



Research Article

Relationship of High Sensitivity C-Reactive Protein and Other Biochemical Parameters of Metabolic Syndrome in Women with Polycystic Ovarian Syndrome and BMI Matched Controls

Vaidyanathan Gowri, Gauhar Rizvi and Shabnam Saquib

Sultan Qaboos University, Oman

Correspondence should be addressed to: Vaidyanathan Gowri; gowrie61@hotmail.com

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is characterized by hyperandrogenism, chronic anovulation and infertility. In addition to reproductive abnormalities, a significant proportion of women suffer from obesity, insulin resistance and other features of metabolic syndrome. Metabolic complications associated with insulin resistance are increased in PCOS independent of obesity including an adverse cardiovascular risk profile. **Methods:** High sensitivity CRP (hs CRP) was measured in 60 PCOS women and 60 age and BMI matched controls with regular menstruation. Other biochemical parameters like fasting blood glucose (FBS), lipid profile (Low density lipoprotein-(LDL), high density lipoprotein (HDL) and triglycerides (TG)) were measured in a subset of 18 PCOs women and age and BMI matched controls. **Results:** A significant positive relationship was observed between BMI & hs CRP ($P < .001$); the degree of relationship was stronger among PCOS cases than controls. Relationship of hs-CRP and FBS was stronger among cases ($P < .001$) than controls ($P = 0.03$) A significant relationship was observed between LDL and hs-CRP among cases ($P .001$) and inverse but insignificant ($p=0.110$) relationship was found among controls. **Conclusion:** Though hs-CRP significantly correlated with obesity, other biochemical parameters like fasting blood glucose and LDL correlated with hs CRP significantly in PCOS women.

Keywords: C- reactive protein, Controls, Metabolic syndrome, Obesity, Polycystic Ovarian syndrome (PCOS)

Introduction

POLYCYSTIC OVARY SYNDROME (PCOS) is the most common endocrinopathy of women

in the reproductive age group (Carmina 1999). Hyperinsulinemia independent of obesity and impaired glucose tolerance in obese PCO women were reported by Duniaf

et al., (Dunaif 1987). Many women with PCOS have additional features of the metabolic syndrome like diabetes and obesity... Lean women with PCOS were found to have a higher prevalence of hyperinsulinemia and ovarian stimulation by insulin appeared to be independent of luteinizing hormone in these women. (Conway 1990) PCO women were found to have significant insulin resistance than weight-matched control subjects (Dunaif 1989, Rajkhowa 1994, Morales 1996). Legro et al., reported in women who have PCOS, as many as 30% have impaired glucose tolerance (IGT) and an additional 7.5% have diabetes and even among non obese women with PCOS, 10.3% have IGT, and 1.5% have diabetes and that PCOs is a more important risk factor in young women to develop glucose intolerance (Legro 1999). Low-grade systemic inflammation, as indicated by elevated hsCRP levels, with Type 2 diabetes mellitus (T2D) was demonstrated in the North Indian population by Mahajan et al., (Anubha 2009). This association was independent of obesity.

Elevated high sensitivity C- reactive protein (hs-CRP) was found to be associated with cardiovascular risk factors in normoinsulinemic PCOS women (Verit 2010). We intended to study the relationship of elevated hs CRP and other biochemical parameters of metabolic syndrome like lipids and fasting blood sugar in PCOS women and age and BMI matched controls.

Methods

Sixty women with Polycystic Ovary syndrome (menstrual irregularity due to oligomenorrhea or anovulation, clinical or biochemical evidence of hyperandrogenism and or polycystic ovaries on ultrasound examination – two of the three criteria to be met as per Rotterdam criteria) were recruited from the infertility clinic. Sixty healthy controls with regular menstruation, matched for age (± 1 year margin) and body mass index (BMI ± 1 margin) were recruited. hs-CRP was measured in all women (cases and controls) and the blood venous sample was drawn in the morning. Women with

Cushing's syndrome, late onset 21-hydroxylase deficiency, thyroid dysfunction and androgen secreting tumours were excluded. Patients and controls on hormonal contraceptives, statins, and aspirin were excluded and so were women with any acute infection.

