the control group which was statistically significant. Similarly, a study by Ghadimi *et al.* observed that vitamin D levels in the PCOS group were considerably lower than in the healthy control group. However, research from British revealed no discernible variation in vitamin D levels between PCOS patients and those without it.[17] On the other hand, a study by Hahn *et al.* and Wehr *et al.* discovered that thin women have much greater levels of vitamin D3 than obese women. They came to the conclusion that obesity and IR, but not PCOS *per se*, are linked to low levels of vitamin D3 in PCOS women.[18] The controversy is still present, whether vitamin D3 levels rise or fall in PCOS women is still up for dispute. In their review study from 2012, Thomson *et al.* made the claim that the data currently available are insufficient to determine the causes of the variation in vitamin D status in women with PCOS.[19]

Leptin levels were shown to be considerably higher in the PCOS group compared to the non-PCOS group, indicating that it may have a role in the pathogenesis of PCOS. Previous research on serum leptin levels in PCOS women has produced mixed findings, with some studies finding noticeably greater levels of leptin in PCOS women than in non-PCOS women.[20] On the other hand, in some studies there was no distinction between women with PCOS and those without PCOS in terms of blood leptin levels.[21,22] Leptin levels were considerably greater in PCOS patients than in controls, according to a meta-analysis of all pertinent studies.

A study by Rizk *et al.* examined the levels of leptin and its receptors in PCOS and their relationships to obesity, IR, and androgens. They discovered that PCOS is linked to higher levels of leptin, indicating that leptin plays a part in the pathogenesis of PCOS. Additionally, they discovered that, as compared to lean non-PCOS individuals, leptin levels in thin PCOS patients are not significantly higher.[23] Similar to this, Olszanecka-Glinianowicz *et al.* found that PCOS patients had greater leptin levels than an age- and BMI-matched control group. Furthermore, they found that obese patients' leptin levels were higher than those of lean PCOS patients.[19] However, other investigations found no discernible difference in leptin levels between PCOS patients and those without it.[24,25] IR, inflammation, dyslipidaemia, and obesity—diseases linked to PCOS—have all been linked to vitamin D insufficiency. According to studies, women with PCOS had considerably lower serum 25 (OH) D levels than fertile controls. In order to optimise these parameters in PCOS therapy, family medicine practitioners can play a critical role in measuring vitamin D and leptin levels and integrating dietary and lifestyle therapies. For young women with PCOS, a comprehensive strategy that takes into account both hormonal and metabolic factors may lead to better overall health results.

From a family medicine standpoint, treating PCOS in young Indian women entails taking into account a number of variables, such as cultural quirks, leptin dynamics, and vitamin D status. Family doctors in India are vital to the adoption of a comprehensive strategy that incorporates dietary advice, lifestyle changes, and cultural awareness to control PCOS and enhance the general health and wellbeing of young women.

Conclusion

Patients with PCOS are a special population with distinctive hormonal profiles that differ from typical profiles in healthy populations. Comparing PCOS to healthy individuals, leptin levels were higher while vitamin D3 levels were lower. It is

necessary to conduct more extensive research on the involvement of leptin and vitamin D3 in the aetiology of PCOS.

Limitation of the study

The study's biggest drawback is the small sample size in both the study and control groups. This is a retrospective study and may not reflect the true distribution of the general population.

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Conflicts of interest

There are no conflicts of interest.

