

SERUM LIPID STATUS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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Summary:

Objective: The aim of this study was to evaluate the serum lipid status in patients with PCOS and to compare the lipid status between PCOS patients and woman without PCOS.

Methods: This cross sectional analytical study was carried out in 50 women diagnosed as polycystic ovary syndrome on the basis of Rotterdam Criteria (group I) and 50 women of reproductive age group without polycystic ovary syndrome (group II) attending the outpatient department of Obstetrics and Gynaecology of Dhaka Medical College Hospital, Dhaka during the period of July 2013 to June 2015.

Results: The mean total cholesterol, triglycerides and LDL were significantly ($p < 0.005$) higher in group I but mean HDL cholesterol was not significantly ($p > 0.05$) associated with PCOS. Patients with raised total cholesterol : HDL ratio having the risk of developing dyslipidemia estimated to be 11.16 (95% CI = 3.9-33.1) times higher in PCOS patients than that in the group II. In multivariate logistic regression analysis of lipid profile, only raised LDL-C (> 130 mg/dl) was found to be significantly associated with PCOS ($p < 0.05$).

Conclusion: High LDL level was more associated with PCOS followed by TC, TG and TC:HDL ratio. This study demonstrated a higher level of dyslipidemia specially in PCOS with higher BMI.

Key words: Polycystic Ovary Syndrome, Dyslipidemia.

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Introduction:

Polycystic ovary syndrome (PCOS) is the most prevalent female endocrinopathy and the largest single cause of anovulatory infertility¹. Its association with menstrual disturbance and altered hormonal parameters leads many affected women of reproductive age to attend a gynaecology, endocrinology or infertility clinic. The incidence of polycystic ovary syndrome (PCOS) is 5-10% in women of reproductive age¹. Insulin resistance is a key pathophysiology of PCOS and dyslipidemia in women with PCOS may therefore be consistent with that found in the insulin resistant state: decreased levels of high density lipoprotein-cholesterol (HDL-C) and apolipoprotein (Apo) A-I and increased

levels of triglycerides (TG), ApoB and very low-density lipoprotein^{2,3,4}. There may be a disturbance of adrenocortical function in the prepubertal and postpubertal phase of life initially, followed by a shift to the ovarian dominance, which is associated with a non-cyclical pattern of ovarian function⁵. The end result would be the increased androgen production in the ovary and the increased peripheral production of oestrogen⁵.

Women with polycystic ovary syndrome appear to be at increased cardiovascular risk due, in part, to dyslipidemia characterized by increased plasma triglyceride and reduced high density lipoprotein (HDL) cholesterol levels.

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A recent study of premenopausal women showed that those with the polycystic ovary syndrome had a higher prevalence of coronary artery calcification as detected by electron-beam computed tomography⁷. A predisposition to macrovascular disease and thrombosis in women with the polycystic ovary syndrome has also been described^{8, 9}.

Both insulin resistance and hyperandrogenemia contribute to this atherogenic lipid profile. Testosterone decreases lipoprotein lipase activity in abdominal fat cells and insulin resistance impairs the ability of insulin to exert its antilipolytic effects^{10, 11, and 12}. Insulin resistance leads to increased catecholamine induced lipolysis in adipocytes resulting in increased free fatty acids in circulation. This results in increased VLDL production by the liver resulting in hypertriglyceridemia¹³. Efforts should be directed toward reducing obesity in PCOS to improve the metabolic disturbance in addition to ameliorating the presenting symptoms¹³.

Materials and Method:

This cross sectional analytical study was carried out in the Obstetrics and Gynaecology department of Dhaka Medical College, Dhaka, during July 2013 to June 2015 with an aim to evaluate the lipid status in patients with PCOS and to compare the lipid status between PCOS patients and women without PCOS.

According to the Rotterdam criteria (ASRM/ESHRE, 2003), patients with following characteristics were included in the study as PCOS patients.

1. Oligomenorrhoea (Menstrual cycle interval more than 35 days but less than 6 months).
2. Elevated LH level and LH/FSH ratio ≥ 2 with one or some of the following features:
 - Characteristic enlargement of ovaries by USG.
 - Hirsutism
 - Obesity
 - Infertility
 - Stria

In this study, dyslipidemia were considered if Total cholesterol (TC)/HDL ratio is >4.5 .

