DETERMINATION OF LIPID PROFILE AND INSULIN RESISTANCE IN NON-OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME

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ABSTRACT

Background: Dyslipidemia is a very common metabolic abnormality in women with polycystic ovary syndrome (PCOS). Insulin resistance is a key pathophysiology of PCOS, thus dyslipidemia in women with PCOS may be consistent with those found in an insulin resistant state. The objective of this study was to find changes in lipid profile in non-obese Pakistani women with Polycystic Ovary Syndrome.

Methods: Subjects enrolled for the study included 50 patients diagnosed with PCOS and 30 healthy women (control group) who showed no history of drugs affecting lipid metabolism. They were divided into two groups; Group 1 included 50 women of age 20-39 years with PCOS. Group 2 included 30 healthy subjects of corresponding age group. Weight (Kg) with a potable scale and height (cm) in the standing position with a portable stadiometer was measured. The body mass index (BMI) was calculated as weight in kg/height in square meters, for all subjects. Five ml fasting blood samples were collected by venipuncture and was centrifuged at 3000 rpm for 10-15 minutes to obtain serum. The serum samples were aliquoted and glucose levels were measured immediately. The remaining serum was stored at -80º C until analyzed**. Conclusion:**The level of triglycerides (TAG), low-density lipoprotein (LDL) and

cholesterol were 26 mg/dL and 12 mg/dl higher, and high-density lipoprotein (HDL) cholesterol concentration was 6 mg/dL lower in women with PCOS than those of controls.

Keywords: Dyslipidemia, Insulin resistance, Metabolic syndrome, Polycystic ovary syndrome
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INTRODUCTION

Polycystic ovary syndrome (PCOS) is one of the most common causes of endocrine dysfunction in women of reproductive age with a prevalence that ranges from 4% to 7% [1,2].PCOS was first described in 1935 by Stein and Leventhal, and this condition is also known as polycentric ovaries, sclerocystic ovarian disease, Stein–Leventhal syndrome, chronic anovulatory syndrome, and polycystic ovarian disease (PCOD)[3]. In women with PCOS, abnormal lipid levels are seen with a prevalence of 70% [4]. The diagnosis of polycystic ovary syndrome is usually made based on combination of clinical, ultrasonographic and biochemical criteria. PCOS is associated with a wide range of clinical presentations including hirsutism, menstrual irregularities, and infertility. Most women with PCOS have hyperandrogenemia, elevated luteinizing hormone (LH), and normal or decreased follicle-stimulating hormone (FSH)[5]Ahigh prevalence of insulin resistance and hyperinsulinemia is a key pathophysiology of PCOS, and dyslipidemia in women with PCOS may therefore be consistent with that found in the insulin resistant state. Insulin resistance and dyslipidemia play a key role in the risk of cardiovascular pathology in women with PCOS. The extent to which dyslipidemia leads to this risk is still not well understood [6]Dyslipidemia is the most common abnormality in PCOS,with elevated levels of total cholesterol, triglycerides (TGs), and low-density lipoprotein cholesterol (LDL-C) and with low levels of high-density lipoprotein cholesterol (HDL-C).[7,8]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 is also increased in women with PCOS in not clear yet, but increased LDL-C levels in women with PCOS may be related to hyperandrogenism or genetic factor.As stated above, LDL-C is increased in women with PCOS; however, recently, alterations in LDL quality also been reported in women with PCOS [9-10].However, all of these studies are based primarily on obese or over-weight PCOS women, but prevalence of obesity in Korean women with PCOS is low [11]. Thus, we tried to investigate whether altered LDL profiles are also observed in non-obese women with PCOS.

MATERIALS AND METHODS

A case-control, hospital-based study carried out in a teaching hospital of Pakistan. All patients with history of PCOS were included. Study participants were non-obese with a BMI < 30. A written informed consent was obtained from all the participants. A total of 50 patients diagnosed with PCOS and 30 healthy women (control group) who showed no history of drugs affecting lipid metabolism were included in the study.Participants were divided into two groups; Group 1 included 50 women of age 20-39 years with PCOS. Group 2 included 30 healthy subjects of corresponding age group. The protocol of the study was approved by the Ethical Review Committee, University of Health Sciences, Lahore.Weight was measured in Kg with a potable scale and height in cmin standing position with a portable stadiometer was measured. The body mass index (BMI) was calculated. Five ml fasting blood samples were collected by venipuncture and was centrifuged at 3000 rpm for 10-15 minutes to obtain serum. The serum samples were aliquoted and glucose levels taken immediately. The remaining serum was stored at -80º C until analyzed.

