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C-Reactive Protein And Plasminogen Activator Inhibitor-1 A Cardiovascular Risk Predictor In Women With Polycystic Ovarian Syndrome

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ABSTRACT

Background: A diverse endocrine condition known as polycystic ovarian syndrome (PCOS) affects 6 to 10% of women of reproductive age. Menstrual irregularity, hyperandrogenism, insulin resistance, anovulatory infertility, and other endocrinopathy known as PCOS are some of its symptoms. There is mounting evidence that cardiovascular disease is becoming more common (CVD) in PCOS females.

Material & method: Our study was prospective case-control research 75 healthy women were included as BMI-matched controls since they had no male-type baldness, hirsutism, acne, or hirsutism. hyperandrogenism symptoms or a family history of PCOS, as well as normal menstrual periods.

Result: In present study when compared to control patients, PCOS patients had substantially higher mean blood levels of TSH, FSH, LH, PRL, hs-CRP, and PAI-1 (p 0.000). In comparison to the healthy controls, the mean fasting blood sugar was considerably higher (p 0.01). 54.16% of all patients had hs-CRP levels more than 3 mg/L, placing them at an increased risk of cardiovascular disease.

Conclusion: Women with the lean phenotype of PCOS have multiple metabolic problems, including abdominal obesity, dyslipidemia, hyperandrogenemia, and insulin resistance. The conclusions of the According to the study, a milieu of continual low-grade inflammation caused by macrophage infiltration in peripheral organs exacerbates metabolic derangements and cardiovascular risk.

Keywords: *PCOS, TSH, LH, CVD, PAI-1*

1. INTRODUCTION

A diverse endocrine condition known as polycystic ovarian syndrome (PCOS) affects 6 to 10% of women of reproductive age.[1] Menstrual irregularity, hyperandrogenism, insulin resistance, anovulatory infertility, and other endocrinopathy known as PCOS are some of its symptoms. On ultrasound, several little ovarian cysts were visible.[2,3] Lean (BMI of normal or below)

and overweight/obese are the two phenotypes of PCOS.[4] Furthermore, the etiology of this disorder may be different from that of its obese counterparts because 20 to 50% of women with PCOS have the lean PCOS phenotype. The diagnostic assessment and management of PCOS patients are made more challenging by the fact that a sizable part of them have normal body mass index (BMI; 25 kg/m2).[5] The examples included for the research are therefore of the lean phenotype. Stein-Leventhal syndrome is another name for PCOS, which was originally. Evaluation of the cardiovascular risk factors in lean PCOS is the goal of the current investigation. There is mounting evidence that cardiovascular disease is becoming more common (CVD) in PCOS females.[6,7,8] In addition, women with PCOS have a cluster of risk factors for cardiovascular disease, including obesity, lipid abnormalities, impaired glucose tolerance (IGT), and hypertension[9]. Proinflammatory markers, including as high sensitivity C-reactive protein (hs-CRP), have been identified as surrogate predictors of future coronary heart diseases in women with lean PCOS and offer an additional tool for global evaluation of cardiovascular risk. Furthermore, in the Indian community, it is still unclear how cardiovascular risks and the lean PCOS phenotype are related. This study is the first to our knowledge to evaluate the cardiovascular risk associated with the lean type of PCOS. CRP is a period of acuteness. By triggering the production of soluble adhesion molecules, secreting monocyte chemoattractant protein, and encouraging low-density macrophages, it also promotes endothelial dysfunction. LDL (lipoprotein) uptake.[10] This study examines CRP in the form of hs-CRP, which more precisely identifies low protein quantities. The recognized CVD risk factor plasminogen activator inhibitor-1 (PAI-1) is a protein.[11] Increased PAI-1 plasma concentrations have been related to type 2 diabetes, insulin resistance, abdominal obesity, the metabolic syndrome, and type 2 diabetes mellitus[12], as well as an increased risk of thrombotic vascular events[13]. The purpose of the current study was to assess the serum PAI-1 activity in PCOS-afflicted women of normal weight and to evaluate if PAI-1 serves as a cardiovascular risk factor for PCOS.

