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Research article

STUDY OF SERUM LIPID PROFILE AND FASTING BLOOD SUGAR IN POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is the multisystemic disorder and most common reproductive endocrinopathy of women during their childbearing years, expressed in wide varieties of clinical signs and symptoms. It is characterized by a varied and often complex array of metabolic and endocrine abnormalities, including hyperinsulinaemia, hyperglycaemia, glucose intolerance and obesity which put women with PCOS at a higher risk for diabetes, hypertension, dyslipidemia, and cardiovascular disease. **Objectives:** To estimate Fasting blood glucose and lipid profile in women with PCOS and normal females. **Materials and Methods:** After Ethical Committee Approval, blood samples were collected from 50 diagnosed PCOS cases and 50 healthy controls (premenopausal women); aged 18 to 40 years. Fasting plasma glucose and lipid profile were investigated in both PCOS patients and controls. The correlation between these biochemical parameters were then studied in the PCOS group. Data analysis done using student‘ t’ test. **Result:** There was a significant increase in fasting plasma glucose levels in PCOS patients as compared to controls. PCOS women had higher BMI with increased total cholesterol, TGL, LDL-C, VLDL-C and lower HDL-C ($P < 0.05$) as compared to the controls which was statistically significant. The levels of glucose showed significant positive correlation with total cholesterol($P<0.01$), triglycerides($P<0.05$), LDL-C ($P<0.01$) whereas non-significant negative correlation with HDL-C. **Conclusion**: The findings of this study confirms the association between Glucose, BMI and dyslipidaemia in PCOS and may help to identify women with PCOS at risk of cardio metabolic syndrome thereby confirming the association between PCOS and cardiovascular risk factors.

Keywords: Polycystic Ovarian Syndrome, Dyslipidaemia, Cardio Metabolic Syndrome, Insulin Resistance.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is the multisystem reproductive endocrinopathy with ovarian expression of metabolic disturbances and a wide spectrum of clinical features characterized by increased ovarian and adrenal androgen secretion, hyperandrogenic metabolic syndrome symptoms such as hirsutism, acne and/or alopecia, menstrual irregularity and polycystic ovaries. It is not only a reproductive endocrinopathy but also a metabolic disorder.[1,2]

The exact prevalence of PCOS is not known as the syndrome has not been precisely defined. The estimated prevalence in women of reproductive age is 5-10%.[3]The pathophysiology is complex involving the hypothalamus-pituitary-ovarian axis, ovarian theca cell hyperplasia, hyperinsulinemia and a multitude of other cytokine and adipocyte-driven factors.[4]

Women with PCOS share many features in common with the metabolic syndrome[1] and It is also associated with an increased risk for metabolic complications like insulin resistance (IR) with consequent compensatory hyperinsulinaemia, dyslipidaemia and cosmetic problems.[5]One of the most prominent metabolic symptoms of PCOS is insulin resistance, which includes hyperinsulinaemia and impaired glucose tolerance.They also develop abnormal glucose metabolism at a younger age and may demonstrate a more rapid conversion from impaired glucose tolerance to type2 diabetes mellitus.[6]Impaired glucose tolerance and diabetes are not only known risk factors for

cardiovascular disease but also present with their own morbidity.

Obesity increases hyperandrogenism, hirsutism, infertility and pregnancy complications both independently and by exacerbating PCOS. Likewise, in PCOS obesity worsens insulin resistance and exacerbates reproductive and metabolic features.[7]Adiposity plays a vital role in the development and maintenance of PCOS and it strongly influences the severity of both its clinical and endocrine features. In addition to abnormal distribution of adipose tissue in women with PCOS, there may also be inherent abnormalities of lipolysis within adipocytes that are site specific[8]. Women with PCOS have disturbed lipid profiles. The causes of dyslipidaemia in PCOS are again multifactorial. Insulin Resistance appears to have a important role; mediated in part by stimulation of lipolysis and altered expression of lipoprotein lipase and hepatic lipase.[9]

IR and dyslipidemia seem to have an important role on the risk of cardiovascular pathology in women with PCOS. It is still not known to what degree dyslipidemia contributes to this risk.[10]

PCOS may represent the largest under-appreciated segment of the female population at risk of Type2 Diabetes Mellitus and cardiovascular disease. So, it is recommended that women with PCOS be routinely screened for indicators of early metabolic changes in order to anticipate early diagnosis and management. In view of this, the present study was undertaken to estimate and correlate the fasting blood sugar levels and lipid profile that may help to identify women with PCOS at risk of Cardiometabolic syndrome.

