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# DYSLIPIDEMIA AND ATHEROGENIC RISK IN NON-OBESE PCOS PATIENTS.

Biochemistry

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## ABSTRACT

With a background of few observations of lipid profile and testosterone in non-obese polycystic ovary syndrome(PCOS) females at our region, we have initiated the study. 52 non-obese PCOS female subjects (BMI<25) and 50 control subjects were selected for the study. (S) total cholesterol, VLDL, LDL, HDL, TG and testosterone were measured in PCOS subjects and compared with controls. Significant increase of (S) VLDL, TG, testosterone and significant decrease of (S) HDL were observed in non-obese PCOS female group when compared with non-obese controls. Elevated serum lipids reflected the metabolic state in those patients; all non-obese PCOS patients should be screened for dyslipidemia and serum testosterone for effective cardiovascular risk prevention.

## KEYWORDS

PCOS, Non-obese,Dyslipidemia,testosterone

**Introduction:**
Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorder in adolescence and reproductive age in women. It occurs in 5%-10% of women of same age group. Furthermore, It is one of the predominant cause of female infertility [1,2]. This condition is characterized by chronic anovulation, hyperandrogenism and polycystic ovarian changes found by ultrasound examination [3]. Clinical and biochemical features of PCOS are, acne, hirsutism, irregular menstruration, infertility, obesity, glucose intolerance, and hyperinsulinemia [4,5].

Increased risk of diabetes mellitus and cardiovascular disorder were observed in PCOS patients with obesity[6]. Dyslipidemia, Insulin resistance, and hyperandrogenism, are presumed to be the major risk factors for cardio vascular disease (CVD) in women with PCOS [7,8]. Insulin resistance and dyslipidemia allegedly plays a key role in the development of CVD in PCOS women [9]. The extent to which the alteration of lipid profile leads to this risk is still not well understood, being the major fact is that dyslipidemia is one of the most common abnormality in PCOS with increase in serum triacylglycerol(TGs), cholesterol, low density lipoprotein(LDL-C) and decrease in high density lipoprotein(HDL-C)[10]. These alteration of lipid profile may be a risk factor of CVD in younger age group with normal BMI [11].

Obesity itself may be a cause of dyslipidemia, furthermore, there is a very little review found regarding dyslipidemia among non obese PCOS females at our region.

Those facts encouraged us to undertake the work of evaluation of lipid profile in non-obese PCOS female and to compare them with weight matched controls.

**Materials and methods:** This cross sectional, hospital based study was carried out in the Department of Biochemistry, Calcutta National Medical College Kolkata, West Bengal.

**Inclusion criteria:** 52 PCOS non obese patients age group 20-45 years,BMI<25 kg/m2 were recruited from Outpatient department of Endocrinology ,Calcutta National Medical College. Diagnosis was based on Rotterdam criteria (2003) with any two of the following. (1) Chronic anovulation presented by either oligomenorrhoea or amenorrhoea. (2)Clinical/Biochemical signs of hyperandrogenism (hirsutism/obvious acne/elevated testosterone. (3)Polycystic ovaries on USG (multiple small follicles).

**Selection of controls:** 50 Healthy female matched for age and BMI<25 kg/m2 without PCOS, having normal menstrual cycle.

**Exclusion criteria:** Study subjects taking oral contraceptive pills. Pregnancy, taking any medications to affect endocrine parameters or lipid profile, smokers, hypertension, diabetes, dyslipidemia, thyroid diseases, hyperprolactenemia, ovarian tumour.

**Sample collection and processing:** The blood samples were drawn after overnight fasting of 12 hours, in the morning; 5 ml of blood were collected from the study population. The blood samples were centrifuged at 3000 rpm for 10 mins and serum was obtained. Samples were analysed in the same day by automatic analyser and ELISA reader.

Analysis was done for (S) cholesterol,triglyceride,VLDL,HDLC, LDLC, and testosterone.

**Ethical permission:** The study was approved by Institutional ethics committee. Written consent was taken from the patients.

**Statistical analysis:** The results were expressed in terms of mean±SD. The test of significance used was student t test and p value <0.05 was cocsidered statistically significant.

**Observations and results:**
**Table 1- Anthropometric parameters of subjects :**

| Age/BMI | Non-obese PCOS cases(n=52) | Non-obese Controls(n=50) | Statistically significance |
|---|---|---|---|
| Age in yrs-mean±SD | 38.09±2.05 | 38.02±3.6 | NS |
| BMI kg/$m^2$ mean±SD | 21.36±1.54 | 22.39±1.87 | NS |

