

Dyslipidemia in Women with Polycystic Ovary Syndrome: Comparison between Obese Cases and Obese Controls in a Government Hospital in West Bengal

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Abstract

Introduction: Polycystic ovarian syndrome (PCOS) causes dyslipidemia. The aim of this study was to compare plasma lipid profiles in women with obese PCOS with body mass index (BMI) matched women without PCOS inpatient in government hospital in West Bengal.

Purpose: A total of 75 obese PCOS cases and 75 BMI matched and obese controls were recruited in the study. Blood samples were taken during the 3rd day of the menstrual cycle. After 12 h of fasting cholesterol, triglycerides (TG), very-low-density lipoprotein-cholesterol (VLDL-C), LDL-C, and high-density lipoprotein-C (HDL-C) were measured. Statistical analysis was done by descriptive statistics in independent group *t*-test between two means of both cases and controls and $P < 0.05$ was considered as statistically significant.

Result: No difference was observed between groups in terms of total cholesterol levels ($P = 0.28$) or LDL-C ($P = 0.342$). In PCOS, HDL-C level is lower than controls ($P = 0.001$). No difference was observed between groups in terms TG level ($P = 0.33$) and VLDL-C ($P = 0.358$), respectively.

Conclusion: A more atherogenic lipid profile with low HDL-C was found in women with PCOS.

Key words: Polycystic ovarian syndrome, Dyslipidemia and obesity,

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most frequently encountered endocrine disorder in women of the reproductive age.^[1] It has been suggested that this condition occurs in as many as 4%–10% of women of the reproductive age with onset manifesting as early as puberty.^[2,3] Because of diversity of clinical and metabolic

findings in PCOS, there has been a great debate as to whether it represents single disorder or multiple associated pathological disorder. PCOS is primarily characterized by hyperandrogenism, insulin resistance, and chronic anovulation.^[4] However, PCOS was not described until 1935 when Stein and Leventhal described the syndrome as having pathognomonic ovarian finding (multiple cysts) and clinical triad of hirsutism, amenorrhea, and obesity.^[5] The term PCOS came in use in 1960, when it was understood and clinical and histological diversity was typical of syndrome.^[6] In 1990, PCOS should be defined by National Institute of Health-National Institute of Child Health and Development. PCOS was defined as clinical and/or biochemical evidence of hyperandrogenism and anovulation and exclusion of some known disorder. This disorders are hyperprolactinemia, thyroid disorder, adrenal

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hyperplasia, androgen producing ovarian tumor chronic anovulation.

Hyperandrogenism is usually suggested by the presence of hirsutism (occurs in approximately 80% of PCOS women) and can be documented by measuring androgen levels in the blood. Free testosterone is the most frequently elevated steroid in the blood in PCOS. Circulating levels of total testosterone, androstenedione, and dehydroepiandrosterone are also elevated.^[7]

PCOS is associated dyslipidemia. Lipid abnormalities in PCOS include lower high-density lipoprotein (HDL) and HDL2-cholesterol (HDL2-C), higher total and low-density lipoprotein-cholesterol (LDL-C), and higher triglycerides (TG) and very-LDL-C (VLDL-C) levels (210,211).

Women with polycystic ovary syndrome (PCOS) are dyslipidemic with high total cholesterol, increased small dense LDL-C. High TG reduced HDL-C.^[8-10] Obesity is a common finding in women with PCOS. Many women with PCOS (between 38% and 88%) are overweight^[11,12] or obese. Adiposity plays a crucial role in PCOS and influences the clinical and endocrine features in many women with the condition.^[13] Obesity itself causes the metabolic syndrome, which includes insulin resistance, Type 2 diabetes mellitus, hypertension, non-alcoholic fatty liver disease, and dyslipidemia, all risk factors for cardiovascular disease (CVD).^[14,15] The typical dyslipidemia of obesity consists of increased TG, VLDL-C, and FFA, decreased HDL-C with HDL-C dysfunction and normal or slightly increased LDL-C with increased small dense LDL-C. The concentrations of plasma apolipoprotein (apo) B are also often increased, partly due to the hepatic overproduction of apo-B containing lipoproteins.^[16,17] Adipokines such as resistin and retinol-binding protein 4 decrease insulin sensitivity, in addition, cytokines such as tumor necrosis factor- α and interleukin-6, which originate from macrophages in adipose tissue.^[18] Obesity causes dyslipidemia irrespective of PCOS. Dyslipidemia is also due to its association with insulin resistance that frequently encountered in PCOS. Dyslipidemia also observed in lean PCOS.

Aims and Objectives

The aims of this study were planned to determine the lipid profile in obese women with PCOS to identify the cardiovascular risk early.

