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Original Article

Relationship of Polycystic Ovarian Syndrome with Cardiovascular Risk Factors

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ABSTRACT

Background: Polycystic ovary syndrome (PCOS) is the most common endocrine disorder affecting women of reproductive age. The two main documented pathogenic mechanisms are hyperinsulinemia and hyperandrogenemia but there is growing evidence for increased predisposition to cardiovascular disease, dyslipidemia, and type 2 diabetes mellitus. Our study aims to analyze the association of PCOS with cardiovascular risk factors.
Methods: This is a prospective study which targeted 100 PCOS patients from Civil Hospital Karachi over a period of one year (July 2016 to July 2017). An equal number of age-matched healthy control participants were also included in the study. The student's *t*-test was used to assess the significance of differences using SPSS version (19). The statistical significance was set at a *p*-value of $<.05$.
Results: The most frequently presented feature associated with PCOS was primary infertility seen in 72% of the patients. Mean arterial pressure, fasting glucose and insulin levels and insulin resistance was found to be significantly different in PCOS patients as compared to their controls. A classic atherosclerotic lipid profile demonstrating elevated total cholesterol and low-density lipoprotein-C (LDL-C) levels and decreased serum high density lipoprotein-C(HDL-C) was observed in our study.
Conclusion: This study established a significant yet independent association of PCOS with major cardiovascular risk factors. This association can effectively progress into CVD outcomes which necessitates early intervention programs and preventative strategies to reduce mortality from cardiovascular events. This study lays out the framework for conducting further researches on the PCOS women while exploring novel cardiovascular risk factors.

1. Introduction

Polycystic ovary syndrome (PCOS) is a common endocrinopathy which is characterized as a mix of symptoms including hirsutism, amenorrhea and enlarged polycystic ovaries [1]. The 2003 Rotterdam conference presented a diagnostic criterion which requires a compulsory presence of at least two of the following symptoms for a definite diagnosis: oligovulation or anovulation, hyperandrogenemia (clinically presented as hyperandrogenism) and ultrasonographical presentation of polycystic ovaries [2]. The etiology of PCOS is uncertain, but hyperinsulinemia and hyperandrogenemia constitute the two principal features of the disease [3]. These characteristics can have significant associations with oxidative stress and greater cardiovascular risk [4]. It has been documented that increased oxidative stress contributes to higher chances of cardiovascular disease development in females [5]. The occurrence of PCOS is also highly influenced by a variety of environmental characteristics such as diet, exercise and stress while also being polygenically determined [3]. Insulin resistance and abdominal obesity play a crucial role in increasing the risk of cardiovascular disease, hypertension, dyslipidaemia, metabolic syndrome and type 2 diabetes mellitus in patients with PCOS [6]. These cardiovascular risk factors are present even in younger patients which is indicative of the fact that patients with PCOS are at a potential risk of developing heart disease during the earlier stages of life.

Abbreviations: PCOS, polycystic ovary syndrome; BMI, mody mass index; HDL-C, high density lipoprotein-C; LDL-C, low density lipoprotein-C; CVD, cardiovascular disease; FSH, follicle stimulating hormone; LH, luteinizing hormone; T2DM, type 2 diabetes mellitus; GPO-PAP, glycerol-3-phosphate oxidase- phenol + amino phenazone; SHBG, sex hormone binding globulin; MAP, mean arterial pressure; HOMA-IR, homeostasis model assessment-insulin resistance; TAG, triacyl Glycerol; OGTT, oral glucose tolerance test; TC, total serum cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure.

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Polycystic ovary syndrome has a published prevalence of 4–15%, subjected to the diagnostic method used [7]. PCO is the most common endocrine disease affecting women of reproductive age [7]. A predominance of 5–10% was reported in Pakistan in 2009 [7]. It is significant to note that while there are documented statistics, the prevalence of PCOS is not comprehended well in diverse populations and primary care setups [2]. Consequently, 70% of PCOS cases fail to get diagnosed in primary care settings [8].

The published literature on the association of PCOS with cardiovascular risk factors has been variable. Moreover, long-term follow up examinations reveals an inconstant relation of PCOS with cardiovascular outcomes [4]. Also, there is a dearth of local literature as only one study has been conducted in Pakistan regarding the connection between PCOS and cardiovascular risk factors [9]. Hence, the inconsistency in data necessitates a more comprehensive understanding of the characteristics of CVD risk factors in patients with PCOS and amongst healthy women. This constitutes the aim of our study which focuses on identifying the relationship between cardiovascular risk factors and PCOS.