High sensitive C - reactive protein (hs -CRP) was estimated in 60 women with polycystic ovarian syndrome (PCOS) and 60 women matched for age and weight with regular menstruation. In a subset of 18 women other parameters like fasting blood sugar (FBS), low density lipoproteins (LDL), triglycerides and high density lipoprotein were estimated.

Statistical Analysis

Kolmogorov-Smirnow test was used to test the normality of the variables under study and it showed that all the parameters were obeying the normal distribution pattern among cases and controls. Pearson coefficient of correlation was used to obtain the degree of relationship between hs-CRP and other parameters and independent sample t -test was applied to test the significance of difference of hs-CRP means between normal and abnormal parameters among cases and controls. A p value of 0.05 has been taken as significant.

Assays

High sensitive C reactive protein was assayed using Cobas Integra systems. (Cobas Integra C-Reactive Protein Latex; Roche Diagnostics). The test principle was based on particle enhanced turbimetric assay. Human CRP agglutinates with latex particles coated with monoclonal anti CRP antibodies. The precipitate is determined turbimetrically at 552nm. All samples were analyzed in one assay. The samples were stored – 80 degree Celsius. The intra-assay coefficient of variation was 1.8% and the interassay coefficient of variation was 2.9% at a mean level of 0.62 mg/dl CRP (similar to the manufacturers). HDL cholesterol (HDL), Low density Lipoprotein (LDL) and triglycerides were measured using Cobas Integra 800

(Roche diagnostics) by homogenous enzymatic colorimetric method.

Fasting blood glucose also was estimated with Cobas Integra 800 (sensitivity 0-40mmol/L, coefficient of variation 0.72% to 1.5%).

Results

The mean age of (PCOS) patients was calculated as 27.00 ± 5.21 and for controls it was 27.35 ± 4.87 . The mean BMI of the PCOS women and controls were found as 28.65 ± 5.63 and 28.75 ± 5.22 respectively. A significant positive relationship was observed between BMI & level of hs-CRP in the whole sample, 114 ($r = .520$, $P < .0001$). This relationship was found stronger among (PCOS) patients ($r = .625$, $P < .00001$) than controls ($r = .393$, $P = .003$). These findings have already been published (Gowri 2010).

In a subgroup of 18 cases and 18 controls fasting blood glucose (FBS), Low density cholesterol (LDL), high density cholesterol (HDL) and triglycerides (TG). The mean age of the controls and cases subgroups was 28.3 ± 6.2 years and cases are 28.8 ± 5.4 years respectively. The mean BMI in controls was 30.1 ± 4.2 and in cases was 31.0 ± 5.2 . The mean hs CRP in controls was 4.2 ± 4.0 iu and cases was 6.1 ± 5.4 iu.

The relationship of hs CRP with FBS, LDL, HDL and TG among cases and controls is presented graphically in table 1. Fig. 1 and table 2 display the impact of lipids and glucose on hs-CRP among cases and controls. The hs CRP was significantly more in PCOS women when the LDL was more than 3 mmol/l and the FBs was equal to more than 5.5 mmol. This effect was not seen in controls.