References

1. Mahde A, Shaker M, Al-Mushhadani Z. Study of omentin1 and other adipokines and hormones in PCOS patients. Oman Med J 2009;24:108–18.
2. March WA, Moore VM, Willson KJ, Phillips DIW, Norman RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod 2010;25:544–51.
3. Amsterdam ESHRE/ASRM-Sponsored 3rd PCOS Consensus Workshop Group. Consensus on women's health aspects of polycystic ovary syndrome (PCOS). Hum Reprod 2012;27:14-24.
4. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, *et al.* Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An androgen excess society guideline. J Clin Endocrinol Metab 2006;91:4237–45.
5. Lizneva, D, Suturina L, Walker W, Brakta S, Gavrilova-Jordan L, Azziz R. Criteria, prevalence, and phenotypes of polycystic ovarian syndrom. Fertil Steril 2016;106:6-15.
6. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet 2007;370:685–97.
7. Adams J, Franks S, Polson DW, Mason HD, Abdulwahid N, Tucker M, *et al.* Multifollicular ovaries: Clinical and endocrine features and response to pulsatile gonadotropin releasing hormone. Lancet 1985;2:1375–9.
8. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome. Fertil Steril 2004;81:19–25.
9. Barber TM, Dimitriadis GK, Andreou A, Franks S. Polycystic ovary syndrome: Insight into pathogenesis and a common association with insulin resistance. Clin Med (Lond) 2015;15(Suppl 6):s72-6.
10. Spritzer PM, Lecke SB, Satler F, Morsch DM. Adipose tissue dysfunction, adipokines, and low-grade chronic inflammation in polycystic ovary syndrome. Reproduction 2015;149:R219-27.
11. Lathief S, Pal L. Emerging concepts: Role of Vitamin D deficiency in the pathogenesis of PCOS. In: Polycystic Ovary Syndrome. New York, NY: Springer; 2014. p. 317-31.
12. Grundmann M, von Versen-Höynck F. Vitamin D – Roles in women's reproductive health? Reprod Biol Endocrinol 2011;9:146.
13. Butts S, Seifer D, Senapati S, Koelper NC, Legro RS, Diamond MP. Vitamin D deficiency is associated with poor reproductive outcomes in PCOS but not unexplained infertility. Fertil Steril 2017;108:e69-70.
14. 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.
15. Stovall DW, Bailey AP, Pastore LM. Assessment of insulin resistance and impaired glucose tolerance in lean women with polycystic ovary syndrome. J Womens Health (Larchmt) 2011;20:37-43.
16. Legro RS, Arslanian SA, Ehrmann DA, Hoeger KM, Murad MH, Pasquali R, *et al.* Diagnosis and treatment of polycystic ovary syndrome: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2013;98:4565–92.
17. Ghadimi R, Esmaeilzadeh S, Firoozpour M, Ahmadi A. Does vitamin D status correlate with clinical and biochemical features of polycystic ovary syndrome in high school girls? Caspian J Intern Med 2014;5:202-8.
18. Hahn S, Haselhorst U, Tan S, Quadbeck B, Schmidt M, Roesler S, *et al.* Low serum 25-hydroxyvitamin D concentrations are associated with insulin resistance and obesity in women with polycystic ovary syndrome. Exp. Clin. Endocrinol. Diabetes 2006;114:577-83.
19. Wehr E, Pilz S, Schweighofer N, Giuliani A, Kopera D, Pieber TR, *et al.* Association of hypovitaminosis D with metabolic disturbances in polycystic ovary syndrome. Eur J Endocrinol 2009;161:575-82. doi: 10.1530/EJE-09-0432.
20. Thomson RL, Spedding S, Buckley JD. Vitamin D in the aetiology and management of polycystic ovary syndrome. Clinical Endocrinol 2012;77:343-50.
21. Pusalkar M, Meherji P, Gokral J, Savardekar L, Chinnaraj S, Maitra A. Obesity and polycystic ovary syndrome: Association with androgens, leptin and its genotypes. Gynecol Endocrinol 2010;26:874–82.
22. Telli MH, Yildirim M, Noyan V. Serum leptin levels in patients with polycystic ovary syndrome. Fertil Steril 2002;77:932–5.
23. Pirwany IR, Fleming R, Sattar N, Greer IA, Wallace AM. Circulating leptin concentrations and ovarian function in polycystic ovary syndrome. Eur J Endocrinol 2001;145:289–94.
24. Rizk NM, Sharif E. Leptin as well as free leptin receptor is associated with polycystic ovary syndrome in young women. Int J Endocrinol 2015;2015:927805.
25. Hofman-Hutna J, Hutny M, Matusik E, Olszanecka-Glinianowicz M, Matusik P. Vitamin D deficiency in obese children is associated with some metabolic syndrome components, but not with metabolic syndrome itself. Metabolites 2023;13:914.