2. MATERIALS AND METHODS

All women between the ages of 18 and 35 who visited the Department of Obstetrics and Gynecology's outpatient department (OPD) with the primary complaint of menstrual abnormalities (amenorrhea or oligomenorrhea) and/or hirsutism with or without infertility were assessed for these conditions. Women (n = 25) who had been diagnosed with PCOS and PCOS were included in the research. According to the Rotterdam revised criteria, PCOS was confirmed by high-resolution ultrasonography in the follicular phase when at least two out of the following three features were present: (1) oligo- or anovulation; (2) clinical and/or biochemical evidence of hyperandrogenism; and/or (3) ultrasonographic[14] findings of polycystic ovaries with exclusion of other known disorders of hyperandrogenism. By using simple random selection, PCOS patients and healthy controls were chosen.

75 healthy women were included as BMI-matched controls since they had no male-type baldness, hirsutism, acne, or hirsutism. hyperandrogenism symptoms or a family history of PCOS, as well as normal menstrual periods. It was prospective case-control research carried out at Sunkar Hospital Department of Obstetrics and Gynecology.

Those who have been diagnosed with diabetes mellitus, hypertension, severe insulin resistance, cardiovascular disease (CVD), congenital adrenal hyperplasia, androgen-secreting tumors, Cushing's syndrome, a history of smoking or drinking, abuse of androgenic or anabolic drugs, hyperprolactinemia, or any combination of these conditions and thyroid problems were left out of the investigation. The number and size of follicles, as well as the number and volume of the ovaries, were observed. Menstrual irregularities, hirsutism, alopecia, infertility, voice changes, weight increase, the presence of acne, a nd obstetric history were all documented in the detailed history.

3. CLINICAL LABORATORY ANALYSIS

Approximately 5 mL of venous blood samples were taken in simple tubes following a 12-hour overnight fast (to estimate the lipid profile and hormone levels profile) and in a tube containing oxalate and sodium fluoride (for plasma glucose estimation). For further examination, serum was extracted and stored at -80°C. In a fully automated ERBA XL (EM-200) Biochemistry analyzer, estimates of fasting plasma glucose, serum total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) concentrations were performed using commercial kits available for standard photometric procedures. Using the Fredrickson-Friedewald formula, LDL was determined. 1. Serum levels of the hormones luteinizing hormone (LH), follicle-stimulating hormone (FSH), prolactin (PRL), and thyroid-stimulating hormone (TSH) were measured using the Advia Centaur CP kit from Siemens. The accuracy and precision of the analyzer, reagents, and test results were examined using quality controls. The Institutional Ethical Review Board gave the study approval. After explaining the purpose and scope of the study to each participant, the Institutional Ethics Committee (IEC) received their informed written permission. The Statistical Package for the Social Sciences (SPSS) version 24.0, for Windows, was used to conduct the statistical analysis (SPSS, Inc., Chicago, IL). Using the Kolmogorov-Smirnov test, the normality of the distribution of all the variables was examined. The numerical information was presented as mean standard deviation (SD). Un paired data (PCOS vs. controls) were compared using Student's t-test, and the correlation between the variables was explained using Pearson's correlation coefficient. p-values less than 0.05 at a 95% confidence interval are Statistical significance was set at 0.05.

4. RESULTS

We assessed fasting blood sugar, lipid profile, TSH, FSH, LH, PRL, hs-CRP, and PAI-1 in both PCOS patients and controls (Fig. 1). There were contrasts between Table 2 displayed both the groups and the findings. In comparison to controls, cases had substantially higher mean blood total cholesterol and LDL levels (p 0.01). When compared to control patients, PCOS patients had substantially higher mean blood levels of TSH, FSH, LH, PRL, hs-CRP, and PAI-1 (p 0.000). In comparison to the healthy controls, the mean fasting blood sugar was considerably higher (p 0.01). 54.16% of all patients had hs-CRP levels more than 3 mg/L, placing them at an increased risk of cardiovascular disease.

