JOURNAL OF DYNAMICS AND CONTROL

VOLUME 8 ISSUE 8

COMPARATIVE STUDY ON THE ASSESSMENT OF LIPID PROFILE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND HEALTHY CONTROLS

Ramadoss Priyadarshini[1], Mamta Singh[1], Praveen Kumar[1], Ben Ashok[1,2]

[1]Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai – 600116, India
[2]NURA - Ai Health Screening Center, Bengaluru - 560038, India

COMPARATIVE STUDY ON THE ASSESSMENT OF LIPID PROFILE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME AND HEALTHY CONTROLS

Ramadoss Priyadarshini[1], Mamta Singh[1], Praveen Kumar[1], Ben Ashok[1,2]
[1]Sri Ramachandra Institute of Higher Education and Research, Porur, Chennai – 600116, India
[2]NURA - Ai Health Screening Center, Bengaluru - 560038, India.

ABSTRACT: *PCOS, or Polycystic Ovary Syndrome, is a relatively common endocrinological disorder in women of childbearing age. It is a disease entity characterized by irregular menstrual cycles, from amenorrhea to periods that occur at very prolonged intervals. Besides menstrual irregularity, PCOS is associated with clinical and biochemical hyperandrogenism, which means an overabundance of the male sex hormone, leading to symptoms like hirsutism, acne, and oily skin. Another hallmark of PCOS is the presence of polycystic ovaries, in which a lot of small cysts can be seen on the ovary by using ultrasound. This pattern of symptoms makes PCOS a heterogeneous condition that has far-reaching impacts on the health of a woman. In the present study, the lipid profile of 40 women with PCOS was compared to that of 40 healthy controls at Sri Ramachandra Institute of Higher Education and Research. We found that the PCOS group had significantly higher levels of triglycerides, total cholesterol, LDL, and Chol/HDL ratio and lower HDLs. This study has reiterated the dyslipidemia noted by previous studies as the major risk factor of CVD in PCOS subjects. Routine lipid screening, along with lifestyle changes, may help in reducing cardiovascular risks associated with PCOS. This study established that the concentration of triglycerides, total cholesterol, LDL, and Chol/HDL ratio was significantly higher, where the HDL concentration was lower in women with PCOS, showing an increased risk for CVD. It therefore points to a need for regular screenings of lipid profiles and lifestyle modifications in the management of dyslipidemia for reducing long-term risks to health.*

KEYWORDS: *PCOS, or Polycystic Ovary Syndrome, dyslipidemia, CVD, Chol/HDL*

1. INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a widespread illness that affects many elements of a woman's general health and has long-term repercussions that go beyond her reproductive age [1,2)]. This is an imbalance of female sex hormones, including the follicle-stimulating hormone, progesterone, luteinizing hormone, and estrogen. Infertility, irregular menstruation, numerous ovarian cysts, and other health issues could result from this [3]. The prevalence of this heterogeneous endocrine disorder is so common that 1 in almost 15 premenopausal women

is affected around the world [4,5,6] Nonetheless, 8.2% to 22.5% of women in India have been diagnosed with PCOS [7].

It is estimated that up to 70% of PCOS is associated with a metabolic anomaly in women, one whose hallmark is dyslipidemia [8]. Women with PCOS are expected to have a seven-fold increased risk of myocardial infarction and a higher prevalence of atherosclerosis and cardiovascular disorders [9]. The exact causes are yet unknown, but they might be associated with high levels of testosterone; often, the syndrome is combined with obesity [10].

More than 40% of women with PCOS in the U.S. population have obesity, although prevalence varies significantly among ethnically diverse populations and geographic regions. Visceral or central fat accumulation is often excessive in women presenting with PCOS. Obese women with PCOS had evidence of a greater degree of reproductive abnormality, with increased hirsutism, infertility, and irregularity of the menstrual cycle. They also had higher free testosterone levels with lower levels of SHBG. Moreover, the miscarriage rate is higher and the conception rate after ovulation induction is poor. Weight reduction may help improve reproductive as well as metabolic obesity-related complications like diabetes and dyslipidemia Central obesity results from a reduction in lipoprotein lipase (LPL) activity in belly fat cells caused by elevated testosterone levels [11]. In the United States, almost 40% of women with PCOS are obese. Ethnicity and geography are two different influences. It is common for visceral or core fat to build. Obese women with PCOS have a more severe reproductive phenotype, which includes a higher occurrence of irregular menstruation, hirsutism, and infertility. These women also get inferior results from ovulation induction and a higher chance of miscarriage. Reproductive problems and the metabolic consequences of obesity, such as dyslipidemia and diabetes, can be lessened by losing weight.

