MARKERS OF OXIDATIVE STRESS AND SERUM LIPIDS IN PATIENTS WITH POLYCYSTIC OVARIAN SYNDROME

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ABSTRACT: Dyslipidemia and oxidative stress were evaluated in patients with polycystic ovarian syndrome. **MATERIALS AND METHODS:** Total cholesterol, Triglyceride, HDL cholesterol, LDL cholesterol, Malondialdehyde (MDA) and Total antioxidant capacity were measured in serum of PCOS subjects and age matched controls. **RESULTS:** Study group comprised of 31 women with PCOS and control group with 31 healthy volunteers. Mean serum levels of MDA, Cholesterol, Triglycerides and LDL cholesterol were significantly increased and TAC and HDL cholesterol were significantly decreased in PCOS subjects compared to controls.
CONCLUSION: Our results revealed that PCOS is associated with dyslipidemia and altered oxidative status.
KEY WORDS: MDA, PCOS, TAC.

INTRODUCTION: Polycystic ovary syndrome (PCOS) is a syndrome of ovarian dysfunction that is characterized by anovulation, hyperandrogenism, and/or the presence of polycystic ovary (PCO) morphology [1].Obesity and insulin resistance occur frequently in association with this syndrome. A wide variety of risk factors have been studied in association with PCOS, including obesity, insulin resistance, dyslipidemia, endothelial dysfunction, and the presence of the metabolic syndrome [2,3,4,5].

Women with PCOS would be predicted to be at high risk for dyslipidemia because they have elevated androgen levels and are frequently obese. Moreover, since they are also often hyperinsulinemic and insulin resistant, they would also be expected to be at increased risk for the dyslipidemia associated with insulin resistance. Insulin, rather than androgen, levels correlate best with lipid abnormalities, and suppressing androgen levels does not alter lipid profiles in PCOS. Insulin resistance and hyperinsulinemia are also associated with an atherogenic plasma lipid profile. Elevated plasma insulin concentrations enhance very low density lipoprotein (VLDL) synthesis, leading to hypertriglyceridemia. Progressive elimination of lipid and apolipoproteins from the VLDL particle leads to an increased formation of intermediate-density and low-density lipoproteins, both of which are atherogenic. Last, insulin, independent of its effects on blood pressure and plasma lipids, is known to be atherogenic. The hormone enhances cholesterol transport into arteriolar smooth muscle cells and increases

endogenous lipid synthesis by these cells. Insulin also stimulates the proliferation of arteriolar smooth muscle cells, augments collagen synthesis in the vascular wall, increases the formation of and decreases the regression of lipid plaques, and stimulates the production of various growth factors[6,7].

In summary, insulin resistance appears to be a syndrome that is associated with a clustering of metabolic disorders, including non-insulin-dependent diabetes mellitus, obesity, hypertension, lipid abnormalities, and atherosclerotic cardiovascular disease. Oxidative stress, which is generally known to be present in women with PCOS regardless of whether they are lean or have metabolic abnormalities, has been documented in infertile women[8]. And it is also reported to affect IR in these patients[9].

Oxidative stress may influence not only cardiovascular system but also female reproductive system[10].

Products of lipid peroxidation reactions have been widely employed as biomarkers for oxidative stress. MDA, produced during the decomposition of polyunsaturated fatty acids, is one of the stable end products of lipid peroxidation that can serve as a good biomarker. Various studies have measured antioxidant markers to correlate oxidative stress and PCOS and the diverse clinical manifestations of metabolic syndrome including diabetes, obesity and cardiovascular diseases. Total antioxidant capacity is the ability of serum to quench free radical production, protecting the cell structure from molecular damage. Various detection assays for TAC assay measures the combined antioxidant capacity of all its components including vitamins, proteins, lipids, glutathione, uric acid, etc[11].

The aim of our study was to investigate the relationship between PCOS, oxidative stress status and lipid profile in patients with polycystic ovary syndrome.

MATERIAL AND METHODS: In the present study, 31 PCOS patients in the age group of 21-40 years who were admitted to Gynaecology Unit of Mamata General Hospital, Khammam were recruited for the study after obtaining written informed consent (Study group). 31 healthy persons in the corresponding age group were selected from the patient's attendants and hospital staff were recruited as controls (control group).

