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A Study on the Influence of Long-Term Complications of PCOS (Poly Cystic Ovarian Syndrome) in Overweight Patients in Comparison with Short-Term PCOS Patients in Tamil Nadu, India

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Abstract: Poly Cystic Ovarian Syndrome (PCOS) is a female endocrine disorder which affects around 10 - 20% of the reproductive women in India when diagnosed using Rotterdam criteria. The common symptoms include weight gain, hirsutism, and irregular periods. As hormonal imbalance and increased weight contribute to cardiovascular diseases, this study aims to analyse the long-term complications of PCOS in overweight patients in comparison with short-term PCOS patients with similar BMI. A questionnaire was circulated to women volunteers, with the reproductive age group between 19 and 43 years old. From this, 30 early PCOS patients aged between (19-22) years with 3 years of PCOS and 30 prolonged PCOS patients aged between (40-43) years with 15 years of PCOS were selected, and blood samples were collected for the lipid profile and early cardiac marker analysis. From the results, it has been observed that the levels of total cholesterol ($p<0.001$), LDL ($p<0.001$), triglycerides ($p<0.5$) and VLDL ($p<0.5$) showed significantly higher and HDL ($p<0.001$) showed significantly lower level in prolonged PCOS patients when compared to the early PCOS patients. In the cardiac markers, the levels of Lipoprotein A ($p<0.001$), Apolipo A1 ($p<0.001$), Apolipo B ($p<0.001$), Apo b/apo A1 ($p<0.001$), Total cholesterol/HDL ($p<0.001$), LDL/HDL ($p<0.001$), LDL/APO B ($p<0.5$), Homocysteine ($p<0.001$) and hsCRP ($p<0.001$) showed significantly higher values in prolonged PCOS patients when compared to the early PCOS patients. Hence, this study recommends that PCOS patients manage it effectively by controlling weight to combat the consequences of the disorder.

Keywords: PCOS, Total cholesterol, hs-CRP, Homocysteine, Rotterdam criteria, Cardiovascular diseases, Lipid profile, Cardiac marker

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Introduction

Polycystic ovarian syndrome is a prevalent endocrine condition affecting women of reproductive age. It is a multifaceted ailment characterized by an extensive array of symptoms,

such as irregular menstrual cycles, alopecia, hirsutism (excessive facial hair growth), acne, and weight gain. Rotterdam criteria need at least two of the following three features: polycystic ovaries on ultrasonography, evidence of increased androgen production, and irregular or non-existent menstrual periods. The pathophysiology of PCOS involves insulin resistance and hyper-insulinemia, highlighting the connection between metabolic disruptions and reproductive failure. The risk factors include obesity, insulin resistance, or the body's inability to use insulin efficiently, which is a common condition among women with PCOS. Increased risk of type 2 diabetes, cardio-vascular disease, and infertility are among the long-term health consequences of uncontrolled PCOS (Mather *et al*., 2000).

Lipid metabolism changes are a significant component of metabolic dysfunction in individuals who have PCOS, which raises the risk of cardiovascular disease. Altered androgenism has been demonstrated to affect lipolysis and lipogenesis, which affects lipid metabolism and may be a factor in PCOS-related dyslipidaemia (Kim and Choi, 2013). Dyslipidaemia in PCOS may be caused by several processes, including insulin resistance, causing adipose tissue to undergo more lipolysis, raising free fatty acid levels and increasing triglyceride biosynthesis in the liver and blood. Numerous risk factors that may have an impact on the development of cardiovascular issues with hormonal abnormality are linked to PCOS. Consequently, the risk of heart disease may rise due to these diseases. Weight gain and obesity are frequently linked to PCOS, which increases the risk of heart disease and raises blood pressure and cholesterol levels. Elevated androgens, or male hormones, and decreased estrogen levels are among the hormones that may impact lipid metabolism and increase the chance of cardio-vascular disease and atherosclerosis, or the hardening of the arteries. Inflammation markers are frequently seen in greater concentrations in women with PCOS, and prolonged inflammation raises the risk of cardiovascular issues and damages blood vessels (Zhang *et al.*, 2012). This study aims to analyse the long-term complications of PCOS in overweight patients in comparison with short-term PCOS patients with similar BMI.