Mixed hyperlipidemia is common in women with PCOS, with low levels of HDL and increased triglycerides, VLDL, and LDL. The LDL particles are often small and dense and have enhanced atherogenic potential. These lipid abnormalities persist after adjustment for degree of obesity. Increased triglyceride levels correlate with increased androgen levels but not with other lipid disorders. Women with both irregular menstruation and hirsutism tend to have the lowest levels of HDL and the highest triglyceride levels [12]. In women with PCOS, hyperlipidemia is often associated with other cardiovascular risk factors such as hypertension, endothelial dysfunction, and inflammation. In obese women with PCOS, higher systolic blood pressure has been reported compared with weight-matched controls. In women with oligomenorrhea and hirsutism, both systolic and diastolic blood pressure values are increased. In addition, in the absence of obesity, increased C-reactive protein and endothelin-1 levels in women with PCOS are indicative of endothelial dysfunction and inflammation [13]. This, therefore means that women suffering from PCOS are prone to such cardiovascular complications that arise due to hypertension and inflammation, both of which are pegged on obesity.

In this framework, the present study is undertaken to assess the lipid profile in women with PCOS. The study aims to measure the serum lipid profile levels in patients with PCOS (cases) and compare them with normal healthy subjects (controls).

2. METHODS

The study was conducted in the Department of Biochemistry in collaboration with the Department of Obstetrics and Gynecology, Sri Ramachandra Institute of Higher Education and Research, Chennai (India). In this prospective case-control study, we enrolled 40 patients with PCOS cases and compared them with 40 healthy controls. The duration of the study was between June 2023 and May 2024. The study was conducted after obtaining ethical clearance from the Institutional Ethics Committee, Sri Ramachandra Medical College & Research Institute and written informed consent was given by all patients before enrolment into the study.

2.1 Inclusion and Exclusion criteria

The cases were selected based on the criteria set by ESHRE and ASRM from the Rotterdam PCOS Consensus Workshop Group, 2004. Diagnosis of PCOS was accepted if at least two of the following three criteria were fulfilled: the presence of polycystic appearance of ovaries on ultrasound, defined as the presence of twelve or more follicles measuring 2-9 mm in diameter and an ovarian volume >10 cm^3; anovulation or oligo-ovulation; biochemical or clinical signs of hyperandrogenism. The controls taken were normal, healthy females of childbearing age. The exclusion criteria for cases included a history of taking oral contraceptive agents, anticoagulants, anti-platelet agents, insulin sensitizers, anti-androgens, anti-lipidemic drugs, anti-hypertensive drugs, and glucocorticoids. The exclusion criteria for controls included pregnancy, hypothyroidism, Cushing's syndrome, non-classical congenital adrenal hyperplasia, current or recent (in the last three months) use of oral contraceptive or other hormonal drugs and anti-diabetic or anti-obesity drugs, and autoimmune disorders.

2.2 Method of data and sample collection

Serum samples were obtained from the study subjects fulfilling the required criteria for PCOS who were visiting the Sri Ramachandra Medical Hospital, after getting informed consent for estimation of serum lipid profile. Procedures for routine blood draws were followed. The serum samples were aliquoted in 2ml polypropylene tubes after centrifugation and stored at -80ºC till analysis. In the Beckman Coulter AU680 Automated Clinical Chemistry analyzer, Total Cholesterol was measured by Enzymatic CHOD-POD (Cholesterol oxidase – peroxidase) endpoint method. Triglycerides were measured by Enzymatic GPO – POD (glycerol phosphate oxidase – peroxidase) endpoint method. HDL& LDL levels were assessed by colorimetric assay techniques. Cho/HDL ratio was calculated.

2.3 Statistical analysis

Statistical analysis was done using SPSS Version 23.0 software. Results The results have been presented in mean ± S.D. Student t-test was performed to find out the mean differences between cases and controls. A p-value of <0.05 was statistically significant.

