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Study of Lipid Profile and High Sensitivity C Reactive Protein in Women with Polycystic Ovary Syndrome

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ABSTRACT

Background: *This study was undertaken to assess the lipid profile parameters and serum levels of high sensitivity C reactive protein (hsCRP) in women with polycystic ovary syndrome. (PCOS).* ***Methods****: 80 women diagnosed with PCOS based on Rotterdam ESHRE/ASRM criteria and 40 age matched healthy controls were selected for the study. Anthropometric and biochemical parameters like serum lipid profile and hsCRP were evaluated among these women.* ***Results****: Women with PCOS were found to have significantly higher levels of total cholesterol, triglycerides, LDL-C and hsCRP and significantly lower levels of HDL-C as compared to controls.* ***Conclusions****: Targeted screening and timely interventions to reduce cardiovascular risk in women with PCOS is necessary to attenuate the complications of the disease.*

Key words: *PCOS, Lipid profile, hsCRP.*

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INTRODUCTION

PCOS is a common metabolic abnormality affecting 10% of female patients of reproductive age.[1,2] In the last few years, there has been growing evidence suggesting the effects of PCOS not only on female reproductive function, but also its metabolic and cardiovascular implications.[3]

Women with PCOS show evidence of insulin resistance, metabolic syndrome, IGT and T2DM, and cardiovascular risk factors such as inflammation, oxidative stress and impaired fibrinolysis. Also, presence of obesity in PCOS further exacerbates increased early clinical and subclinical markers of atherosclerosis like endothelial dysfunction, impaired pulse wave velocity, increased carotid intima media wall thickness, presence of carotid plaque and increased coronary artery calcification.[4] Women with PCOS also show deranged lipid profile characterized by high concentrations of serum triglycerides and total and low-density lipoprotein cholesterol and suppressed levels of high density lipoprotein (HDL), particularly HDL2 subfraction. It seems that significant risk factors for developing atherosclerotic conditions, hypertension and myocardial infarction, are present at an earlier age than women without PCOS. There is thus evidence for an increased risk of developing cardiovascular disease in PCOS.[5]

This study therefore aimed to evaluate the relationship between hsCRP and lipid profile to assess risk for

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cardiovascular diseases in women with PCOS.

METHODS

The study was conducted in Department of Biochemistry, Government Medical College, Aurangabad, with the prior approval of the institutional ethical committee. A total of 80 women, in the age group of 18 – 35 years, diagnosed with PCOS based on Rotterdam ESHRE/ASRM diagnostic criteria were selected for the study. According to Rotterdam consensus criteria commonly used in clinical practice, two of the following three must be fulfilled for the diagnosis of PCOS: polycystic ovaries (12 or more follicles in each ovary, each follicle measuring 2–9mm in diameter and/or ovarian volume >10 mL, one polycystic ovary is sufficient for the diagnosis), oligo-/anovulation clinically diagnosed as oligo-/amenorrhea (menstrual cycles longer than 35 days or less than 10 menstruations per year) and hyperandrogenism (clinical or biochemical).[6] 40 apparently healthy age matched women with BMI between 18.5 – 24.99 kg/m2 were included as controls in the study. They constituted the group 1 of the study. Cases of PCOS were divided into two groups on the basis of BMI: Group 2 – PCOS with BMI 18.5-24.99 kg/m2 and Group 3 – PCOS with BMI ≥ 25 kg/m2.

Detailed history of the participants was taken with respect to marital status, history of any medications, addictions. Cases with history of type 1 or types 2 diabetes mellitus, alcoholism, cardiovascular diseases, renal diseases, any endocrinological disorders were excluded.

After overnight fasting, venous blood samples were collected in plain vacutainers. Serum hsCRP quantitative estimation was done by Chemiluminescence Immunoassay (CLIA) using Acculite CLIA microwells. Assay kits from Monobind INC., Lake Forest, CA 92630, USA. Estimation of lipid profile parameter including total cholesterol, triglyceride and HDL was done using commercially available enzymatic kits. VLDL was calculated using Friedewald's formula.

The results were analyzed by Graphpad prism software, version 5. The results were interpreted as mean ± S.D. Unpaired t test was applied for comparing between the groups and correlation coefficients (r value) were calculated. P value was obtained from unpaired t test and < 0.05 was considered statistically significant. Correlation coefficients (r) were calculated among various parameters in group 2 and group 3. Positive and negative r values were interpreted as follows: r: 0 (no correlation), r: 0- 0.3 (poor correlation), r: >0.3- 0.7 (considerable correlation) and r: 0.8 or more (strong correlation).

RESULTS

Table 1 shows that values of the demographic characters in controls (Group 1) and lean women with PCOS (group 2) did not differ significantly among the groups. Lean women with PCOS (Group 2) and overweight and obese women with PCOS (group 3) showed highly significant difference in the mean values of weight, BMI, waist circumference(WC) and waist hip (W/H) ratios (p2 < 0.0001). Also the mean values of hip circumference (HC) (p2= 0.04) differed significantly among the two groups.

