High sensitivity–c reactive protein as an additional marker for increased risk of cardiovascular disease in patients of polycystic ovary syndrome

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Abstract

Background: **Polycystic ovary syndrome (PCOS)** is the most common endocrine disorder affecting women of reproductive age group with a worldwide prevalence of about 4 to12%[1,2]. PCOS is seen in up to 25% of the Caucasians and 50% of the South Asian women respectively[3,4]. It is a heterogeneous disorder of unknown aetiology with a strong genetic element[5]. PCOS does not exclusively involve the reproductive apparatus; it has a complex number of systemic relevancy symptoms. It leads to Metabolic Syndrome with severe consequences on the cardiovascular system[6]. The precise cardiovascular disease (CVD) risk in women with PCOS remains unclear because there are no longitudinal studies pertaining to cardiovascular events. There is a paucity of data in regard to cardiovascular event rates and mortality in PCOS hence the present study was aimed to assess cardiovascular disease risk in women with PCOS.

Aim: To evaluate cardiovascular disease risk in women with Polycystic ovary syndrome.

Materials and Methods: 50 diagnosed cases of PCOS and 50 age matched healthy females were included in this study. Cases were diagnosed based on new Rotterdam criteria formulated by the American Society for Reproductive Medicine (ASRM) and the European Society for Human Reproduction and Embryology (ESHRE). Blood samples were collected after overnight fasting. Serum High sensitivity-C Reactive Protein (hs-CRP), Total Cholesterol(TC), Triglycerides(TG), HDL Cholesterol(HDL-C), VLDL Cholesterol(VLDL-C), LDL Cholesterol (LDL-C) were estimated. Body Mass Index (BMI) was calculated for women in both the groups.

Statistical analysis: Results were analyzed using unpaired t-test and p-value was calculated. BMI was correlated with hs-CRP using one way ANOVA test.

Statistically non-significant increased levels of serum total cholesterol, Triglycerides, HDL cholesterol, LDL cholesterol, VLDL cholesterol and hs-CRP in PCOS cases as compared with control were observed. BMI was found to be significantly increased in cases as compared to control.

Conclusion: hs-CRP is a known cardiovascular risk marker. In this study though hs-CRP was increased in the case group compared to controls but it was not statistically significant. hs-CRP levels vary with age, sex and BMI. Therefore, age, sex and BMI should be considered when interpreting hs-CRP. Women with PCOS who participated in our study were quite young (15-35years) and majority of them had a normal BMI and this may be the reason for a relatively smaller risk of CVD compared with other studies.

Keywords: Lipid Profile, PCOS, hs-CRP, BMI.

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Introduction

The polycystic ovary syndrome (PCOS) is a common endocrine disorder in women characterized by hyperandrogenism and oligomenorrhoea. Classical features of PCOS include anovulation, obesity, high LH/FSH ratio and high testosterone levels.[7] The etiology of PCOS has not been exactly elucidated but it is clear that hyperandrogenism plays a central role in its manifestations as it is present in 60-80% of cases of PCOS[4]. Insulin resistance is another common finding in PCOS that is thought to promote hyperandrogenism through the compensatory hyperinsulinemia.[5,6] Most women with PCOS also exhibit features of the metabolic syndrome, including insulin resistance, obesity and dyslipidaemia[8]. While the association with type 2 diabetes is well established, whether the incidence of cardiovascular disease is increased in women with PCOS remains unclear. Because of the fact that patients with PCOS are at higher risk of the earlier development of complications such as diabetes type 2, atherosclerosis, hypertension and cardiovascular system diseases, it is important to carry out metabolic disorders diagnosis in every patient with PCOS. It will help to estimate the risk of complications and allow for the implementation of prevention or treatment of cardiovascular diseases belonging to the image of PCOS.

The current study is aimed to evaluate and correlate BMI, serum levels of hs-CRP and lipid profile in PCOS patients.

Materials and Methods

This study was conducted in the Department of Biochemistry, at Lokmanya Tilak Municipal medical college and General hospital, Sion, Mumbai. Approval from institutional ethical committee was taken 50 PCOS cases and 50 age matched healthy controls were chosen for this study. This sample size was calculated from desired CI of the study and estimated prevalence of the condition.