MATERIAL AND METHODS

Study Design

A community-based, cross-sectional study was carried out from 2007 to 2011 among women aged 20–35 years who were permanent residents of West Bengal. PCOS patients

with body mass index (BMI) ($\geq 30 < 35 \text{ kg/m}^2$) were recruited from the outpatient department clinics of the Department of Gynecology in Institute of Postgraduate Medical Education and Research (IPGME&R), Kolkata. This clinical study was approved by the Institutional Ethics Committee, (IPGME&R) Kolkata. All of the participants signed informed consent to be included in the study.

Selection of Cases and Control from Sources

Operational definition

Amenorrhea

Amenorrhea was defined as the absence of periods for at least 3 of the previous cycle in patient who had been menstruating previously.

Oligomenorrhea

Oligomenorrhea was considered when length of menstrual cycle was greater than 35 days.

Obese

Obesity was considered when BMI was between 30-35 kg/m².

Clinical hyperandrogenism

Hyperandrogenism was defined as presence of hirsutism (modified Ferriman-Gallwey score > 5) and or severe acne.

Polycystic ovaries

Polycystic ovaries was defined having follicles 2–9mm in diameter and ≥ 12 in number or ovarian volume $\geq 10 \text{ cm}^3$ in one or both ovaries on transabdominal pelvic ultrasonography (USG). There should be no dominant follicle with size greater than 10 mm in diameter.

Participants selected were undergone three stages of operation.

Stage I: Questionnaire

“Probable cases” and “probable controls” were identified during the cross-sectional survey after administration of the questionnaire. A “probable case:” A “probable case” was defined as a woman with symptoms suggestive of PCOS (i.e., oligo/amenorrhea according to menstrual cycle length and/or clinical features of hyperandrogenism) as defined above.

A probable control: A “probable control” was defined as a woman with regular menses and no clinical features of hyperandrogenism who was not a relative of a probable case. Probable controls were selected by drawing lots among eligible women from the same age and BMI.

The process was repeated until the desired number of controls was obtained at a 1:1 ratio.

All “probable cases” and randomly selected “probable

controls” were invited to undergo further evaluation (Stages 2 and 3).

Stage 2: Clinical examination and biochemical investigations

Selected women were examined for the presence of hirsutism, acne, or alopecia. Hirsutism was routinely graded by two physicians independently using the common modified Ferriman–Gallwey (FG) score. If the FG score differed by >2, reevaluation by a third physician was done and median values were used. Nine areas were examined: Upper lip, chin, chest, upper abdomen, lower abdomen, upper back, lower back, thighs, and upper arms. Each area is scored 0–4, resulting maximum score 36. Hirsutism was diagnosed when a score above 5 was evaluated.

Biochemical Investigations

Venous blood (5 ml) was drawn from both probable cases and probable controls. Blood samples were taken during the 3rd day of the menstrual cycle. Hemolyzed sera were discarded. Serum total testosterone was measured to diagnose biochemical evidence of androgen excess or hyperandrogenemia. Hyperandrogenemia was diagnosed when serum total testosterone level was greater than 55ng/dl. Upper normal level of serum total testosterone level was 55ng/dl mentioned by kit supplier. Kit was supplied by Radio-pharmaceutical and isotope technology, BARC, Mumbai.

Stage 3: Ultrasound scanning

Women identified as probable cases and probable controls were invited to undergo pelvic ultrasound scanning within the first 5 days of commencement of their next menstrual period.

Polycystic ovaries on ultrasound sonography (USG) - multiple small follicles (> 10–12) and (2–9 mm in diameter) tightly spaced along the periphery of the ovary. Ovaries which contained cysts >10 mm in diameter were excluded from then calculations as per diagnostic recommendation, since they do not represent immature follicles of PCOS.

Inclusion Criteria of Cases

The diagnostic criteria for PCOS were based on the unified standards formulated by the Rotterdam International Conference in 2003. Patients with any two of the following three conditions were diagnosed with PCOS: (1) Infrequent ovulation or anovulation; (2) hyperandrogenism or clinical manifestations of high blood androgen; and (3) polycystic ovaries on USG - multiple small follicles (>10–12) and (2–9 mm in diameter) tightly spaced along the periphery of the ovary. Exclusion criteria included congenital adrenal hyperplasia, androgen-secreting tumors, Cushing

syndrome, thyroid dysfunction, hyperprolactinemia, and other diseases.^[12]

Inclusion Criteria of Controls

Patients in the control groups exhibited normal menstruation, no clinical or biochemical signs of hyperandrogenism, normal ovaries as defined by B-mode ultrasonic examination, no family history of endocrine and metabolic diseases, and no family history of PCOS including age and BMI matched with cases.

Participants on OCP or conceived were excluded from the study.

A total of 75 obese PCOS patients between age group between 20 and 35 years were recruited. Healthy age and BMI matched (*n* = 75) women without PCOS enrolled as controls.

Other Biochemical Parameters

Blood samples were taken during the 3rd day of the menstrual cycle after 12 h of fasting. Hemolyzed sera were discarded. Serum HDL-C, LDLC, VLDL-C, and total cholesterol TG were measured.