Materials and Methods

A questionnaire was circulated to women volunteers in the age group between 19-43 years with written consent (Ethical Clearance-ARCIEC/others/001/2001), and the overweight PCOS patients were selected (Christ and Cedars, 2023). Based on the questionnaire, the patients (with PCOS- duration 3 years) aged between 19-23 years and prolonged PCOS patients (with PCOS-duration 15 years) aged between 38-43 years with similar BMI (25.0 to <30) were selected for the analysis. The venipuncture method collected 5 ml of venous blood during their follicular phase, and the levels of TG, HDL, VLDL, Total Cholesterol, LDL/HDL ratio, LDL/APO B ratio, Lipoprotein A, Apolipo A1, Apolipo B, Apo b / apo A1, hsCRP and homocysteine were carried by standard proven methods.

Statistical Analysis

The values are expressed as Mean ± SD, and the significance level was determined between early PCOS and prolonged PCOS by the Student t-test using Microsoft Excel.

Results and Discussion

The levels of total cholesterol, LDL, and HDL in early PCOS patients were found to be 135.4 ± 4.5, 83.1 ± 6.9, and 51.4± 9.25, and in prolonged PCOS patients, the levels were 195 ± 16.38, 117± 17.74, and 35.9 ± 6.4, respectively (Table 1).

The levels of LDL/APO B, VLDL, and Triglycerides in early PCOS patients were found to be 1.17 ± 0.2, 31.1 ± 1.7, and 155 ± 8.5 and in prolonged PCOS patients, the levels were 1.20 ± 0.2,33.04 ± 4.3, and 165 ± 20.6, respectively (Tables 1, 2).

The levels of lipoprotein, apolipo A1, apolipo B, apo B/apo A1, Total cholesterol/HDL, LDL/HDL, homocysteine and hsCRP in early PCOS patients were found to be 27 ± 2.1, 101.7 ± 5.9 , 71.9 ± 8.6 , 0.7 ± 0.1, 2.73 ± 0.6, 1.67 ± 0.4, 16.58 ± 2.5, and

Table 1: Lipid profile parameters of early and prolonged PCOS patients

S. No.	Parameters	Early PCOS patients	Prolonged PCOS patients
1.	Total cholesterol	135.4±4.5	195 ± 16.38***
2.	Triglycerides	155 ± 8.5	165 ± 20.6*
3.	LDL	83.1 ± 6.9	117± 17.74***
4.	HDL	51.4± 9.25	35.9 ± 6.4***
5.	VLDL	31.1 ± 1.7	33.04 ± 4.3*

n=30; ns -non significant; *p<0.5; **p<0.01; ***p<0.001

Table 2: Cardiac risk parameters of early and prolonged PCOS patients

S. No.	Parameters	Early PCOS Patients	Prolonged PCOS Patients
1.	Lipoprotein A	27 ± 2.1	36.1 ± 4.1***
2.	Apolipo A1	101.7 ± 5.9	114 ± 9.3***
3.	Apolipo B	71.9 ± 8.6	98.4± 10.1***
4.	Apo b / apo A1	0.7 ± 0.1	0.8 ± 0.07***
5.	Total cholesterol / HDL	2.73 ± 0.6	5.57 ± 0.9***
6.	LDL/HDL	1.67 ± 0.4	3.35 ± 0.7***
7.	LDL/ APO B	1.17 ± 0.2	1.20 ± 0.2*
8.	Homocysteine	16.58 ± 2.5	28.16 ± 5***
9.	hsCRP	3.78 ± 0.6	6.8 ± 1.9***

n=30; ns -non significant; *p<0.5; **p<0.01; ***p<0.001

3.78 ± 0.6 and in prolonged PCOS patients the levels were 36.1 ± 4.1,114 ± 9.3, 98.4 ± 10.1, 0.8 ± 0.07 5.57 ± 0.9, 3.35 ± 0.7, 28.16 ± 5, 6.8 ± 1.9, respectively (Table 2).

The results of our lipid profile analysis indicate the association between prolonged PCOS and dyslipidaemia, following the reports of Bozdag *et al*. (2016), who mentioned that women with PCOS were frequently reported to have lipid abnormalities, including reduced levels of high-density lipoprotein.Women with PCOS have higher LDL-C levels, but more recently, it has also been noted that these women have different LDL quality levels, such as size, density, and atherogenicitically different LDL subclasses. Large buoyant LDL particles are not as atherogenic as small dense ones and are closely linked to coronary artery disease. The proportion of atherogenic small dense LDL in women with PCOS is higher, and their mean LDL particle size is lower, and these changes may be linked to a higher risk of cardiovascular disease (Wild *et al*., 2011). The degree of the significant risk variables, including LDL-C, HDL-C, blood pressure, triglycerides, and length of exposure, most likely influence the development of atherosclerosis.