Serum Total cholesterol (by Cholesterol Oxidase - Peroxidase)[9], Triglycerides (by Glycerol kinase, Glycerol oxidase Peroxidase)[10], HDL cholesterol(by Polyanionic Precipitation)[11] were estimated on Olympus AU680 autoanalyser. Serum VLDL cholesterol and LDL cholesterol were Calculated by Friedwald's Formula.[12] hs-CRP was measured by Latex enhanced immunoturbidimetric method on nephelometer Mispa i2[13]. BMI for the two groups was calculated by the formula weight in Kilograms/ (height in meter)^2 and gradation of BMI was done as per WHO guidelines.

Subjects with any known cardiovascular pathology or taking any medications affecting cardiovascular functions like beta blockers, sympathomimetic drugs and women smokers were excluded from this study.

Results

Table 1 shows a non significant (p=0.0688) increased levels of hs-CRP in the PCOS patients (0.89±0.73 mg/dl) as compared to healthy controls (0.69±0.19mg/dl). BMI levels were significantly (p=0.002) increased in the PCOS patients (24.96±2.609) as compared to healthy controls (23.12±2.1541).

Table 1: Comparison of hs-CRP and BMI in Cases (PCOS) and Controls

Parameters	Controls (Mean±SD) N=50	Cases (Mean±SD) N=50	p value
hs-CRP(mg/dl)	0.69±0.19	0.89±0.73	0.0688**
BMI	23.12±2.1541	24.96±2.609	0.002*

*p value statistically significant

**p value statistically non- significant

Table 2 shows significant positive correlation between hs-CRP and BMI in PCOS cases (r=0.594) as compared to control group (r= -0.187).

Table 2: Correlation of hs-CRP with BMI

Correlations	BMI	
	Cases	Control
hs-CRP [Pearson Correlation Sig. (2-tailed)]	.594**	-0.187*
N	50	50

*Negative significant correlation at the 0.01 levels

** Positive significant correlation at the 0.01 levels

Table 3 shows statistically significant increase (p value = 0.002) in the mean values of BMI in cases of PCOS (24.96±2.609) as compared to the healthy controls (23.12±2.1541).

Table 3: BMI distribution in Controls and Cases(PCOS)

BMI (kg/m2)	Controls		Cases	
	No.	%	No.	%
Under weight	1	2.0	-	-
Normal	40	80.0	26	52.0
Over weight	9	18.0	22	44.0
Obese	-	-	2	4.0
Total	50	100	50	100
Mean ± SD	23.12±2.1541		24.96±2.609	

One way analysis of variance (ANOVA) was carried out between the means of 4 independent BMI groups UW -Underweight, N- Normal, OW-Overweight, Obese and the dependent variable hs-CRP. The result showed highest hs-CRP mean levels among the obese class. There is an increase in hs- CRP with increase in BMI