3. RESULTS

A total of 80 populations were considered for this study; the age of most of the subjects ranged from 20 to 32 years. According to Table 1, the mean±SD values of SBP, DBP, BMI, and WHR in the case group were significantly higher, that is, 124.7±4.3, 82.7±2.8, 30.7±3.2, and 0.89±0.06, respectively, compared to the control group, in which the mean±SD values of SBP, DBP, BMI, and WHR were 117.1±3.7, 76.1±4.0, 24.3±3.2, and 0.81±0.03, respectively. The differences in all these parameters were highly statistically significant with a p-value of <0.05. As in Table 2, mean±SD triglyceride levels were higher in the case group, at 110.1±54.7, when compared to the control group at 88.5±37.2. Similarly, the Cholesterol/HDL ratio was higher in cases at 4.3±0.8 compared to controls at 3.7±0.7, both being statistically significant with p<0.05. However, the mean±SD HDL levels were lower in the case group 42.5±9.3 than the control group 47.9±8.1, and this difference was statistically significant at p<0.05. The mean±SD total cholesterol levels were 178.4±38.6 and 176.3±35.9 in the case and control groups respectively, while that of LDL were 116.5±30.1 in cases and 111.9±27.1 in controls.

4. DISCUSSION

Obesity is one of the leading causes of PCOS and is associated with impairment of lipid profile. Few reports have shown that dyslipidemia and insulin resistance occur in PCOS subjects. However, the cause of PCOS remains still obscure. We, therefore attempted to assess the lipid profile level in both the case and control groups and, in mind, their abnormalities contribute to

Table 1: Demographic characteristics of study groups

Variables	***PCOS Case (n=40)***	***Control (n=40)***	***p-value***
Age (years)	*26.8±6.3*	*24.6±4.4*	*0.0667*
SBP(mmHg)	*124.7±4.3*	*117.1±3.7*	*<0.0001***
DBP(mmHg)	*82.7±2.8*	*76.1±4.0*	*<0.0001***
BMI (Kg/m^2)	*30.7±3.2*	*24.3±3.2*	*<0.0001***
WHR	*0.89±0.06*	*0.81±0.03*	*<0.0001***

Table 2: Biochemical characteristics (Lipid Profile) of study groups

Variables	***PCOS Case (n=40)***	***Control (n=40)***	***p-value***
TC (mg/dl)	*178.4±38.6*	*176.3±35.9*	*0.8087*
TG (mg/dl)	*110.1±54.7*	*88.5±37.2*	*0.0423**
LDL (mg/dl)	*116.5±30.1*	*111.9±27.1*	*0.4815*
HDL (mg/dl)	*42.5±9.3*	*47.9±8.1*	*0.0075**
Cho/HDL ratio	*4.3±0.8*	*3.7±0.7*	*0.0023**

the development of PCOS. In our results, the mean age in the case group was 26.8±6.3 years, while that in the control group was 24.6±4.4 years; however, the difference between these two age groups was not statistically significant, p=0.0667. This observation is consistent with the study by Bashir et al., who found the maximum prevalence of PCOS to be 50% in the age group of 15-24 years [14]. The trend may be due to the reason that PCOS is commonly diagnosed during the early reproductive years, particularly in those women who are suffering from oligomenorrhea or have primary infertility and hence approach early medical assistance.

We also observed that BMI and WHR were found to be quite high among the case group at 30.7±3.2 and 0.89±0.06, respectively, while it was recorded as low among the control group at 24.3±3.2 and 0.81±0.03, respectively. These differences were found to be statistically significant with a p-value of <0. In addition to that, Yadav et al. similarly reported increased anthropometric measures of height, weight, BMI, and WHR in women with PCOS compared to the non-PCOS counterpart [15].

The current study also demonstrated that systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly high in the case group, with mean values of SBP (124.7±4.3) and DBP (82.7±2.8), in comparison to the control one, with mean values of SBP (117.1±3.7) and DBP (76.1±4.0), which is also highly significant ($p<0.05$). These results are identical to Wu et al.'s observations, where more cases of hypertension were reported in subjects who had PCOS compared with controls [16]. The higher prevalence of hypertension in PCOS has been associated with a number of variables, including obesity, insulin resistance (IR), hyperandrogenism, and cardiac autonomic dysfunction. Because PCOS is hyperandrogenic, there is an increased risk of cardiovascular disorders, which can lead to endothelial dysfunction and high blood pressure.

In our study, we observed that women with PCOS exhibited dyslipidemic profiles characterized by elevated levels of total cholesterol, triglycerides, LDL, and the Chol/HDL ratio.