The current study's PCOS women seem to have a much higher risk of coronary heart disease and cholesterol problems at a younger age. The slower rate of growth in LDL-C with age in PCOS cases may be explained by the lack of change in ovarian function if the increase in LDL-C was primarily related to reduced ambient estrogen levels with time. Most likely, the LDL-C and total cholesterol with age among PCOS cases account for the diminishing difference (Rashad *et al*., 2019).

There is growing evidence that changes in lipoprotein patterns considerably raise cardio-

vascular risk in addition to plasma lipids (Jeanes and Reeves, 2017). Dyslipidemia in PCOS is due to insulin resistance, a key factor in PCOS. HDL-cholesterol levels are reduced, but concentrations are often within the normal range and considerably higher when compared to controls. Compared to women with anovulatory PCOS, ovulatory PCOS women have lower levels of total cholesterol, triglycerides, and LDL cholesterol and greater levels of HDL cholesterol; also, they have higher concentrations of Lp(a) and decreased lipoprotein levels. Hepatic lipase typically forms small, dense LDL particles from lipoprotein precursors enriched in triglycerides, and this process may be primarily caused by elevated triglyceride levels.

Several interconnected pathogenic modalities, such as obesity, hyperinsulinemia, oxidative stress, anovulation, and hyperandrogenaemia, are associated with dyslipidaemia in PCOS. A low amount of Apo-AI can cause hyperandrogenism in PCOS patients. Apo-AI is involved in the synthesis of androgen. Both inflammation and oxidative stress have high levels of ROS, and inflammatory variables are connected to HDL-C and HDL antioxidant/anti-inflammation impairment. Furthermore, it is challenging to identify the causal connections between these variables. Because oxidized LDL affects follicle formation, it is linked to impaired ovarian function. In PCOS patients, the widely used cholesterol-lowering medications statins, omega 3 f fatty acids, and niacin enhance the lipid profile and prevent long-term illness (Rashad *et al*., 2019).

Women with PCOS had lower concentrations of high-density lipoprotein cholesterol and greater levels of triglycerides and low-density lipoprotein (LDL) cholesterol. Studies have looked into the levels of apolipoprotein (Apo) A-I and ApoC-I in PCOS-affected women. They found that the cardio-protective effects of ApoA-I were significantly lower in PCOS-affected women than in controls. ApoC-I may be the first instance of lipid abnormalities in women with PCOS. ApoC-I is known to raise the postprandial blood lipid level, typical in individuals with coronary artery disease. Lipid levels can be lowered by modifying day-to-day habits, reducing the amount of total and saturated fat in the diet, losing weight, regular aerobic exercise, and eating plenty of fruits and vegetables. Patients with PCOS tend to be heavier, more sedentary, have higher blood pressure and eat diets high in saturated fats and low in fibre. Therefore, it is reasonable to advise against smoking, drinking alcohol, changing one's diet, and engaging in physical activity to lower the risk of cardiovascular issues.

When there is insulin resistance, the body may produce more insulin to help regulate blood sugar, but this can also lead to increased production of androgens, which can disrupt the menstrual cycle and contribute to the symptoms of PCOS. It is like a domino effect where one thing impacts the other. Insulin resistance and dyslipidaemia often go hand in hand. When the body becomes resistant to insulin, it can lead to higher insulin levels in the blood. This, in turn, can affect lipid levels, causing dyslipidemia, where the cholesterol and triglyceride levels may be imbalanced. They work together to cause health issues. Insulin resistance can be avoided by doing some modifications. Over time, these lifestyle modify-cations can increase insulin sensitivity (reduce insulin resistance), Lower blood glucose levels, decrease blood pressure, decrease triglyceride and LDL (“bad”) cholesterol levels, and raise HDL (“good”) cholesterol levels. Variations in dietary consumption, patient groups, or other factors may be responsible for variations in lipoprotein lipid concentrations. Still, they do recommend a masculine trend in PCOS individuals' lipoprotein lipids. The contents of lipoprotein lipids indicate a masculine pattern when the androgen-to-estrogen ratio is changed toward androgenicity in women (as in PCOS). Despite low absolute values in each group, obese women with polycystic ovarian syndrome paradoxically had considerably higher HDL-C levels than did control women.