Statistical Analysis

Statistical analysis was done by descriptive statistics in statistical analysis was carried out using Microsoft Excel sheet 2003. Descriptive statistics are presented as mean ± standard deviation for normally-distributed variables. Student *t*-test was used to compare variables with normal distribution and *P* < 0.05 was considered as statistically significant.

RESULTS

Baseline Characteristic

The present analysis evaluates 75 women with PCOS (PCOS group) and 75 healthy controls matched for age and BMI. [Table 1] There was no age difference between groups (*P* = 0.86) and no difference in term of BMI (*P* = 0.27).

Table 1: Age and BMI of the study population

Age/BMI	Obese PCOS <i>n</i> =75	Obese controls <i>n</i> =75
Age in years <i>P</i> =0.86		
Range	20–35	20–35
Mean±SD	27.8±3.4	28.65±2.7
BMI kg/m ² <i>P</i> =0.27		
Range	30–35	30–35
Mean±SD	31.08±1.76	30.98±1.32

BMI: Body mass index, SD: Standard deviation, PCOS: Polycystic ovarian syndrome

Table 2: Lipid profiles of women with obese PCOS and control

Lipid mg/dl	Obese PCOS, n=75 Mean±SD	Obese Controls, n=75 Mean±SD	P value P<0.05 Significant	Significant or not
Total cholesterol	197.55±11.2	189.25±24.7	P=0.28	Not significant
VLDL	35.5±9.98	37.5±4.09	P=0.358	Not significant
LDL	116.2±12.32	109±16.24	P=0.342	Not significant
HDL	42.05±3.34	47.75±3.32	P=0.001	Significant
TG	130±22.7	137±32.3	P=0.35	Not significant

PCOS: Polycystic Ovarian Syndrome, VLDL: Very-low-density lipoprotein-cholesterol, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, TG: Triglycerides

Lipid Parameters [Table 2]

No difference was observed between groups in terms of total cholesterol levels ($P = 0.28$) or LDL-C ($P = 0.342$). In PCOS, HDL-C level is lower than controls ($P = 0.001$). No difference was observed between groups in terms TG level ($P = 0.33$) and VLDL-C ($P = 0.358$).

DISCUSSION

Decrease in HDL-C and increase in TG levels are well-known lipid profile characteristics in women with PCOS.^[19-21] Decrease in HDL-C is only lipid abnormalities in our finding. Many studies have reported that LDL-C is increased in women with PCOS, which is usually not noted in insulin-resistant states. The reason why LDL-C in also increased in women with PCOS is not clear yet, but increased LDL-C levels in women with PCOS may be related to hyperandrogenism or genetic factor.^[22] Another study shows that no differences were observed in the incidence of high total cholesterol, HDL cholesterol level, LDL-C level; TG, and homocysteine levels did not differ between PCOS and control groups.^[23] Further study is needed why HDL is decreased in our study. Insulin resistance is cause of dyslipidemia in PCOS. Obesity is important cause of dyslipidemia. Obesity is associated with dyslipidemia and it plays a major role in the development of atherosclerosis and CVD. Obesity causes higher TG, decreased HDL-C levels, and increased small, and dense LDL particles and these have been shown to be atherogenic.^[24,25] Several recent studies have suggested that insulin resistance causes dyslipidemia and insulin resistance is associated with hypertriglyceridemia and high levels of VLDL-C and low levels of HDL-C cholesterol and apo A-I.^[26,27] Dyslipidemia is associated with insulin resistance in women with PCOS. The mechanisms by which PCOS exerts an effect on lipoprotein metabolism independent of insulin resistance are not known, but hyperandrogenemia may cause dyslipidemia. However, plasma androgen levels do not always correlate closely with clinical hyperandrogenemia, and it is thought that other factors such as tissue sensitivity to androgens are involved. Hyperandrogenemia is a risk factor for dyslipidemia, which was altered only in the phenotypes with elevated androgen levels.^[28] The mechanism by which hyperandrogenism

may contribute to the development of lipid abnormalities in PCOS is not clear. Hyperandrogenism may lead to the abnormalities in lipoprotein profile by working directly at the liver by acting on hepatic lipase by mediating central obesity.^[29-33] A higher prevalence of dyslipidemia in women and men with androgenic alopecia has been found.^[34] Hence, we can conclude that androgen itself causes dyslipidemia. We did not measured central obesity in both cases and controls. Hence, further study is needed. In my study, HDL-C level correlates with androgen not with insulin resistance. It cannot be explained. It may be due to clearance of HDL-C by hepatic lipase that is up regulated by androgen.

CONCLUSIONS

A more atherogenic lipid profile, in particular related to low HDL-C, was found in women with PCOS. The results of this study may indicate increased risk for CVD in obese women with PCOS than BMI matched obese women without PCOS.

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