A total of 50 women diagnosed as polycystic ovary syndrome on the basis of Rotterdam criteria considered as group I and 50 women of reproductive age group without polycystic ovary syndrome considered as group II attending the out patient department were enrolled in this study.

Patients with adrenal or ovarian androgen producing tumours, hypothyroidism, overt diabetes, cardiovascular disease, Cushing's syndrome, familial hypercholesterolemia or hypertriglyceridemia, hyperprolactinaemia, postmenopausal women, pregnant and lactating women, those on lipid lowering drug, androgen containing drug, oral contraceptives, cortisone, synthetic progestogen or danazol were excluded from the study.

Data were collected using a structured questionnaire containing all the variables of interest, by interview and laboratory investigations. Statistical analyses were carried out by using the Statistical Package for Social Version (SPSS) version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all data. The mean values were calculated for continuous variables. The quantitative and qualitative observations were indicated by frequencies, percentages with 95% CI. Chi square test and odds ratio with 95% CI were used to analyze the categorical variables shown with cross tabulation and unpaired t-test was used to analyze the continuous variable expressed as mean (\pm SD). Multiple logistic regression analysis was done for prediction of dyslipidaemia in PCOS. A P-value was considered to be statistically non significant if >0.05 and statistically significant if ≤ 0.05 .

Ethical consideration:

Prior permission was taken from Ethical Review Committee (ERC), Dhaka Medical College (DMCH) Hospital, Dhaka to undertake this study. Keeping compliance with Helsinki Declaration for Medical Research Involving Human Subjects 1964, all the study subjects were informed verbally about the study design, the purpose of the study and potential benefits for the community. PCOS patients and women

without PCOS who gave informed consent to participate in the study were included as study sample.

Results:

Majority 19 (38.0%) patients belonged to age 26-30 years in group I and 18(36.0%) in group II. Mean age was found 27.98±4.5 years in group I and 26.92±4.8 years in group II. Mean age difference was not statistically significant (p>0.05) between two groups. Almost three-fourth (74.0%) patients belonged to BMI e”25.0 kg/m² in group I and 38(76.0%) patients belonged to BMI 18.5-24.9 kg/m² in group II (table 1). Mean BMI was found 28.0±3.7 kg/m² in group I and 24.4±2.8 kg/m² in group II. Mean BMI was statistically significant (p<0.05) between two groups. Mean total cholesterol was found 217.7±21.8 mg/dl in group I and 180.5±17.7 mg/dl in group II. Mean triglycerides were found 193.4±25.6 mg/dl in group I and 140.5±12.8 mg/dl in group II. Mean

LDL-cholesterol was found 171.0±21.0 mg/dl in group I and 117.6±28.4 mg/dl in group II which were statistically significant (p-value, 0.001) but mean HDL-cholesterol was not statistically significant (p>0.05) between two groups. (Table 2)

The risk of developing dyslipidemia with raised total cholesterol, triglyceride, LDL and total cholesterol / HDL ratio was estimated to be 47.25(95% CI = 12.69-100.0), 23.92(95% CI = 7.58-79.70), 82.25(95% CI = 18.02-100.0) and 11.16(95% CI = 3.90-33.10) times higher in PCOS patients than that in the group II. More than two-third (68.0%) of the patients had raised total cholesterol: HDL ratio in group I and 8(16.0%) in group II. (Table 3) In multivariable logistic regression analysis of lipid profile, only raised LDL-C (>130mg/dl) was found to be statistically significant (p < 0.05). Other lipid profiles were not significantly associated with PCOS. (Table 4)

Table 1
Distribution of the study patients by BMI (n=100)

BMI (kg/m ²)	Group I (n=50)		Group II (n=50)		OR	95% CI (lower-upper)	P
	n	%	n	%			
≥25.0 (over weight & obese)	37	74.0	12	24.0	9.01	3.34-24.96	^a 0.001 ^s
18.5-24.9 (normal)	13	26.0	38	76.0			
Mean±SD	28.0	±3.7	24.4	±2.8			^b 0.001 ^s
Range (min-max)	20.3	-34.7	20.3	-32.1			

s= significant, OR= odds ratio, ^aP value reached from chi square test

^bP value reached from unpaired t-test

Table-II
Distribution of the lipid profile of study patients (n=100)