Adolescents with PCOS exhibit unfavourable cardiometabolic biomarkers, such as overweight/

obesity and hyperandrogenism, more frequently than controls. Women with PCOS experience the development of new cardiometabolic indicators, including metabolic syndrome, insulin resistance, and hypertension, when they reach reproductive age. An increasing body of research demonstrates the critical function of inflammatory cytokines in these women's cardiovascular health. Certain PCOS traits improve when a woman enters menopause, whereas other biomarkers—like body mass index, insulin resistance, type 2 diabetes, and hypertension—rise. Compared to controls, children of PCOS-afflicted mothers have lower birth weights and higher body mass indices later in life (Rashad *et al*., 2019).

Our results are supported by Zhang *et al.* (2012), who reported that a significantly high correlation exists between hsCRP level and PCOS due to hyperandrogenism, hyperinsulinemia, and insulin resistance seen in PCOS women. An increased hsCRP level in PCOS women may increase the risk of cardiac disease. A variety of metabolic disorders are common in women with PCOS, and there is conflicting data about their risk of cardiovascular disease. A number of research from the past ten years indicate that PCOS may be linked to an increase in endothelial dysfunction and preclinical atherosclerosis disease. Numerous investigations have revealed that women with PCOS had higher serum levels of hs-CRP, a sensitive indicator of long-term, low-grade inflammation and a mediator of atherosclerotic disease.

One of the main characteristics of PCOS is hyperandrogenism, which has been linked to higher cardiovascular risk in PCOS-affected individuals. It has been proposed that elevated levels of inflammatory mediators in the blood of PCOS patients are linked to insulin resistance, another prominent metabolic disturbance feature of the disease. Additionally, there are theories that both hyperinsulinemia and insulin resistance independently raise the risk of cardiovascular disease (Bozdag *et al*., 2016).

Women with PCOS exhibit hyperresistinaemia, and this conclusion holds regardless of how obese a woman is. Several increased indicators, including CRP levels, indicated chronic inflammation in PCOS. Women with PCOS have higher hsCRP levels. Indian women with PCOS have higher serum hs-CRP levels than Indian women who appear to be in good health, which suggests that low-grade chronic inflammation is linked to this condition. Raised hs-CRP is more common in obese PCOS women. A positive connection between hsCRP and TC and LDL in the context of a standard lipid profile and elevated hs-CRP levels suggests that chronic inflammation takes precedence over dyslipidemia in PCOS. The association between hs-CRP and age indicates that conditions associated with chronic inflammation, such as PCOS, should be identified and treated early. Examining PCOS women's serum hs-CRP levels may have predictive significance given the usefulness of the marker in predicting risk for cardiovascular illnesses and its correlation with insulin resistance.

Higher BMI, fasting insulin, and triglyceride levels indicate dysregulated lipid metabolism. In contrast, higher hsCRP levels indicate chronic low-grade inflammation. This study found a substantial difference in hsCRP levels between obese PCOS and normal PCOS, as well as between obese PCOS and obese controls. This suggests that obesity may contribute to or worsen chronic inflammation in PCOS and the rise of the markers CRP, TNF-α, and IL-6; adipose tissue is a known source of TNF-α and IL-6, which encourages the liver's production of CRP. The primary marker of the onset of inflammation in PCOS is an elevated CRP level. Therefore, PCOS has effects that go beyond the reproductive system, and it is linked to comorbid conditions, including obesity, hypertension, breast, endometrial, and cardiovascular cancer, complications from pregnancy and obstructed sleep Apnea(Kim and Choi, 2013).

The primary atherogenic and prothrombotic characteristics of hcy play a crucial role in the morbidity and mortality associated with

cardiovascular disease. Leucocyte recruitment, smooth cell proliferation, increased collagen synthesis, foam cell generation, disruption of blood clotting mechanics, endothelial cell damage, and impaired nitric oxide production are some ways it works. Diastolic dysfunction and elevated levels of hcy in PCOS individuals may raise the risk of cardiovascular disease (Christ and Cedars, 2023).

The activation of apoptosis, oxidative stress production, increased inflammatory cytokine expression, and aberrant methylation are some of the molecular pathways of homocysteine-induced cellular dysfunction. Homocysteine's metabolite can react with LDL cholesterol to form atherosclerotic plaques and foam cells. The oxidation of reduced homocysteine produces free radicals, which have the potential to damage endothelium cells directly. Significant platelet aggregation might be a byproduct of homocysteine's pro-aggregatory actions. Extended homocysteine exposure to endothelial cells reduces their ability to produce nitric oxide. Recurrent coronary events and myocardial infarction have been associated with hyperhomocysteinemia. By increasing the expression and secretion of interleukin-8 and monocyte chemoattractant protein-1, homocysteine facilitates the recruitment of leukocytes. Homocysteine promotes the growth of smooth muscle cells and boosts the synthesis of collagen. Homocysteine has prothrombotic effects that include decreased endothelial antithrombotic activity because of altered thrombomodulin function, activation of factor VIIa and V, inhibition of protein C and heparin sulphate, increased fibrinopeptide A and prothrombin fragments 1 and 2, increased blood viscosity, and attenuation of endothelial cell tissue plasminogen activator binding sites. The fasting serum TC, LDL-C, and Apo B values of obese PCOS participants and obese controls were comparable. However, TG and Lp(a) levels were considerably higher in obese PCOS patients, while HDL-C and Apo A levels were strikingly reduced compared to the control group.