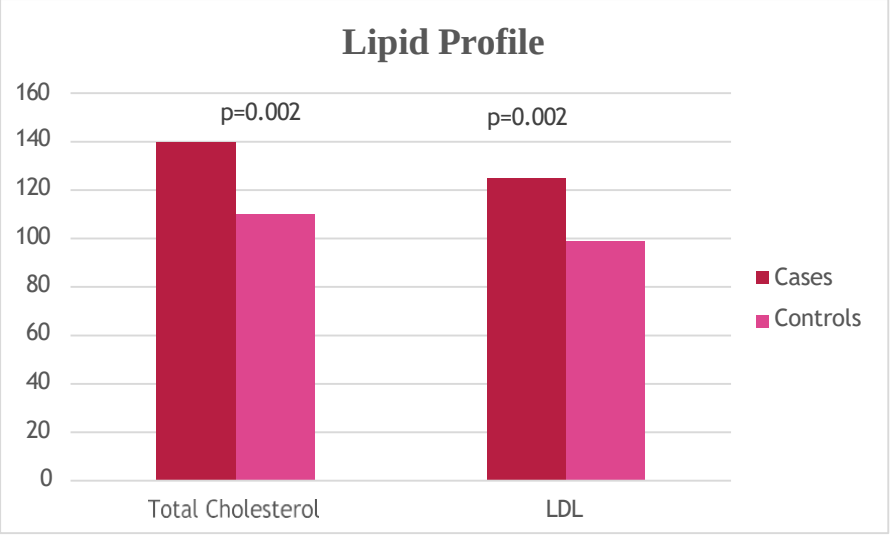
Table 1: Demographic characteristics

Variable	Cases	Control	p-value
BMI	20.96 ±1.62	20.11 ± 2.64	0.14
Height	1.57 ± 0.05	1.57 ± 0.05	0.73
Weight	51.39 ± 5.65	49.64 ±6.43	0.07
Age	20.50 ± 2.81	22.57 ± 2.21	0.84

Table 2: Correlation of PAI-1, LDL, TSH, WHR

Variables	Cases r-Value	Cases p-Value
PAI-1	0.41	0.000
LDL	0.2	0.03
TSH	0.41	0.00
WHR	0.22	0.02

Fig 1: Comparison among PCOS patients & Controls



5. DISCUSSION

When compared to healthy controls of same age and BMI, slim PCOS women had a WHR that was considerably greater. An essential part of metabolic syndrome is the WHR. Hyperinsulinemia and insulin resistance are Because theca cells produce more androgens, PCOS causes a rise in their levels in the blood[15].The dyslipidemia and central obesity are predisposed by the hyperandrogenemia. According to a 2012 theory put out by Lim et al, elements of the metabolic syndrome that were more common in PCOS than in controls were linked to adipose tissue malfunction[16]. This buildup of visceral adipose tissue, which is connected to elevated WHR, may play a major role in the development of metabolic syndrome and low-grade chronic inflammation[17]. WHR exhibits a substantial association with hs-CR on Pearson's correlation analysis. (r ¼ 0.22, p ¼

0.02). 2009 research by Oh et al. In 39 slim PCOS patients discovered a positive correlation between hs-CRP levels and waist circumference (r 14 0.46, p 0.01). Women with certain PCOS phenotypes are more likely to experience metabolic syndrome and long-term cardiovascular disease. In comparison to controls, cases had substantially higher mean blood total cholesterol and LDL levels (p 0.01). According to studies, women with PCOS show signs of the metabolic syndrome, particularly dyslipidemia, which is a common finding[18,19]. According to Xia et al 2012 hypothesis, LAP is a potent measure for identifying insulin resistance in non-diabetic people[20]. In 2009, Wiltgen et al[21], hypothesized that LAP has a favorable correlation with the HOMA index in PCOS and that it may be used to correctly measure insulin resistance in female PCOS. In comparison to control individuals, slim PCOS patients had higher mean blood TSH levels (p 0.000). The relationship between elevated TSH and the lean PCOS phenotype can be linked to insulin resistance because the patient's BMI is within normal bounds. Maratou et al. hypothesized in 2009 that impaired glucose transporter (GLUT)-4 glucose transporter translocation may contribute to increased insulin resistance[22].Additionally, the pituitary's deiodinase 2 activity is lowered in this situation for unexplained reasons.[23] Because of the low T3 levels, this may cause a spike in TSH. Furthermore, research indicates that women with PCOS had greater thyroid antibody levels compared to controls, which is indicative of autoimmune thyroiditis[24]. Additionally, PCOS's hyperestrogenic condition is known to cause autoimmunity since it causes B-lymphocyte, T-cell, and macrophage growth due to the estrogen receptors they possess[25].