Lipid profile	Group I(n=50)		Group II(n=50)		P value
	Mean	±SD	Mean	±SD	
Total cholesterol (mg/dl)	217.7	±21.8	180.5	±17.7	0.001 ^s
Range (min-max)	160	-260.0	130	-210.0	
Triglycerides (mg/dl)	193.4	±25.6	140.5	±12.8	0.001 ^s
Range (min-max)	126.0	-218.0	120.0	-176.0	
HDL-cholesterol (mg/dl)	46.84	±4.0	47.35	±6.4	0.633 ^{ns}
Range (min-max)	38.0	-56.0	32.0	-60.0	
LDL-cholesterol (mg/dl)	171.0	±21.0	117.6	±28.4	0.001 ^s
Range (min-max)	124.0	-202.0	68.0	-178.0	

s=significant; ns=not significant P value reached from unpaired t-test

Table-III
Risk of developing dyslipidemia in subjects with PCOS (n=100)

Lipid profile	Group I(n=50)		Group II(n=50)		OR	95% CI (lower-upper)	P value
	n	%	n	%			
Total cholesterol (mg/dl)							
>200	42	84.0	5	10.0	47.25	12.69-100.0	0.001 ^s
≤200 (normal)	8	16.0	45	90.0			
Triglycerides (mg/dl)							
>150	42	84.0	9	18.0	23.92	7.58-79.70	0.001 ^s
≤150 (normal)	8	16.0	41	82.0			
HDL-cholesterol (mg/dl)							
<40	1	2.0	5	10.0	0.18	0.01-1.73	0.092 ^{ns}
≥40 (normal)	49	98.0	45	90.0			
LDL-cholesterol (mg/dl)							
>130	47	94.0	8	16.0	82.25	18.02-100.0	0.001 ^s
≤130 (normal)	3	6.0	42	84.0			
Total cholesterol: HDL ratio							
>4.5 (dyslipidemic)	34	68.0	8	16.0	11.16	3.90-33.10	0.001 ^s
≤4.5 (normal)	16	32.0	42	84.0			

s=significant; ns=not significant, P value reached from chi square test

Table-IV
Multivariable logistic regression analysis of Lipid Profile (n=100)

	B	S.E	P value	OR	95% CI for OR	
					Lower	Upper
LDL-cholesterol (>130 mg/dl)	3.268	0.865	0.001 ^s	26.3	4.8	143.1
Triglycerides (>150 mg/dl)	-2.848	2.127	0.181 ^{ns}	0.1	0.0	3.7
Total cholesterol (>200 mg/dl)	2.728	1.508	0.070 ^{ns}	15.3	0.8	293.8
HDL-cholesterol (<40 mg/dl)	-2.517	1.468	0.086 ^{ns}	0.1	0.0	1.4
Total cholesterol/HDL ratio (>4.5 mg/dl)	1.026	2.019	0.611 ^{ns}	2.8	0.1	145.8

s=significant; ns= not significant

Discussion:

Insulin resistance is a key pathophysiology of PCOS and dyslipidemia in women with PCOS may therefore be consistent with that found in the insulin resistant state: decreased levels of high-density lipoprotein-cholesterol (HDL-C) and apolipoprotein (Apo) A-I, and increased levels of triglycerides (TG), ApoB and very low-density lipoprotein (VLDL) ^{4,14}.

Three-fourth (74.0%) patients belonged to BMI ≥25.0 kg/m² in group I and 38(76.0%) patients belonged to BMI 18.5-24.9 kg/m² in group II. Mean BMI was found 28.0±3.7 kg/m² in group I and 24.4±2.8 kg/m² in group II. Mean BMI

was statistically significant (p<0.05) between two groups. Overweight or obese had 9.01 times increased risk to develop PCOS with 95% CI 3.34-24.96% in this study. Similarly, in another study the mean BMI was 26.76 ±6.08 kg/m² in PCOS group and 24.73±5.66 kg/m² in control group¹⁵. The difference was statistically significant (p<0.05) between two groups. On the other hand, Manjunatha et al. (2014), Fulghesu and Magnini (2012) and Iuhas et al. (2012) observed statistically significant difference between two groups regarding the mean BMI^{16, 17, 18}.