Conclusion

Cardiac issues in PCOS women increase tremendously. So, this study aims to analyse the long-term PCOS patients who are overweight in comparison with PCOS patients with similar BMI and a short time history of the syndrome. The patho-physiology of PCOS indicates that long-term PCOS patients might end up with severe complications, including metabolic and cardiovascular disorders. Patients with similar BMI (25.0 to <30) were selected for the analysis based on the questionnaire. From the results in the lipid profile, it has been observed that the levels of total cholesterol ($p<0.001$), LDL ($p<0.001$),triglycerides ($p<0.5$) and VLDL ($p<0.5$) showed significantly higher levels and HDL ($p<0.001$) showed significantly lower level in prolonged PCOS patients when compared to the early PCOS patients. In the cardiac markers, the levels of Lipoprotein A ($p<0.001$), Apolipo A1($p<0.001$), Apolipo B ($p<0.001$),Apo b / apo A1($p<0.001$), Total cholesterol / HDL($p<0.001$), LDL/HDL ($p<0.001$), LDL/ APO B ($p<0.5$), Homocysteine ($p<0.001$), hsCRP ($p<0.001$) showed significantly higher levels in prolonged PCOS patients when compared to the early PCOS patients. Hence, this study recommends that PCOS patients manage their hormonal levels and weight to avoid cardiovascular and metabolic consequences in future. Also, it is suggested that long-term PCOS patients have regular blood lipid profiles and cardiac marker analyses with the consultation of physicians. In general, it is recommended to have a healthy weight and PCOS-friendly diet, exercise, yoga and meditation to avoid the unwanted complications associated with it. More research is needed to reveal the molecular mechanism behind the complications linked.

Ethical Statement

The study was carried out with IAEC approval (Ethical Clearance- ARCIEC/others/001/2001). In the presence of a medical physician, the individuals were informed about the study and written consent was obtained.

Author Contributions

All authors have equally contributed to this study and manuscript preparation. They have read and agreed to the published version of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

References

Bozdag G, Mumusoglu S, Zengin D, Karabulut E and Yildiz BO. (2016) The prevalence and phenotypic features of polycystic ovary syndrome: a systematic review and meta-analysis. Human Reproduction (Oxford, England) 31(12): 2841–2855.

Christ JP and Cedars MI. (2023) Current guidelines for diagnosing PCOS. Diagnostics (Basel) 13(6): 1113..

Jeanes YM and Reeves S. (2017) Metabolic consequences of obesity and insulin resistance in polycystic ovary syndrome: diagnostic and methodological challenges. Nutrition Res Rev. 30(1): 97-105.

Kim JJ and Choi YM. (2013) Dyslipidemia in women with polycystic ovary syndrome. Obstetrics Gynecol Sci. 56(3): 137-142.

Mather KJ, Kwan F and Corenblum B. (2000) Hyperinsulinemia in polycystic ovary syndrome correlates with increased cardiovascular risk independent of obesity. Fertility Sterility 73(1): 150-156.

Rashad NM, El-Shal AS, Abomandour HG, Aboelfath AMK, Rafeek MES, Badr MS, Ali AE, Yousef MS, Fathy MA and Sharaf El Din MTA. (2019) Intercellular adhesion molecule-1 expression and serum levels as markers of pre-clinical atherosclerosis in polycystic ovary syndrome. J Ovarian Res. 12(1): 97.

Wild RA, Rizzo M, Clifton S and Carmina E. (2011) Lipid levels in polycystic ovary syndrome: systematic review and meta-analysis. Fertility Sterility 95(3):1073-9.e1-11.

Zhang J, Fan P, Liu H, Bai H, Wang Y and Zhang F. (2012) Apolipoprotein A-I and B levels, dyslipidemia and metabolic syndrome in south-west Chinese women with PCOS. Human Reproduction (Oxford, England) 27(8): 2484-2493.