MATERIAL AND METHODOLOGY

The observational case-control study was conducted at Raichur institute of medical sciences teaching Hospital, and OPEC super specialty Hospital Raichur from September 2014-September 2015. Study consists of 50 female patients newly diagnosed with PCOS based on Rotterdam criteria in the age group of 18-40 years as cases and 50 age matched healthy female volunteers with regular menstrual cycles and with no clinical evidence of hyperandrogenism or PCOS were taken as control subjects. Institutional ethical committee approved the study and informed consent obtained from all the study subjects. All subjects answered a questionnaire which contained details of age, menstrual history, medical history and family history of type2 diabetes mellitus or polycystic ovarian syndrome.

Inclusion criteria:

Cases: Female patients newly diagnosed with PCOS based on Rotterdam Criteria, in the age group of 18-40 years.

Women with oligomenorrhoea/Amenorrhoea, clinical/Biochemical signs of hyperandrogenism (including: Hirsutism, Acne, Alopecia etc.), elevated androgen levels, Presence of Polycystic ovaries on USG were included in the study.

Controls: Age matched healthy female volunteers with regular menstrual cycles and no signs of clinical hyperandrogenism or PCOS.

Exclusion criteria:

Women with Diabetes mellitus, hypertension, thyroid disorders, renal diseases, cardiovascular diseases, cushing syndrome, pregnant/lactating women, women on drugs (oral contraceptives, hypoglycemic agents/ lipid lowering drugs), hormonal medicines within 6 weeks were excluded from the study.

Method of collection of data:

A pre-structured and pretested proforma was used to collect the data. Baseline data including age, BMI, detailed medical history, family history, clinical examinations were included as part of the methodology.

Anthropometric data:

Body Mass Index:

All the subjects' height and weight were recorded using standard apparatus.

Body mass index (BMI) was calculated by dividing weight (kg) by height (m2).

Normal weight was defined as BMI < 25, Overweight as BMI between 25.0-29.9 and Obesity as BMI > 30.

Waist circumference and waist:hip ratio

Waist circumference was measured mid-way between the last palpable rib and the top part of the iliac crest and the hip circumference was taken around the widest portion of the buttocks.

Blood Pressure:

Blood Pressure was measured in the right arm, with the subjects in a relaxed sitting position using a mercury sphygmomanometer.

Sample Collection and Storage:

5 ml of venous blood samples was collected from healthy controls and women with PCOS after 12 hrs overnight fast. 1 ml of sample was taken in a tube containing anticoagulant and analysed for plasma glucose. 4 ml of sample was taken in a plain tube. After centrifugation at 3000 rpm for 10 minutes, the serum samples were incubated for 15 minutes at room temperature and analysed.

Biochemical Method:

Lipid Profile using standard kits (ERBA: Glucose,Total-Cholesterol, Triglycerides, High Density Lipoprotein-Cholesterol [HDL-C]) in Semi- Auto analyser (Mannheim Erba chem5X) either on the same day of collection or stored at 2-8^{0}C until further analysis.

I. Plasma glucose was analysed by Glucose Oxidase-Peroxidase Method

II. Serum sample was used for following biochemical assays:

Lipid Profile:

Total Cholesterol (Cholesterol Oxidase Method);

Triglycerides (Glycerol Phosphate Oxidase and Peroxidase Method);

High Density Lipoprotein Cholesterol (Phosphotungstic Acid Method);

LDL-C and VLDL-C were calculated using the Friedewald's formula:

LDL Cholesterol = [Total cholesterol] - [HDL cholesterol] [TRIGLYCERIDE]/5;

VLDL Cholesterol = [Triglyceride]/5 (Where all concentrations are given in mgs/dl)

Statistical Analysis: Data Analysis was performed using SPSS 16 Software. The values were expressed as mean ± Standard Deviation. Deviation and the findings were analysed by student "t" test. Pearson's correlation coefficients were calculated to assess the correlation between the biochemical parameters in the study group. A 'P' value of < 0.05 was considered statistically significant.

RESULTS

Table I shows the mean, standard deviation and P values of anthropometric measurement, FBS and Lipid profile in PCOS patients and controls. The mean age of the PCOS group and the control group were not statistically significant. PCOS patients had significantly high BMI (p < 0.01), waist circumference (p<0.001), Systolic Blood Pressure (P<0.001) and diastolic blood pressure (P < 0.001) as compared to controls.

The PCOS group showed a significantly higher fasting glucose (P < 0.001). PCOS patients had increased total cholesterol, triglycerides, LDL-C, VLDL-C and decreased HDL-C as compared to the controls which were statistically significant.

Table II: shows correlation between various parameters in PCOS cases. From the table it can be inferred that BMI (kg/m^2) has significant positive correlation with Fasting blood glucose, total cholesterol, triglyceride, LDL-c and VLDL-c where as significant negative correlation with HDL-c. From the table III it can be inferred that Fasting blood sugar level has significant positive correlation with serum total cholesterol, serum triglyceride, serum LDL-c and serum VLDL-c whereas non significant negative correlation with serum HDL-c.