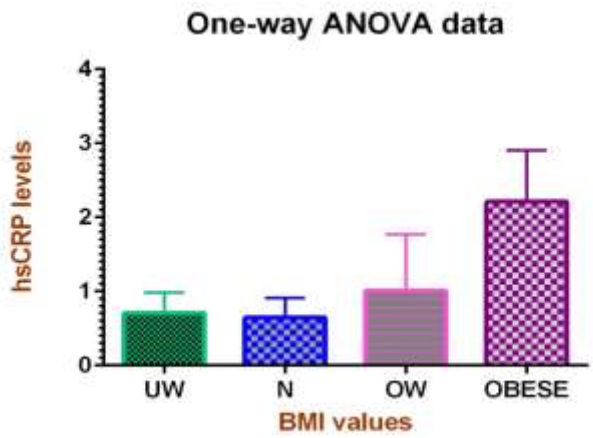

Fig. 1: ANOVA between BMI and hs-CRP

Table 4 shows a non significant (p=0.0610) increased levels of Total Cholesterol in the PCOS patients (167.24±20.49 mg/dl) as compared to healthy controls (159.88±18.27mg/dl). Triglycerides levels were non-significantly (p=0.1866) increased in the PCOS patients (114.9±20.47 mg/dl) as compared to healthy controls (109.78±17.95 mg/dl).There were also a non-significant (p=0.7536) increased levels of HDL- Cholesterol in the PCOS patients (64.2±8.54 mg/dl) as compared to healthy controls (64.92±10.43mg/dl). LDL-Cholesterol levels were non-significantly (p=0.1236) increased in the PCOS patients (82.19±25.60mg/dl) as compared to healthy controls (73.00±21.04mg/dl). A non-significant (p=0.1866) increased levels of VLDL Cholesterol in the PCOS patients (23.07±4.09mg/dl) as compared to healthy controls (21.96±3.59 mg/dl).

Table 4: Comparison of Lipid Profile in Cases (PCOS) and Controls

Parameters	Controls (Mean±SD) N=50	Cases (Mean±SD) N=50	p value
Total Cholesterol(mg/dl)	159.88±18.27	167.24±20.49	0.0610**
Triglycerides(mg/dl)	109.78±17.95	114.9±20.47	0.1866**
HDL-C(mg/dl)	64.92±10.43	64.2±8.54	0.7536**
LDL-C(mg/dl)	73.00±21.04	82.19±25.60	0.1236**
VLDL-C(mg/dl)	21.96±3.59	23.07±4.09	0.1866**

*p value statistically significant
** p value statistically non- significant

Discussion

In the present study hs-CRP showed statistically non-significant increase in PCOS cases as compared to healthy controls. This is in accordance with the previous studies done by Mohlig M, et al whose findings showed neither hs-CRP nor IL-6 were significantly elevated in lean or obese PCOS women compared with age-matched lean or obese controls[14].

Wild RA et al. showed no significant difference in CRP levels between PCOS females and controls[15].

As CRP levels vary with age, sex and BMI; these factors should be considered when interpreting hs-CRP[16]. Women with PCOS who participated in our study were quite young (15-35years) and majority of them had a lean body this may be the reason for a relatively smaller risk of CVD compared with other studies. Collectively, these factors appear to contribute to the low hs-CRP levels observed in this study. Our findings are contradictory to the study done by Kelly CCJ et al, who showed that low grade chronic inflammation as reflected by increased C-reactive protein concentrations independently predicts those at risk for coronary heart disease and type 2 diabetes[17]. PCOS per se is not associated with increased hs-CRP levels rather documented risk factors for CVD such as increased BMI levels may be responsible for raised hs-CRP in patients[18]. The probable cause of rise in hs-CRP in obese individuals is due to an increase in the secretion of cytokines from adipose tissue.[19]

In the present study though serum triglycerides, cholesterol, LDL, VLDL was increased in cases, it was not statistically significant. Lipid metabolism in PCOS is dependent on several related factors, subjects with PCOS who are obese show a specific reduction in HDL lipid, suggesting a reduced capacity for cholesterol removal from tissues with diminished antiatherogenic

potential[20].

Data on CVD and cardiovascular mortality in women with PCOS are thus insufficient. This paucity of data is, in part, due to the fact that most studies in this population are conducted at a time when women are young, before an age when CVD would be expected to develop. Majority of cases in our study group were lean females with normal BMI and lipid profile.

Conclusion

Women with PCOS are more prone for cardiovascular disease risk[21]. In this study though hs-CRP was increased in the case group, it was not statistically significant. hs-CRP levels vary with several factors like age, sex and BMI. Therefore, these factors should be considered when interpreting hs-CRP values. Women with PCOS who participated in our study were quite young (15-35years) and majority of them had a normal BMI and this may be the reason for a relatively smaller risk of CVD as shown by non significant increase in hs-CRP compared with other studies.

Hence these cardiovascular risk predictors along with other documented traditional risk factors for CVD, if studied in a larger population of PCOS women with different BMI, will help in early diagnosis, early management and reduce mortality, morbidity due to CVD in PCOS women.

Limitations of our study

1. Small sample size
2. Women from varied age group

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