Association of BMI with Serum Homocysteine in Polycystic Ovarian Syndrome Women

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Abstract

Background: Women of reproductive age group are prone for Polycystic ovarian syndrome (PCOS). Recent studies have shown that hyperhomocysteinemia is a risk factor for cardiovascular diseases. Prevalence of cardiovascular disease and cardiovascular morbidities in women with PCOS are increased nowadays. The purpose of the study is to assess correlation of BMI with serum homocysteine in PCOS females.

Materials and Methods: This is done on 50 PCOS patients and 50 voluntary age matched healthy women with no menstrual abnormalities as controls. The age group for the cases and controls is 18-35 years. The study was conducted at Biochemistry Department, SBKS MI & RC, Piparia, Vadodara, Gujarat, India. Measurements of BMI and waist circumference were taken. Fasting blood samples were collected for estimation of FBS, Lipid profile and homocysteine. Medcalc software was used for all statistical analysis. A p-value less than 0.05 ($p < 0.05$) is considered as statistically significant.

Conclusion: Our study has shown significant higher levels of homocysteine in obese PCOS cases when compared with non-obese PCOS cases. Also, significant higher level of homocysteine and triglyceride are seen in PCOS cases compared to controls. Regular follow up for lipid profile and homocysteine is required for PCOS patients to prevent CVS complications.

Key Words: *BMI, Homocysteine, Lipid profile, PCOS.*

Introduction

Women of reproductive age group are prone for Polycystic ovarian syndrome (PCOS), an endocrine disease. Rotterdam criteria were used for PCOS diagnosis. According to that presence of any 2 of the following: oligomenorrhoea or amenorrhoea, hyperandrogenism (clinical and/or biochemical), and polycystic ovaries (≥12 follicles of the ovaries measuring 2–9 mm in diameter, or volume of ovary is 0.10 ml in at least one ovary) are the requirement for the diagnosis of PCOS[1,2]. Clinical features seen in PCOS are menstrual irregularities, hirsutism, obesity, infertility, anovulation, and acne. PCOS is also linked with obesity, insulin resistance, and metabolic syndrome leading to complications like cardiovascular diseases and diabetes mellitus[3].

Homocysteine (hcy), an amino acid, is an intermediary product of methionine metabolism. The only source of homocysteine is methionine which is an essential amino acid. Major causes of homocysteinemia include the imbalance in intake of folate, cobalamine, pridoxine and methionine or genetic variations[4]. Recent studies have shown that hyperhomocysteinemia is a risk factor for cardiovascular diseases. Homocysteine plays an important role in endothelial injury. Hyperhomocysteinemia leads to impairment of

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endothelial dependent vasoreactivity and due to it, endothelium thromboresistance is also decreased. And because of all these events, atherogenesis is developed in hyperhomocysteinemia patients[5]. If the homocysteine level in the blood is more than15 micromol/L, then it is considered as hyperhomocysteinemia[6]. Prevalence of cardiovascular disease and cardiovascular morbidities in women with PCOS are increased nowadays[7].

The reason for increased homocysteine in PCOS women is not well-established. Factors affecting serum homocysteine levels are age, gonadocorticoids and gonadal steroids levels, Body Mass Index (BMI), insulin resistance (IR) and chronic inflammatory conditions. Hyperinsulinemia inhibits hepatic cystathionine β-synthase activity which causes increase in serum homocysteine level[8]. The purpose of the study is to assess correlation of BMI with serum homocysteine in PCOS females.

Material and Methods

This is a case control study, which is carried out on 50 PCOS patients and 50 voluntary age matched healthy women with no menstrual abnormalities as controls. The age group for the cases and controls is 18-35 years. The study was done at Biochemistry Department, SBKS MI & RC, Piparia, Vadodara, Gujarat, India. Rotterdam criteria is used for the diagnosis of PCOS. Patients with diabetes mellitus, hypertension, dyslipidemia, renal and liver failure, thyroid disorders and other endocrine diseases and patients which are on treatment for PCOS were excluded from the study.

Informed consent was taken from all the participants in their respective languages. A performa was used to collect the data. Age, BMI, medical history, clinical examinations and investigations were included in performa.

Body weight and height were measured. Calculation of BMI was done as weight (kg) divided by height in meter square (m^2). Centralized obesity also known as waist circumference was measure at middle point between the lower margin of last palpable rib and highest point of iliac crest. FBS (Fasting blood sugar), serum homocysteine and lipid profile were measured in all participants from fasting blood samples. Serum Homocysteine level was measured by Enzymatic Method[9] in the Laboratory of Dhiraj hospital. Serum Total cholesterol was measured by Cholesterol oxidase peroxidase. Serum Triglyceride was estimated by Glycerophosphate oxidase (GPO) end point method. HDL cholesterol was measured by HDL direct reagent based on modified polyvinyl sulfonic acid (PVS) and PEGME coupled classic precipitation principal method. Serum VLDL and LDL were calculated by Friedewalds formula. Lipid profile was performed on EM-200 fully auto chemistry analyzer.

Statistics Analysis

Data was presented as Mean and SD Values. Test of significance was assessed by independent t-test. A p-value less than 0.05 ($p< 0.05$) is considered as statistically significant. Medcalc software was used for all statistical analysis.

Results

Table 1: Biochemical parameters in PCOS cases and controls. All the values are given as means ±SD.