NS- not significant

**Table 2- Serum lipid profile in non-obese PCOS females and non-obese terone controls:**

| Biochemical parameter | PCOS (n=52) | Control (n=50) | P value | 95% CI | t | Standard error of mean |
|---|---|---|---|---|---|---|
| (S)Cholesterol (Mean± SD) | 167.18± 19.38 | 169.60± 17.80 | 0.51 | -9.73 to 4.89 | 0.6561 | 2.68 |
| (S)VLDL(Mean± SD) | 22.94± 5.8 | 19.20± 2.8 | <0.0001 | 1.93± 5.54 | 4.1207 | 0.80 |
| (S)LDLC (Mean± SD) | 98.62 ± 13.5 | 100.35 ± 16.35 | 0.56 | -7.61 to 4.15 | 0.5837 | 1.87 |
| (S)HDLC (Mean± SD) | 44.21± 4.23 | 48.80 ± 4..71 | <0.0001 | -6.34 to -2.83 | 5.1824 | 0.58 |
| (S)Triglyceride (Mean± SD) | 121.32± 27.80 | 96.70± 16.2 | <0.0001 | 15.63 to 33.60 | 5.43 | 3.85 |
| (S) testosterone: (ng/ml) | 0.97±0.11 | 0.51±0.09 | <0.0001 | 0.42 to 0.49 | 23.06 | 0.0153 |

TC- Total cholesterol, VLDL- Very low density cholesterol, LDL- Low density lipoproteins, HDL- High density lipoproteins.

**Observations:** The results of our study have clearly shown that there is no significant difference of (S) TC between PCOS females and control group (p=0.51), as well as in (S) LDLC (p=0.56). Significant difference were observed in (S) VLDL (p<0.0001),(S) HDLC (p<0.0001) and (S) TG (p<0.0001) between PCOS females and controls.

The LDL/HDL ratio in PCOS females is 2.23 (low risk), TG/HDL ratio is 2.74 and NHDL/HDL ratio also 2.74 among the PCOS females are of borderline risk. No correlation found between lipid profile and (S) testosterone in case group.

**Discussion:** From the results of our study we have gathered the following facts.

Significant difference (p<0.0001) were observed in (S) VLDL, HDLC, TG and (S) testosterone between non-obese PCOS females and controls, whereas no such significant difference were observed in case of TC(p=0.51) and LDLC(p=0.56).

Shoaib OM et al [10] found significant increase of TC, TG, and LDL and significant decrease of HDL in PCOS females when compared with controls.We also indicated that trend. In another study, Amini L et al [12] observed the significant increase of TG in PCOS patients with BMI>25 when compared with non PCOS controls. Furthermore, Manjunatha S et al [11]found that the (S) TG,TC, LDLC, VLDLC, were significantly raised while HDLC, significantly decreased in PCOS patients than normal women. These findings corroborated with our study.On the other hand, our results were not concurrent with the study done by Bickerton et al, who demonstrated that there was no significant difference in lipid or lipoprotein concentrations between patients with PCOS and weight matched controls [13].

Cardiovascular risk factors seem to cluster in women with PCOS. Dyslipidemia is one of the important risk factor associated with PCOS. The increase in TG may be due to accumulation of TG, resulting from increased lipogenesis, decreased clearance or reduced fatty acid oxidation. Increased secretion of VLDL particles by the liver results in elevated plasma TG concentrations, this may occur due to insulin resistance found in PCOS. Insulin resistance also contributes more catabolism of HDL particles and formation of LDL particles[10]. Cholesterol ester transfer proteins (CETP) may contribute for this[14].Furthermore, hyperandrogenism also contributes to the altered lipid profile. Hyperandrogenism has been associated with increased hepatic lipase activity which has a role in catabolism of HDL particles [10]. Thus PCOS patients have more atherogenic lipid profile, than controls.

Some authors indicated that, lipid abnormalities were closely related to insulin resistance independent of obesity, this finding enlightens us to evaluate the alteration of lipid profile in non-obese PCOS patients [15]. Wild et al observed that the women with PCOS showed lower HDLC levels, higher LDL/HDL ratios, and higher TG levels than regularly menstruating women [16].

More recently, Slowinska-Srzednicka et al [17] indicated the role of insulin in lipid abnormalities observed in hyperandrogenic women with PCOS. They have included obese and non-obese subjects in PCOS and control groups. Women with PCOS showed significantly lowered levels of HDL2 and higher levels of apoB anf TG.Furthermore they found the insignificant correlation between BMI and serum levels of HDL.

Serum testosterone was significantly increased in non-obese PCOS females in comparision to non-obese controls, rise of testosterone may be contributed by hyperandrogenism. Banu IM et al [18]documented that there is no significant difference of serum testosterone between obese and non-obese PCOS,reflected the fact that PCOS is hyperandrogenic independent of body weight.

Alteration to the atherogenic lipid profile, insulin resistance, and high testosterone all contributes for cardiovascular disease and other complications of PCOS patients. Thus PCOS patients should be screened and monitored regularly, to prevent complications associated with cardiovascular diseases.

**Conclusion:** A more atherogenic lipid profile, particularly related to low HDL and high VLDL along with TG , were found in women with non-obese PCOS compared to non-obese controls. Non obese PCOS females should be screened for dyslipidemia to prevent the early cardiovascular complications.

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