Table 2 shows a significant difference in TC, HDL and LDL between groups 1 & 2 (controls and PCOS with BMI 18.5-24.99). Also, highly significant difference was found in the values of TG and VLDL as well as that of TC/HDL and TG/HDL ratios). Groups 2 & 3 showed highly significant difference in the levels of TC, HDL, LDL, TG, VLDL, and the lipoprotein ratios. Mean values of TC, LDL, TG, TC/HDL and TG/ HDL ratio increased with increasing BMI while HDL levels decreased. The mean values of hs-CRP were significantly increased in cases of PCOS with BMI between 18.5 – 24.99 as compared to their matched controls with a further significant increase in group 3.

Table 1: Comparison of demographic characters in studied groups

Parameter	Group 1 Healthy women with BMI 18.5-24.99 n = 40	Group 2 PCOS with BMI 18.5-24.99 n = 40	p1 value	Group 3 PCOS with BMI ≥25 n = 40	p2 value
	MEAN ± SD			MEAN ± SD	
Age (Years)	25.63±2.38	25.58± 3.90	0.94	27.08 ± 3.94	0.09
Weight(Kg)	57.25± 5.54	57.27± 5.86	0.98	77.75 ± 7.26	<0.0001**
Height(m)	1.59 ± 0.05	1.58 ± 0.06	0.60	1.60 ± 0.04	0.20
BMI(Kg/M²)	22.65± 1.19	22.86± 1.30	0.45	30.48 ± 2.50	<0.0001**
WC (Cm)	76.83± 3.15	78.68± 5.15	0.06	87.85 ± 6.17	<0.0001**
HC (Cm)	95.70± 5.16	96.06± 5.93	0.75	98.63 ± 5.08	0.04*
W/H Ratio	0.80 ± 0.04	0.82 ± 0.04	0.09	0.89 ± 0.07	<0.0001**

(p1 value: p value for group 1 & 2; p2 value: p value for group 2 & 3)
* Significant p value
** Highly significant p value

Table 2: Comparison of lipid profile parameters and hs-CRP in studied groups

Parameter	Group 1 healthy women with BMI 18.5-24.99	Group 2 PCOS with BMI 18.5-24.99	p1 value	Group 3 PCOS with BMI ≥25	p2 value
	MEAN ±SD			MEAN ±SD	
TC (mg%) (Upto 200)	170.35 ± 10.08	176.45 ± 15.71	0.04*	190.58 ± 26.92	0.005**
HDL (mg %) (40 –60)	55.05 ± 3.94	47.75 ± 7.65	<0.0001*	40.55 ± 7.17	<0.0001**
LDL (mg %) (Upto 100)	91.39 ± 11.40	100.32 ± 19.04	0.01*	119.06 ± 27.67	0.0007**
TG (mg %) (Upto 150)	119.58 ± 10.37	141.90 ± 21.48	<0.0001**	154.83 ± 24.34	0.01*
VLDL	23.92 ± 2.07	28.38 ± 4.30	<0.0001**	30.97 ± 4.87	0.02*
TC/HDL	3.11 ± 0.30	3.81 ± 0.83	<0.0001**	4.85 ± 1.13	<0.0001**
TG/HDL	2.18 ± 0.24	3.07 ± 0.79	<0.0001**	3.94 ± 0.97	<0.0001**
hs-CRP(upto 1 mg/L)	0.83 ± 0.17	1.63 ± 0.38	<0.0001**	2.79 ± 0.53	<0.0001**

Table 3: correlation coefficients (r value) in Group 2: PCOS BMI 18.5-24.99

	W/H	hs-CRP	TC	HDL	TG	TC/HDL	TG/HDL
BMI	r= 0.56	0.33	0.28	-0.32	0.13	0.34	0.27
	p=<0.001	<0.05	0.07	<0.05	0.4	0.03	0.10
W/H	-	0.38	0.31	-0.19	0.39	0.26	0.36
		<0.05	<0.05	0.20	<0.05	0.10	0.02
hs-CRP		-	0.44	-0.34	0.35	0.36	0.34
			<0.05	<0.05	<0.05	0.02	0.03

Above table shows that in group 2, hs-CRP shows a positive correlation with BMI, waist/hip ratio, TC and TG, TC/HDL

& TG/HDL ratios and a negative correlation with HDL. BMI is positively correlated with waist/ hip ratio, hs-CRP, and negatively correlated with HDL. Waist/hip ratio is positively correlated with hs-CRP and TC and negatively correlated with HDL.