Rotterdam guidelines suggested evaluation for the metabolic syndrome and indirectly indicated

the need to measure only HDL-C and triglycerides with relatively little attention to other lipid parameters. However, during past decade, a large number of studies found an increase of LDL-C levels in women with PCOS^{28, 19}. Therefore, recently both the American College of Obstetricians and Gynecologists (ACOG) (ACOG practice bulletin 2009) and the Androgen Excess and PCOS Society (Wild et al. 2010) guidelines have recommended that women with PCOS should have a complete fasting lipid and lipoprotein evaluation as part of their cardiovascular risk assessment^{20,21}.

In this study, mean total cholesterol was 217.7 ± 21.8 mg/dl varied from 160 – 260 mg/dl in group I and 180.5 ± 17.7 mg/dl varied from 130 – 210 mg/dl in group II. The mean total cholesterol was significantly (p value-0.001) higher in group I. Similarly, Manjunatha et al. (2014) showed mean serum total Cholesterol 202.16 ± 16.12 mg/dl in study group and 170.8 ± 9.87 mg/dl in control group.

Mean triglycerides was 193.4 ± 25.6 mg/dl varied from 126 – 218 mg/dl in group I and 140.5 ± 12.8 mg/dl varied from 120 – 176 mg/dl in group II which was significantly (p-value 0.001) higher in group I. Manjunatha et al. (2014) found that the mean serum triglycerides was 120.13 ± 12.88 mg/dl and 98.3 ± 18.19 mg/dl in study group and control group respectively¹⁶. The difference was statistically significant (p<0.05) between two groups, which is consistent with the current study.

Mean LDL-cholesterol was 171.0 ± 21.0 mg/dl varied from 124 – 202 mg/dl in group I and 117.6 ± 28.4 mg/dl varied from 68 – 178 mg/dl in group II which was significantly (p-value 0.001) higher in group I.

In this present study, it was observed that the mean HDL-cholesterol was not significantly (p>0.05) associated with PCOS. Manjunatha et al. (2014) found that the mean HDL-Cs were 39.16 ± 6.01 mg/dl and 55.45 ± 4.11 mg/dl in study group and control group respectively¹⁶. The difference was statistically significant (p<0.05) between two groups which is comparable with the current study.

Al-Hakeim et al. (2009) mentioned that there is a significant increase (p<0.05) in total cholesterol, TG and LDL-C in PCOS patients as compared with control group while HDL-C and serum calcium is decreased significantly in patients group in comparing with control group²². Similar observations were also reported by Wild et al. (2010), Moran et al. (2010); Manjunatha et al. (2014)^{10, 23,16}.

However, some other studies showed different profiles. Bickerton et al. (2005) found that there were no significant differences in lipid or lipoprotein concentrations between the women with PCOS group and controls²⁴. Yilmaz et al. (2005) found no difference in serum TC, LDL-C, TG, levels between PCOS and control groups, whereas HDL-C was lower²⁵. Vrbikova et al. (2003) showed serum TC and TG did not differ significantly between PCOS and healthy women groups while HDL-C was lower and LDL-C was higher in PCOS than in controls²⁶.

In this study, the frequency of raised total cholesterol, raised triglycerides and raised LDL were higher in group I compared to group II. More than eighty percent (84.0%) of the patients had raised total cholesterol and raised triglyceride. The risk of developing dyslipidemia was higher in PCOS patients than that in group-II.

Wild et al. (2011) showed triglyceride levels were 26 mg/dl (95% confidence interval [CI] 17–35) higher and HDL-cholesterol concentrations were 6 mg/dl (95% CI 4–9) lower in women with PCOS²⁷. Iuhas et al. (2012) reported that both total cholesterol and LDL-cholesterol were positively associated only with the presence of PCOS (p<0.05 for total cholesterol, p<0.05 for LDL-cholesterol)¹⁸. No association was observed between HDL-cholesterol levels and the presence of PCOS.

Conclusions:

This study was undertaken to evaluate the lipid status in patients with polycystic ovary syndrome. Most of the patients were in 3rd decade. High LDL level was more associated with PCOS followed by TC, TG and TC:HDL ratio. This study demonstrated a higher level of dyslipidemia specially in PCOS with higher BMI.

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