Parameters	PCOS Cases	Controls	P Value
Waist (cm)	80.92 ± 8.47	77.09 ± 9.18	Non significant
BMI (kg/m2)	25.56 ± 4.73	23.64 ± 3.87	Non significant
FBS (mg/dl)	91.44 ± 8.21	86.12 ± 6.78	Non significant
Total Cholesterol (mg/dl)	181.54 ± 8.62	171.89 ± 5.22	Non significant

Cont... **Table 1: Biochemical parameters in PCOS cases and controls. All the values are given as means ±SD.**

Triglyceride (mg/dl)	125.35 ± 18.42	100.28 ± 13.60	<0.01
HDL cholesterol (mg/dl)	45.14 ± 11.72	56.22 ± 5.81	<0.01
LDL cholesterol (mg/dl)	110.24 ± 18.79	96.11 ± 20.97	Non significant
Homocysteine (micromol/L)	13.9 ± 3.29	9.91 ± 2.88	<0.003

$p < 0.05$ - significant, $p < 0.001$ - very significant, $p \geq 0.05$ - not significant

BMI – Body Mass Index, FBS- Fasting Blood Sugar, HDL – High Density Lipoprotein, LDL – Low Density Lipoprotein, PCOS – Polycystic Ovarian Syndrome

Table 2: Comparison of Homocysteine in obese and non-obese PCOS cases based on BMI

Subgroups	**PCOS cases (BMI ≥25) (n=34)**	**PCOS cases (BMI <25) (n=16)**	**P Value**
Homocysteine	11.19 ± 4.97	8.87 ± 3.71	<0.001

$p < 0.05$ - significant, $p < 0.001$ - very significant, $p \geq 0.05$ - not significant

Table 3: Comparison of Homocysteine in obese and non-obese PCOS cases based on Waist circumference

Subgroups	**PCOS cases (Waist ≥ 80) (n=32)**	**PCOS cases (Waist <80) (n=18)**	**P Value**
Homocysteine	9.79 ± 2.14	7.34 ± 2.87	<0.001

$p < 0.05$ - significant, $p < 0.001$ - very significant, $p \geq 0.05$ - not significant

Table 1 showed comparison of different biochemical parameters between PCOS cases and controls. Mean BMI, waist circumference, FBS, Lipid profile and homocysteine were increased in PCOS cases when compared to controls. Significant increase levels of triglyceride and homocysteine were found in PCOS cases compared to controls. HDL levels were significantly decreased in PCOS cases than the controls. In table2 and table 3, Homocysteine was compared between Obese and non-obese PCOS cases based on their BMI and Waist circumference respectively. There was a significant increase in homocysteine in obese PCOS cases compared to non-obese PCOS cases.

Discussion

Polycystic ovarian syndrome women are at considerable risk for the development of metabolic and CVS abnormalities apart from reproductive abnormalities. Reproductive age group women are more prone for the development of insulin resistance, type 2 diabetes mellitus, obesity, hypertension, dyslipidemia[10]. Hyperhomocysteinemia is considered a risk factor for

CVD. Increased homocysteine levels may be seen in nutritional deficiencies of folic acid, pyridoxine, and vitamin B_{12}. Decreased serum vitamin B_{12} level in PCOS patients is linked with insulin resistance and obesity[11].

In our study, waist circumference, BMI and FBS were higher in PCOS cases compared to controls. But difference among them was insignificant. Significant increase levels of triglyceride were found in PCOS cases compared to controls. HDL levels were significantly decreased in PCOS cases than the controls. These findings are similar to study done by Ahmed M. Mohamadin. They also found increase in homocysteine levels in PCOS cases compared to controls which also coincides with our finding of homocysteine[12]. Significant increase in mean BMI, Waist circumference and serum homocysteine are observed in PCOS women then the normal controls in study done by priyanka Maleedhu, et al[7]. While Annamaria Fulghesu, et al showed in their study that total cholesterol, HDL, LDL, triglycerides and homocysteine levels did not differ between PCOS cases and control groups[13]. One meta-analysis study showed that increase in homocysteine was found both in normal and obese women with PCOS. So according to this study, homocysteine concentration was not associated with body weight[11] which is contrast to our study. In our study, there was a significant increase in homocysteine in obese PCOS cases compared to non-obese PCOS cases. BMI and waist circumference affect homocysteine levels in PCOS women. Schachter M, et al concluded in their study that hyperinsulinaemia in PCOS women is correlated with increased serum homocysteine, regardless of BMI[14]. Suleiman RR, et al found significant high homocysteine level in PCOS patients compared to control. They also showed there was no significant difference in homocysteine levels between the BMI categories and marital status in PCOS cases and controls[3]. Our study coincides with study done by Priyanka Maleedhu et al which showed the increase in homocysteine was associated with increase in BMI and waist circumference in PCOS cases. While some studies didn't show any association between PCOS and homocysteine levels in PCOS women[15,16].

Foam cells and atherosclerotic plaques are formed when metabolite of homocysteine combines with LDL-cholesterol. Oxidation of reduced homocysteine forms free radicals which cause damage to the endothelial cells and because of this there is a marked platelet aggregation. Production of nitric oxide is impaired because of long-lasting exposure of endothelial cells to homocysteine. All these events are responsible for cardiovascular complications. Thus hyperhomocysteinemia has been linked to cardiovascular complications[17].

Conclusion

Our study has shown significant higher levels of homocysteine in obese PCOS cases when compared with non-obese PCOS cases. Also, significant higher level of homocysteine is seen in PCOS cases compared to controls. Dyslipidemia is also seen in PCOS cases compared to controls. Hyperhomocysteinemia and dyslipidemia are the risk factors for cardiovascular diseases. Further studies are required to find the correlations between lipid profile and homocysteine levels in PCOS patients so that further CVS complications are prevented in reproductive age women.

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Conflict of Interest: There is no conflict of interest.

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