Table 1. Mean, Standard Deviation and P Values of Anthropometric Measurements, Fasting blood sugar and Lipid profile in PCOS Patients and Control Groups.

Parameter	Cases (n=50)	Controls(n=50)	P value
Age (yrs)	26.16± 3.77	27.38± 5.01	>0.05
BMI (Kg/m^2)	27.50± 2.54	25.9± 2.21	<0.01
Waist circumference (cm)	85.47± 5.46	78.2±4.34	<0.001
Waist Hip ratio	0.786± 0.055	0.7384±0.05	>0.05
SBP (mm Hg)	118.48±8.79	110.96±5.92	<0.001
DBP (mmHg)	78.92±5.47	74.52±4.19	<0.001
FBS (mg/dl)	97.62± 7.19	90.28± 8.52	<0.001
Total cholesterol (mg/dl)	187.44±25.08	165.52± 19.21	<0.001
Triglyceride (mg/dl)	138.3± 40.32	104.69± 32.88	<0.01
HDL-c (mg/dl)	40.64± 8.87	45.78± 5.86	<0.05
LDL-c (mg/dl)	120.17± 28.17	98.79± 19.45	<0.001
VLDL-c (mg/dl)	27.61± 8.91	20.93±6.57	<0.01

P value of <0.05 considered statistically significant

Table 2. correlation of BMI with other parameters in PCOS

Parameter	BMI(kg/m^2)	
	r	p
Glucose	0.687	<0.01
Total cholesterol	0.691	<0.01
Triglyceride	0.568	<0.01
HDL-c	-0.391	<0.05
LDL-c	0.607	<0.01
VLDL-c	0.498	<0.01

P value of <0.05 considered statistically significant

Table 3. Correlation of Glucose and Lipid profile in PCOS

Parameter	Glucose (mg/dl)	
	r	p
Total cholesterol	0.740	<0.01
Triglyceride	0.377	<0.05
HDL-c	-0.251	>0.05
LDL-c	0.699	<0.01
VLDL-c	0.321	<0.05

P value of <0.05 considered statistically significant

DISCUSSION

Considerable evidence has accumulated for the coexistence of the metabolic syndrome and PCOS. A key alteration in the former appears to be insulin resistance which is associated with an increased morbidity and mortality due to coronary artery disease with its enormous public health implications. It has been suggested that inherited defects leading to peripheral insulin resistance and concurrent hyperinsulinaemia are among the causative factors for the development of PCOS. However, due to the heterogeneity of PCOS, it is unclear whether all subjects with this disease are equally susceptible to the symptoms and sequelae of the metabolic syndrome. All in all, the possibility of an increased risk of coronary artery disease in women with PCOS warrants effective diagnostics of the syndrome. Known susceptibility to coronary heart disease should also be kept in mind when designing hormonal therapies for PCOS patients. Clinical manifestations of the metabolic syndrome, i.e. coronary artery disease and diabetes mellitus, have caused it to be referred to as the 'secret killer'. As preventive measures can slow down the appearance of these late symptoms, it is important to recognize at-risk populations during the symptomless period[11]. Cardio metabolic syndrome is a clustering of inter related risk factors that promote the development of atherosclerotic vascular disease and Type 2 DM. These interrelated risk factors have direct effect on atherogenic Dyslipidaemia, elevated blood pressure, and elevated plasma glucose, and promote proinflammatory and prothrombotic states.[12]

Obesity is defined as BMI of > 30 and overweight as BMI of 25-29.9. PCOS patients display central or abdominal or android obesity, which is characterized by an increased waist-hip ratio. This visceral distribution of adipose tissue can be inferred clinically by a waist-hip ratio of more than 0.85.In our study the mean BMI in normal healthy women (controls) is 25.9±2.21(kg/m^2) and in PCOS women (cases) is 27.50±2.54(kg/m^2). The mean BMI was higher in PCOS cases than controls and the mean difference was statistically significant (P<0.01). This is in accordance with other study which showed that excess visceral fat seems to be predictive not only of the metabolic syndrome but also of CVD. A person's waist circumference is the simplest way to assess central obesity. Waist circumference has been shown to be one of the most accurate anthropometrical indicators of abdominal fat.[13]Waist circumference≥80 cm in women is considered as a positive indicator of abdominal obesity as per the consensus India guidelines for Indian population.[14] In our study mean waist circumference for normal healthy women (controls) is 78.2±4.34 cm and in PCOS women(cases) is 85.47±5.46 cm and there was highly significant statistical difference in the mean waist circumference values (P<0.001). In the present study the mean waist hip ratio for normal healthy women (controls) is 0.7384±0.033 and in PCOS women (cases) is 0.786±0.0551. The mean waist hip ratio was higher in cases than controls and the mean difference was not statistically significant.