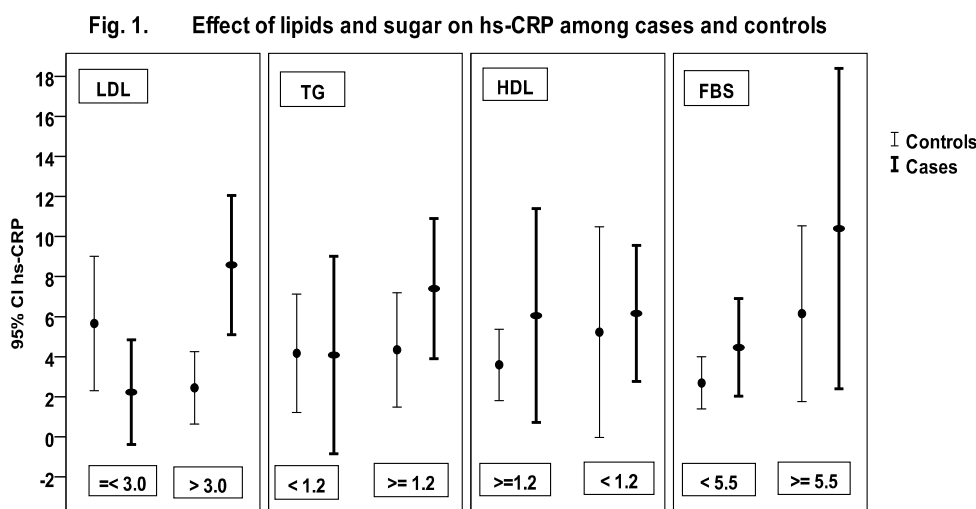


Figure 1: Effect of lipids and sugar on js-CRP among and controls

Table 1: Relationship of hs-CRP with lipids and sugar among cases and controls

	Controls		Cases	
	Correlation	P-value	Correlation	P-value
LDL	-.390	.110	.722	.001
TG	-.025	.923	.383	.117
HDL	-.261	.296	.076	.766
FBS	.512	.030	.775	<.001

Table 2: Impact of Lipids and sugar on hs-CRP among cases and controls

	Cases				Controls				
		n	Mean	SD	P-value	n	Mean	SD	P-value
LDL	≤ 3.0	7	2.23	2.83		10	5.66	4.68	.093
	> 3.0	11	8.58	5.17	.009	8	2.44	2.16	
TG	< 1.2	7	4.08	5.33		12	4.17	4.66	.936
	≥ 1.2	11	7.40	5.20	.210	6	4.34	2.72	
HDL	≥ 1.20	8	6.05	6.38		11	3.60	2.65	.419
	< 1.20	10	6.16	4.75	.968	7	5.23	5.69	
FBS	< 5.5	13	4.46	4.03		10	2.70	1.82	.069
	≥ 5.5	5	10.40	6.44	.030	8	6.15	5.25	

LDL- low density lipoproteins; TG triglycerides; HDL high density lipoproteins; FBS- fasting blood sugar

Discussion

The metabolic syndrome is composed of abnormalities like elevated fasting glucose, hyperlipidemia, obesity and hypertension. There were various definitions for the metabolic syndrome and the National Cholesterol Education Program (NCEP) definition includes fasting glucose, waist circumference, blood pressure, and lipid criteria pertaining to triglycerides and HDL cholesterol (NCEP 2001). Metabolic syndrome is a significant predictor of cardiovascular disease but a stronger predictor of type 2 diabetes.

Many patients with polycystic ovary syndrome (PCOS) also have features of the metabolic syndrome, including insulin resistance, obesity, and dyslipidemia compared to weight matched controls and this contributes to an increased risk for

cardiovascular disease (Sharpless 2003). Obese women with PCOS also have a dyslipidemia. Elevations of low density lipoprotein cholesterol were the main abnormality in women with PCOS. (Legro 2001). However Holte et al., reported plasma free fatty acid correlations were markedly increased in obese women with PCOS closely associated with lower insulin sensitivity and lower glucose tolerance. They did not find the lipoprotein lipid profile significantly abnormal in obese PCOS women compared to weight matched controls. (Holte 1994).

Metabolic complications associated with insulin resistance are increased in PCOS independent of obesity including an adverse cardiovascular risk profile (Lakhani 2004). High sensitivity C-reactive protein (hs- CRP) is an acute phase reactant hepatically synthesized in response to IL6 and TNF- α (Clearfield 2005). Elevated levels of hS CRP

are linked to visceral fat accumulation, Insulin resistance, the metabolic syndrome and type 2 diabetes mellitus (Lemieux 2001). It is still not clear whether elevated hs-CRP in women with PCOS is due to obesity or the disease itself. (Meyer C, 2005). Since the hs-CRP was significantly high in women with obesity, the authors in the present study compared the other parameters contributing to metabolic syndrome in women with PCOS and the controls. We found that hs -CRP significantly more in PCOS women when the LDL was more than 3 mmol/l and the FBS was equal to more than 5.5 mmol, though the effect of obesity was not tested. It is likely that women with PCOS are at increased risk of cardiovascular risk due to elevated LDL and FBS in addition to obesity, but this needs a larger sample size.

The main limitation of the study is sample size. There is an international concern on emerging epidemic of type 2 diabetes and obesity. . Even some others have queried if PCOS is an early manifestation of metabolic syndrome. A larger study is needed to clarify if metabolic syndrome parameters are related only to obesity or PCOS itself.

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