2. Methods and materials

2.1. Subjects

This case-control prospective study analyzed 100 PCOS patients and an equal number of age-matched healthy controls. The study was conducted in Civil Hospital Karachi from July 2016 to July 2017. The subjects were divided into 4 groups in which Groups 1 and 2 each comprised of 25 women with PCOS aged 20–29 years and 30–39 years respectively. Groups 3 and 4 included 100 healthy females from the described age groups.

The presence of PCOS was diagnosed using the Rotterdam consensus criteria [2]. Polycystic ovaries were identified on ultrasound examination if there was a presence of 10 or more cysts measuring 2–9 mm in diameter which would be surrounding a dense connective tissue (stroma) or be dispersed through an increased stromal substance. Oligovulation and/or anovulation was identified in the presence of oligomenorrhea (menstrual cycles of >35 days) or amenorrhea (lack of menstrual period for 6 months or more). The cut off for the Ferriman–Gallwey score was set at ≥8 to determine hirsutism [10]. The health status of the control group was evaluated through assessing their medical history and results of physical examinations, blood serum analysis and pelvic ultrasound. The controls did not fulfill the requirements for the Rotterdam consensus.

The study participants ranged 20–39 years in age. Diabetes mellitus, hyperprolactinemia, congenital adrenal hyperplasia, infectious disease, androgen-secreting tumors, thyroid disorders, smoking history, Cushing syndrome, hypertension, or hepatic or renal dysfunction were all considered as factors in determining the exclusion criteria for our study. Additionally, patients using (within the previous six months) oral contraceptives, glucocorticoids, antiandrogens, ovulation induction agents, other hormones, or anti-diabetic/anti-obesity drugs and anti-hypertensive drugs were also excluded from the study.

2.2. Anthropometric measurements

All study subjects underwent a comprehensive physical examination which determined height, weight, heart rate and systolic and diastolic blood pressure through standard methods. Weight was measured using a digital scale and it was ensured that the participants wore light clothes. Similarly, height was measured without shoes in a standing position and normal posture of shoulders with a tape measure. Weight (kg) divided by height squared (m) to determine the value for Body Mass Index (BMI in kg/m^2). A BMI between 25.0 and 29.9 kg/m^2 was considered as overweight whereas obesity was defined with BMI 30.0 kg/m^2. These definitions were used according to the criteria defined bythe World Health Organization (WHO) [11].

Systolic (SBP) and diastolic blood pressure (DBP) were on the right arm in a seating position (by a qualified physician with a standard mercury sphygmomanometer). The mean arterial pressure was calculated using the formula DBP + 1/3 pulse pressure. Waist and hip circumference were measured at the end of a normal expiration while the subjects were made to stand. Waist circumference was measured at the narrowest point between the iliac crest and the lowest rib margin. The widest level at the greater trochanter was used to measure hip circumference. The waist-to-hip ratio (WHR) was calculated using these two measurements. All of the anthropometric measurements were performed by the same physician.

2.3. Lipid profile and hormonal assays

Venous blood samples from the antecubital vein (5 ml) were drawn from the participants after a 12 h overnight fast. The subjects were at the follicular phase of their menstrual cycle. Whole blood was allowed to clot for 5–10 min in a clot activator tube. The specimens were then centrifuged at a rate of 3000 rotation/min for 10–15 min to obtain serum. The samples were stored at −70° Celsius until assayed.

Serum LH, FSH and insulin were estimated by ELISA using commercially available kits (Monobind, Lake forest, CA).

A 75-g oral glucose tolerance test (OGTT) was conducted in which blood samples were drawn at 30 min intervals for 2 h. A blood sample was also drawn at the baseline. The purpose of the test was to determine levels of glucose and insulin. The American diabetes Association criteria was used to determine the Glucose tolerance state [12]. Insulin resistance (IR) was estimated through the homeostasis model assessment(HOMA)from this formula: HOMA-IR = (Fasting insulin level(mIU/l) × FPG (mmol/l)/22.5 [13]. Insulin resistant was defined if fasting insulin was >25 lIU/mL, peak serum insulin during OGTT was >100 lIU/mL and HOMA-IR was >4. [13]

Table 1
Depicts the percentages of defining features of PCO among study participants.

Symptoms	Group 1 [n = 50] (20–29 y) (%)	Group II [n = 50] (30–39 y) (%)	Group 1 and II (20–39) y [n = 100] (%)
Polycystic ovaries[a]	100	100	100
Oligo-/amenorrhoea	52	64	58
Hirsutism	56	60	58
Hyperandrogenemia[b]	70	62	66
Primary infertility	72	72	72
Secondary infertility	28	28	28
Acanthosis nigricans	10	22	16

[a] Diagnosis made by transvaginal ultrasound.
[b] Diagnosis made by measuring serum DHEA concentrations.

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