Table 4 shows that in group 3 hs-CRP shows a positive correlation with BMI, waist/hip ratio, TC and TG, TC/HDL & TG/HDL ratios and a negative correlation with HDL. BMI is positively correlated with waist/hip ratio, hs-CRP, TC and TG, TC/HDL and TG/HDL and negatively correlated with HDL. Waist/ hip ratio shows a positive correlation with all parameters except for a negative correlation with HDL.

Table 4: Correlation coefficients (r value) in group 3: PCOS with BMI >25

	W/H	hs-CRP	TC	HDL	TG	TC/HDL	TG/HDL
BMI	r= 0.52	0.30	0.47	-0.33	0.41	0.45	0.42
	p=<0.001	0.06	<0.01	<0.05	<0.01	<0.05	0.01
W/H	-	0.35	0.46	-0.42	0.59	0.54	0.60
		<0.05	<0.01	<0.01	<0.0001	<0.01	<0.01
hs-CRP		-	0.53	-0.34	0.33	0.49	0.36
			<0.001	<0.05	<0.05	<0.01	0.02

DISCUSSION

In our study we found that the mean values of the lipid profile parameters and the lipoprotein ratios and hsCRP were significantly higher in the lean women with PCOS group as compared to controls except HDL which was lower in lean PCOS. Also, the mean values of lipid profile parameters were significantly raised in overweight and obese PCOS cases as compared to lean PCOS cases except for HDL which was found to be significantly lower in overweight and obese PCOS. These findings are consistent with those of Djuro Macut et al found that values of TG, HDL, TC/HDL and TG/HDL were significantly higher in overweight PCOS women compared to normal weight PCOS women (P <0.001).[7]

Presence of visceral obesity could lead to increased production of cytokines such as IL-6 and TNF-α by visceral adipocytes, which could induce higher hs-CRP production by liver.[8] Boulman et al found that women with PCOS with normal BMI and obese women with PCOS had raised hs-CRP as compared to matched controls (p <0.001).[9]

TG, HDL and TC/HDL ratio are important predictors of CVD50.[10] Increased TG/HDL-C ratios also indicate the presence of atherogenic small, dense LDL particles and could serve as predictor of myocardial infarction and the presence of coronary atherosclerotic lesions.[11]

In our study we also found that hs-CRP correlated positively with TC, TG, LDL, VLDL and correlated negatively with HDL in lean women with PCOS. hs-CRP also correlated with TC/HDL and TG/HDL ratios in these women. In the overweight and obese women with PCOS also hs-CRP showed positive correlation with TC, TG, LDL, VLDL, TC/HDL and TG/HDL ratios and negative correlation with HDL. This suggests the role of inflammation in deranged lipid profile.

The results of the study are similar with the results of a study by Veritt FF in which it was found that hs-CRP correlated positively with TC (r = 0.56, P <0.0001), LDL (r = 0.62, P <0.0001), and TG (r = 0.38. P <0.0001) and negatively correlated with HDL (r = -0.45, P <0.0001)10. Multivariate regression analysis demonstrated that BMI, WHR, LDL, HDL and PCOS status were also the independent variables that influenced hs-CRP.[12]

The possible explanations for role of hs-CRP in deranged lipid profile are as follows:

1) The primary cytokine involved in the hepatic CRP synthesis is IL-6 which itself is produces in various tissues like activated leukocytes, adipocytes and endothelial cells.

2) IL-6 inhibits lipoprotein lipase activity and increases concentration of non-esterified fatty acids by which IL-6 modifies adipocyte glucose and lipid metabolism.[13]

A positive correlation between inflammatory markers, such as hs-CRP and IL-6, and serum lipids was also found in a study by Yuwen Wu et al., suggesting that PCOS is a state of low-grade chronic inflammation, which stimulates the immune response, increasing inflammatory factors such as C3, CRP, and interleukin-6 and thus contributing to the dyslipidemia.[14] Wahda Basheer Al-Youzbaki et al in their study also found a significant correlation between hs-CRP and atherogenic index (TC/HDL) in women with PCOS.[15]

PCOS is much more than a disorder of excess hair and anovulation.[16] Until now clinicians have mainly focused the management mainly on the specific symptoms of PCOS, however, it is becoming obvious that due to the complex nature of the syndrome, other metabolic implications of PCOS on women's health will have to be confronted in the near future.[5]

Women with PCOS represent an intriguing biological model illustrating the relationship between hormonal pattern and cardiovascular risk profile. Taking into consideration the young age of the patients and the devastating effects of PCOS on hormonal and metabolic pattern, this complex and multifaceted disease requires a comprehensive approach in order to achieve concrete beneficial effects for PCOS.[17]

CONCLUSION

From the above findings we can conclude that in women with PCOS, a state of chronic low grade systemic inflammation may be present leading to early abnormalities in lipid profile parameters. Therefore enhancing awareness of the risk factors amongst the high risk population and the clinicians is the need of the hour for reducing the metabolic and cardiovascular complications of the disease.

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