Hormonal estimation: Serum FSH, LH and insulin levels were determined by ELISA(Appendix 3), using commercially available kits (Monobind Inc, Lake Forest, CA, USA) with an automated EIA analyzer (CODA, Bio-Rad Laboratories, Hercules, CA, USA), [12].Homeostasis model assessment of insulin

resistance (HOMA-IR) was calculated by the following formula: HOMA-IR = Fasting insulin (uU/ml) x Fasting glucose (mmol/l) / 22.5 [13].Triacyl glycerides (TAG), Cholesterol, HDL-C and LDL-C were measured by an automatic chemistry analyzer.All these measured parameters from patients of PCOs werecomparedwith same measured parameters in control participants.Later, the results were collected and presented in graphs and tables, showing the values as mean ± standard deviation.

Statistical analysis: Data was analyzed using student's t test for the significance of differences. P < 0.05 was considered statistically significant. All calculations were carried out with the SPSS version 20 (SPSS, Inc. Chicago, IL, USA).

RESULTS

Lipid Profile

PCOS patients had significantly higher (P <0.005) TAG levels as compared to their age matched controls. Total serum cholesterol was significantly higher (P <0.05) in patients with PCOS as compared to their age matched controls.Patients with PCOS had significantly higher (P <0.05) LDL-C levels and lower HDL- C levels as compared to controls.

Fasting glucose and insulin levels: No significant differences in fasting glucose levels were observed between PCOS patients and controls. However, PCOS patients had significantly higher (P <0.05) fasting insulin levels as compared to their age matched controls.

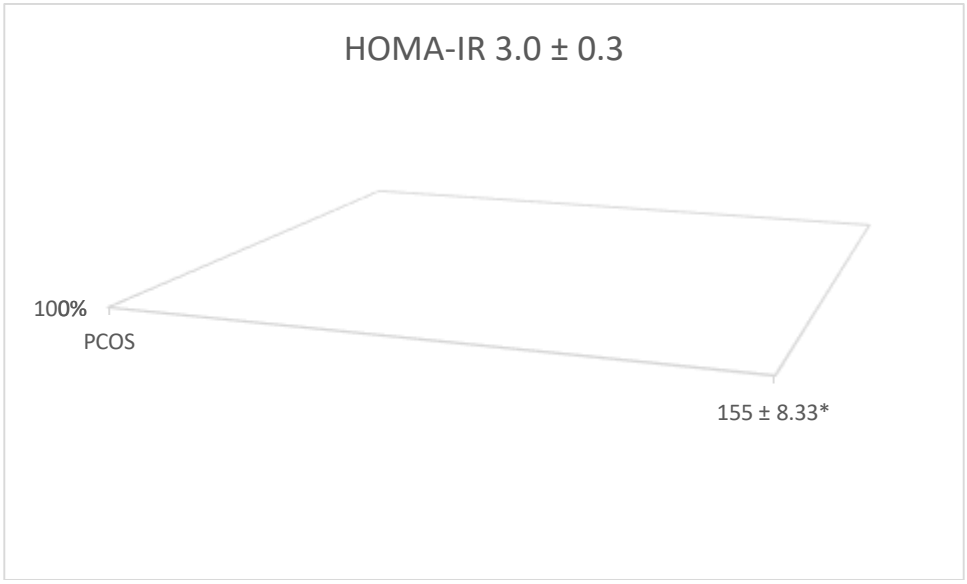
HOMA- IR: Insulin resistance as assessed by HOMA-IR was significantly higher in patients with PCOS as compared to their respective controls.

Gonadotropin levels: Serum FSH levels between patients and their age matched controls were not significantly different whereas serum LH levels were significantly higher (P <0.05) in PCOS patients as compared to their respective control group.

Table 1: Mean ± SEM values of CVD risk factors and endocrinological parameters in subjects with PCOS and controls of 20-29 y age group.