In comparison to healthy women of similar age and BMI, slim PCOS women had a higher mean level of hs-CRP. This substantial distinction can be ascribed to the relationship of PCOS with persistent low-grade inflammation. This proinflammatory condition results in altered adipocytokine profiles and malfunction of adipose tissue, both of which are linked to insulin resistance. . Moreover, the consumption of glucose, which is known to activate the nuclear factor (NF)-kB, a family of proteins, causes slim women with PCOS to experience elevated oxidative stress. Tumor necrosis factor (TNF)-a, interleukins, and transforming growth factor are examples of transcription factors that modulate genes[26]. In the lean phenotype of PCOS, this causes proatherogenic inflammation that results in insulin resistance and hyperandrogenism independent of fat[28]. In line with other research, we found that slim PCOS women had higher hs-CRP levels than age- and BMI-matched controls. Oh et al. recruited in 2009 39 lean PCOS patients and 24 controls were compared, and it was expected that women with PCOS had higher levels of hs-CRP; however, after controlling for BMI, the difference was no longer significant.

In 2011, Makedos et al[28]. also carried out research on 188 PCOS patients with normal weights (BMI 25 kg/m2) and hypothesized that the difference between hs-CRP in patients and controls was substantial. Keskin Kur et al[29]. came to the same conclusion in 2014 that slim PCOS women had considerably higher levels of hs-CRP than controls.Additionally, the difference in hs-CRP levels between IGT and NGT women with PCOS supports the role of glucose metabolism in the development of chronic low-grade inflammation. Similar results were presented by Kim et al[30] in 2012, who similarly concluded that slim PCOS patients were more likely to experience IGT.

WHR, FBS, and LDL all had a highly significant positive connection with hs-CRP. This demonstrates low-grade subclinical inflammation that has previously been associated with visceral obesity and insulin resistance. Insulin sensitivity causes hyperandrogenemia, which makes a woman more likely to have belly fat. Thus, the adipocytokines secreted from adipose tissue might start and maintain chronic inflammation, increasing the risk of cardiometabolic disease in PCOS patients with a lean phenotype[31].

Women with lean PCOS had higher levels of PAI-1 than BMI-matched control women. Previous research has indicated that plasmin is crucial for development and follicular rupture. High levels of PAI-1 have also been linked to the development of ovarian maturation, according to Sampson et al. in 1996[32]. Insulin is known to promote the synthesis of PAI-1 in the liver. Therefore, PAI-1 participation may be a main event in anovulation in PCOS, a condition of hyperinsulinemia. Similar results were reported by Elci et al in 2016 who found that nonobese women with PCOS (BMI 30 kg/m2) had significantly higher levels of the cardiovascular risk marker PAI-1.42 Compared to controls, normal-weight PCOS women had considerably higher levels of PAI-1, according to Orio et al. in 2004[33].

6. CONCLUSION

Women with the lean phenotype of PCOS have multiple metabolic problems, including abdominal obesity, dyslipidemia, hyperandrogenemia, and insulin resistance. The conclusions of the According to the study, a milieu of continual low-grade inflammation caused by macrophage infiltration in peripheral organs exacerbates metabolic derangements and cardiovascular risk. The hs-CRP and PAI-1 tests will aid in the early detection, diagnosis, and treatment of CVDs associated with the lean form of PCOS. These indicators may be useful in monitoring any negative changes in a patient's cardiometabolic profile.

Conflict of interest

No conflict of interest were found. All authors agreed to communicate this article.

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