In our study mean systolic blood pressure in normal healthy women (controls) is 110.96±5.992 mmHg and in PCOS women(cases) it is 118.48±8.795 mmHg. The mean diastolic blood pressure in controls is 74.52±4.19 mmHg and in cases it is 78.92±5.473 mmHg. There is highly significant statistical difference in the mean blood pressure values (P<0.001).

Impaired glucose tolerance (IGT) AND impaired fasting glucose (IFG) are now referred to as "pre-diabetic" indicating the relatively high risk for development of diabetes in these persons. In the absence of pregnancy, IFG and IGT are not clinical entities in their own right but rather risk factors for future diabetes as well as cardiovascular diseases.[15

The results of our study showed mean fasting blood glucose in normal healthy women (controls) as 90.28±8.52 mg/dl and in PCOS women (cases) it was 97.92±7.196 mg/dl. There was very highly significant statistical difference in the mean fasting blood glucose values (P<0.001). Our study also showed significant positive correlation between fasting blood glucose and BMI, TG and VLDL-c (P<0.05) and high significant positive correlation with, TC and LDL-c (P<0.01) whereas non significant negative correlation with HDL-c (P>0.05).

V.M. Vinodhini et al., showed no statistically significant differences in the mean concentrations of fasting plasma glucose between PCOS patients and healthy controls[16] whereas, a study by Azevedo MF et al., reported higher fasting glucose levels in PCOS women which was statistically significant.[17]Our result was consistent with the study of Azevedo MF et al.,. Our study is consistant with the other study conducted among 30 pre-menopausal women and 30 healthy controls, increased fasting glucose levels and decreased magnesium levels were noted in women with PCOS as compared to controls and the differences noted were statistically significant.[3]In another study, impaired glucose tolerance (IGT), fasting insulin and Homeostasis Model Assessment of IR (HOMA-IR) were found to be significantly higher in the study group, when compared to the healthy controls.[18]In a study conducted among 28 PCOS patients and 24 control women who were divided into obese and non-obese groups, 75% of the PCOS subjects presented with insulin resistance suggesting that insulin resistance not only depends on the BMI but also on the presence of PCOS.[19]

Obesity is known to have a strong influence on the prevalence of several metabolic abnormalities in women with PCOS. The syndrome may be associated with a change in both lipid and lipoprotein metabolism (a more atherogenetic lipoprotein pattern is seen in the presence of obesity). Increase in the triglycerides and total cholesterol levels and a greater reduction of high-density lipoproteins (HDLs) have been observed in obese women with PCOS.[20]Our study showed highly significant statistical difference in the mean values of TC, TG, LDL-c and VLDL-c in PCOS cases than controls, the mean values being higher in cases than controls where as mean HDL-c values were lower in PCOS cases than controls and the difference was statistically significant. This is in agreement with the other study which show that there is an elevation of triglycerides, cholesterol and LDL-C in combination with decreased HDL-C and apoA-I.3.

Our study found that HDL-C is lower in PCOS group than in control group whereas higher mean VLDL was seen in PCOS compared to controls. This is consistent with the other study who showed that women with PCOS had higher triglycerides and VLDL-C with lower HDL2-C and apolipoprotein A1:A2 ratios.[21]

Another study compared lean and obese PCOS with control subjects. They also found lower levels of HDL2 cholesterol and higher levels of apolipoprotein B in PCOS. Obese women had lower levels of HDL-C and apoA-I with higher triglycerides and VLDL-C.[22]A study by AnuradhaKalra et al., found no correlation between BMI with various lipid parameters.[2] But in our investigation, we found a significant positive correlation between BMI and total cholesterol, triglycerides, LDL-C, VLDL-C and significant negative correlation between BMI and HDL-C. Our study is in agreement with the another study where the total serum cholesterol, triglycerides, LDL cholesterol (LDL-C) and Very Low-density lipoprotein cholesterol(VLDL-C) were higher in the women with PCOS and higher BMI. Significantly lower levels of serum HDL-C were also noted. Positive correlations were observed between: uric acid and HDL-C, glucose and total cholesterol, triglycerides, LDL-C, and VLDL-C.[3]

Our study showed that PCOS women had higher BMI, significantly increased total cholesterol, triglycerides, LDL-C and VLDL-C. On the other hand, serum levels of HDL-C were significantly lower in this group compared to controls.

CONCLUSION

The use of these simple biochemical parameters might prove to be biomarkers in early detection of these metabolic changes and may help to identify women with PCOS at risk of cardio metabolic syndrome. Based on early recognition of PCOS, efforts may be done to limit or forestall the onset or progression of clinical symptomatology. In addition, treatment may be

instituted in an attempt to prevent or restrict the long-term complications of PCOS namely diabetes and its related complications, including cardiovascular disease. However future prospective studies needed in this aspect. Currently the most effective modalities appear to be life-style modification and ovarian suppression by oral contraceptives.

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