Specifically, the mean±SD levels of total cholesterol (178.4±38.6), triglycerides (110.1±54.7), LDL (116.5±30.1), and the Chol/HDL ratio (4.3±0.8) were higher in the PCOS group compared to the control group, where the corresponding levels were total cholesterol (176.3±35.9), triglycerides (88.5±37.2), LDL (111.9±27.1), and the Chol/HDL ratio (3.7±0.7). The differences in triglycerides and the Chol/HDL ratio were statistically significant ($p<0.05$). Conversely, the level of HDL was significantly lower in the PCOS group (42.5±9.3) compared to the controls (47.9±8.1), with this difference also being statistically significant ($p<0.05$). The findings of our study are consistent with those reported by Manjunatha et al., who observed a significant increase in serum triglycerides, cholesterol, LDL, and VLDL levels, along with a decrease in serum HDL levels among PCOS subjects. Their study highlighted the altered serum lipid profile in PCOS and concluded that dyslipidemia is a key risk factor associated with the condition [17]. Reduced levels of HDL are frequently accompanied with elevated levels of triglycerides, LDL, and Cholesterol-HDL ratio. Moreover, the majority of the LDL particles are dense, tiny particles, which have a higher propensity for atherogenicity. More anomalies are seen even when the degree of obesity is taken into account. High triglyceride levels are associated with androgen levels, but not with other lipid disorders. Lower HDL and higher triglyceride values are found in women who have both irregular menstruation and hirsutism [18]. Other cardiovascular risk factors, such as hypertension, endothelial dysfunction, and inflammation, are more common in conjunction with hyperlipidemia. Blood pressure in women with oligomenorrhea and hirsutism is higher at the systolic and diastolic levels [19].

There are several contributing factors to dyslipidaemia in PCOS. Patients with PCOS often have insulin resistance, which can lead to dyslipidaemia. A key function for insulin resistance seems to be played by lipolysis stimulation and changes in the expression of hepatic and lipoprotein lipases. Increased HDL particle catabolism and LDL particle production are also related to insulin resistance. A changed lipid profile may potentially be a result of

hyperandrogenism in addition to insulin resistance [20]. An increased level of hepatic lipase activity, which is involved in the breakdown of HDL particles, has been linked to hyperandrogenism. Adipocytes were able to release free fatty acids into the bloodstream and undergo enhanced lipolysis brought on by catecholamines due to hyperinsulinemia and hyperandrogenaemia. Through the reverse cholesterol transfer mechanism, hypertriglyceridemia results in decreased HDL cholesterol and increased LDL cholesterol levels reduced fatty acid oxidation, slower clearance, or enhanced lipogenesis could possibly be the cause of the rise in triglycerides [21]. In PCOS women, elevated triglyceride levels may play a role in their obesity. Increased risk of cardiovascular illnesses is attributed to altered lipid profile, obesity, and insulin resistance. To avoid issues linked to cardiovascular disorders, PCOS patients must be routinely checked and monitored [22].

One of the study's drawbacks is the limited sample size. To fully understand the significance of lipid profiles in the prevention and treatment of women with polycystic ovarian syndrome, more research with a larger sample size is required.

6. CONCLUSION

The current study aimed to determine the lipid profile levels in both normal healthy controls and those with polycystic ovarian syndrome (PCOS). According to this study, women with PCOS exhibited an atherogenic lipoprotein profile, which was defined by elevated triglycerides, cholesterol, and LDL and decreased HDL. These findings may be risk factors for the later development of cardiovascular complications. Therefore, to effectively prevent cardiovascular risk, it is advised that all women with PCOS undergo routine screening for dyslipidemia and implement the required dietary restrictions and lifestyle modifications as soon as possible.

ACKNOWLEDGEMENT

The authors thank the department of biochemistry and department of obstetrics and gynaecology, SRMC, India for providing the support in conducting the study. We are thankful to the Sri Ramachandra Laboratory Services for the support extended in doing the biochemical analysis. We extent our gratitude to SRIHER Ethics committe for accepting the research proposal (Reference ID: CSP/23/MAY/128/421).

REFERENCES

1. Puurunen J, Piltonen T, Morin-Papunen L, et al. Unfavorable Hormonal, Metabolic, and Inflammatory Alterations Persist after Menopause in Women with PCOS. The Journal of Clinical Endocrinology & Metabolism. 2011 Jun;96(6):1827–34.
2. Shaw LJ, Bairey Merz CN, Azziz R, et al. Withdrawn: Postmenopausal Women with a History of Irregular Menses and Elevated Androgen Measurements at High Risk for Worsening Cardiovascular Event-Free Survival: Results from the National Institutes of Health—National Heart, Lung, and Blood Institute Sponsored Women's Ischemia Syndrome Evaluation. The Journal of Clinical Endocrinology & Metabolism. 2008 Apr;93(4):1276–84.
3. Kanchan Choudhary, Ranjan Singh, Ajay Garg, Nitesh Verma, Anjali Purohit, Deepika Deora. AN UPDATED OVERVIEW OF POLYCYSTIC OVARY SYNDROME. Innovare Journal of Medical Sciences. 2019 Jun 10;7(3):1–13.
4. Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. Nature Reviews Endocrinology. 2018 Mar 23;14(5):270–84.
5. Azziz R. Polycystic Ovary Syndrome. Obstetrics & Gynecology. 2018 Aug;132(2):321–36.