Parameters	Controls	PCOS
Triglyceride (mg/dl)	121 ± 8.64	155 ± 8.33*
Cholesterol (mg/dl)	143 ± 4.77	162 ± 8.34*
HDL (mg/dl)	45.2 ± 2.08	39.8 ± 1.79*
LDL (mg/dl)	140 ± 11.1	186 ± 10.7*
Fasting glucose (mg/dl)	94.7 ± 3.26	86.7 ± 3.25
Fasting insulin (µIU/ml)	13.01 ± 1.1	32.4 ± 5.94*
LH (mIU/ml)	4.94 ± 0.65	9.42 ± 1.62*
FSH (mIU/ml)	6.76 ± 1.28	6.57 ± 0.55

HOMA-IR	3.0 ± 0.3	7.26 ± 1.45*****



***** Significantly different from the control group; P<0.05 (Student's t test).

DISCUSSION

The study was conducted to evaluate the changes in lipid profile parameters in Pakistani non obese PCOS patients and healthy women as control group. PCOS is one of the important endocrine disorders causing reproductive abnormalities in women, which has heterogeneous clinical features and multifactorial etiology.[14] Dyslipidemia is one of the important risk factors associated with PCOS. Obesity and insulin resistance occur frequently in association with this syndrome. Cardiovascular risk factors seem to cluster in women with PCOS when compared with general population.[15]. Previously, based on observation that obese women with PCOS develop greater degree of insulin resistance have been interpreted as due to increase in body mass [16].This possibility was ruled out in the present study by including non-obese PCOS and their age-matched controls. The present study, therefore, supports the view of hyperinsulinemia and insulin sensitivity as salient features of the syndrome even in absence of obesity.Levels of total cholesterol, TAG, and LDL-C in present study were statistically higher, and level of HDL-C was lower in PCOS patients, when compared with age-matched healthy females [Table 1]. This is like the results observed in PCOS patients in another study.[17].Similar results found by some studies suggest that PCOS patients were hyperlipidemic with higher total cholesterol, LDL-C, and TGs concentrations and lower HDL-C levels than control[18]. In present study women with PCOS showed significantly decreased serum levels of HDL-C [Table 1] when compared with the control subjects; this result was like the study done by Wild et al. [19] in 1985 who found that women with PCOS showed lower serum levels of HDL-C in comparison with healthy control subjects. Fasting insulin levels of PCOS patients in both age groups were significantly and markedly higher than their age-matched controls [20]. Previously, based on observation that obese women with PCOS

develop greater degree of insulin resistance have been interpreted as due to increase in body mass [21].This possibility was ruled out in the present study by including non-obese PCOS and their age-matched controls.Hyperinsulinemia stimulates ovarian cytochrome P450c17 α activity in non-obese women with PCOS, thereby increasing serum androgen concentrations [22] and therefore decreasing serum sex hormone-binding globulin (SHBG) concentration [23]. Hyperinsulinemia has also been reported to stimulate adrenal P450c17 α activity of some affected women [24]. In this study, fasting glucose levels in PCOS patients and controls were within the normal range but insulin levels were significantly raised in women with PCOS compared to controls. These observations indicate a tendency towards insulin resistance that is compensated by increased secretion of insulin sufficient to keep glucose levels in the normal range in these patients.The present study, therefore, supports the view of hyperinsulinemia and insulin sensitivity as salient features of the syndrome even in absence of obesity [25]. The PCOS may itself confer insulin resistance and degree of hyperinsulinemia correlates significantly with cardiovascular risk in PCOS, independent of BMI [26].In our study, mean LH levels were higher in both PCOS groups as compared to their age-matched controls which is in accordance with a previous study, whereas no significant difference was observed between FSH levels. Patients with hyperinsulinemia and excess of LH have been regarded to constitute a distinct subgroup with increased adrenal androgenic activity.

CONCLUSION

From this study, it is concluded that women with PCOS have altered lipid profile, with higher levels of (TGs, total cholesterol, and LDL) and low level of serum HDL; this difference may play a role in the pathophysiology found in women with PCOS. Further studies are needed to clarify the role of lipids in these women. Moreover, elevated serum lipids reflected the metabolic state in those patients; all patients should be screened for dyslipidemia for effective cardiovascular risk prevention.

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