6. Witchel SF, Oberfield SE, Peña AS. Polycystic Ovary Syndrome: Pathophysiology, Presentation, and Treatment With Emphasis on Adolescent Girls. Journal of the Endocrine Society. 2019 Jun 14;3(8):1545-73.
7. Mohan V, S MT, Ranjani H, Kamalesh R, Ram U, M AR. Prevalence of polycystic ovarian syndrome among adolescents and young women in India - Eprints@MDRF. Mdrf-eprintsin. 2021;12(3).
8. Legro RS, Kunselman AR, Dunaif A. Prevalence and predictors of dyslipidemia in women with polycystic ovary syndrome. The American Journal of Medicine. 2001 Dec;111(8):607–13.
9. Kumariya S, Ubba V, Jha RK, Gayen JR. Autophagy in ovary and polycystic ovary syndrome: role, dispute and future perspective. Autophagy. 2021 Jun 23;17(10):2706–33.
10. Elder SJ, Lichtenstein AH, Pittas AG, Roberts SB, Fuss PJ, Greenberg AS, et al. Genetic and environmental influences on factors associated with cardiovascular disease and the metabolic syndrome. Journal of Lipid Research. 2009 Sep;50(9):1917–26.
11. Iuhas CI, Costin N, Mihu D. Lipid Parameters in Patients with Polycystic Ovary Syndrome. Applied Medical Informatics. 2012 Nov 24;31(4):27–32.
12. Kousta E, Tolis G, Franks S. Polycystic ovary syndrome. Revised diagnostic criteria and long-term health consequences. HORMONES. 2005 Jul 15;4(3):133–47.
13. Orio F, Palomba S, Cascella T, De Simone B, Di Biase S, Russo T, et al. Early Impairment of Endothelial Structure and Function in Young Normal-Weight Wome with Polycystic Ovary Syndrome. The Journal of Clinical Endocrinology & Metabolism. 2004 Sep;89(9):4588–93.
14. Talbott EO, Guzick DS, Sutton-Tyrrell K, McHugh-Pemu KP, Zborowski JV, Remsberg KE, et al. Evidence for Association Between Polycystic Ovary Syndrome and

Premature Carotid Atherosclerosis in Middle-Aged Women. Arteriosclerosis, Thrombosis, and Vascular Biology. 2000 Nov;20(11):2414–21.

15. Bashir R, Sideeq K. Prevalence of polycystic ovarian syndrome in women of different age groups in Hazratbal area of Srinagar by ultrasonographic evaluation-hospital data based study. Int J App Res; 2020;6(6):292-5.
16. Yadav S, Tarware R. Waist hip ratio: an anatomical predictive marker of risk of PCOS. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2019 Mar 26;8(4):1630–2.
17. Wu CH, Chiu LT, Chang YJ, Lee CI, Lee MS, Lee TH, et al. Hypertension Risk in Young Women With Polycystic Ovary Syndrome: A Nationwide Population-Based Cohort Study. Frontiers in Medicine. 2020 Sep 23;7(574):1–9.
18. Lambrinoudaki I, Christodoulakos G, Rizos D, Economou E, Argeitis J, Vlachou S, et al. Endogenous sex hormones and risk factors for atherosclerosis in healthy Greek postmenopausal women. European Journal of Endocrinology. 2006 Jun;154(6):907–16.
19. Kousta E, Tolis G, Franks S. Polycystic ovary syndrome. Revised diagnostic criteria and long-term health consequences. HORMONES. 2005 Jul 15;4(3):133–47.
20. Orio F, Palomba S, Cascella T, De Simone B, Di Biase S, Russo T, et al. Early Impairment of Endothelial Structure and Function in Young Normal-Weight Women with Polycystic Ovary Syndrome. The Journal of Clinical Endocrinology & Metabolism. 2004 Sep;89(9):4588–93.
21. Buccola JM, Reynolds EE. Polycystic ovary syndrome: a review for primary providers. Primary Care: Clinics in Office Practice. 2003 Dec;30(4):697–710.
22. Cinar N, Kizilarslanoglu MC, Harmanci A, Aksoy DY, Bozdag G, Demir B, et al. Depression, anxiety and cardiometabolic risk in polycystic ovary syndrome. Human Reproduction. 2011 Oct 7;26(12):3339- 45.