PCOS was diagnosed according to the Rotterdam criteria[12]. The patients having two or more of the following criteria were defined as PCOS:

1. History of oligo and/or anovulation in reproductive age.
2. Clinical and/or biochemical signs of hyperandrogenism: hirsutism score of >6 and/or high total testosterone level.
3. Typical ovarian imaging of polycystic ovaries on ultrasound: multiple follicles in each ovary measuring 2–9 mm in diameter and/or increased ovarian volume (>10ml).

Fasting lipid profile [Total cholesterol, High density lipoprotein Cholesterol (HDL-cholesterol), Triglycerides] was done to all patients by using enzymatic kits on biochemistry autoanalyser [tulip diagnostics, India]. Low density lipoprotein cholesterol values have long been estimated using the Friedwald formula:

[Total HDL cholesterol] – 20% of the Triglycerides value = Estimated LDL-cholesterol [13].

Malonaldehyde (MDA) is determined as Thiobarbituric acid reactive substances (TBARS)[14,15].

Estimation of Total Antioxidant Capacity using the FRAP (Ferric Reducing Ability of Plasma) assay.TAC assay measures the combined antioxidant capacity of all its components.(16)

The subjects having Diabetes mellitus, Hypertension, Coronary heart disease, endocrine disorders, alcohol abuse, and on lipid lowering drugs are excluded from the study.

STATISTICAL ANALYSIS: Mean±S.D values of all biochemical parameters were calculated in study and control groups and the mean difference was compared by using student't' - Test.

Mean serum cholesterol, LDL-Cholesterol, triglyceride levels were significantly increased in study group when compared to controls and mean serum HDL-Cholesterol level was significantly decreased.(TABLE 1)

These observations are consistent with previously mentioned related studies T Valkenburg O et al[17], Djuro Macut et al[18], Anuradha Kalra et al[19].

Mean MDA level in study group was significantly increased when compared with controls. The Total antioxidant capacity in study group was significantly decreased when compared with controls (TABLE 2).

Present results are consistent with the previous studies Zhang D et al[20], Palacio JR et al [21] and Fenkci V et al[22].

DISCUSSION: In our study we tried to assess lipid profile and oxidative stress in PCOS cases. We observed that mean serum levels of total cholesterol, TG, LDL-C, MDA in cases of PCOS have increased significantly, when compared with controls. Mean serum HDL-C & TAC levels are decreased significantly when compared with controls.

Women with PCOS would be predicted to be at high risk for dyslipidemia because they have elevated androgen levels and are frequently obese. PCOS women are often hyperinsulinemic and insulin resistant, which can lead to dyslipidemia . Elevated plasma insulin concentrations enhance very-low-density lipoprotein (VLDL) synthesis, leading to hypertriglyceridemia. Progressive elimination of lipid and apolipoproteins from the VLDL particle leads to an increased formation of intermediate-density and low-density lipoproteins, both of which are atherogenic (6)

ApoA-1 - apolipoprotein A-1; ApoB - apolipoprotein B; CE - cholesteryl ester, CETP - cholesteryl ester transfer protein; FFA - free fatty acid; HL - hepatic lipase; LPL - lipoprotein lipase; SD LDL, - small dense LDL cholesterol; TG - triglyceride.

Insulin resistance initiates the characteristic triad of high triglyceride level, low HDL cholesterol level and high small dense LDL level. If the concentration of VLDL-transported triglyceride is high, CETP promotes the transfer of LDL cholesteryl ester or HDL cholesteryl ester in exchange for triglyceride. Triglyceride-rich HDL cholesterol or LDL cholesterol can undergo hydrolysis by hepatic lipase or lipoprotein lipase. (22)

CONCLUSION: Dyslipidemia and increased oxidative stress is observed in patients with polycystic ovary syndrome. PCOS women should be evaluated for status of serum lipids and oxidative stress, which aids in the management of these cases. Correction of dyslipidemias and antioxidant supplementation can be beneficial in treatment of PCOS cases. It also reduces the overall morbidity and enhances the prognosis of PCOS.

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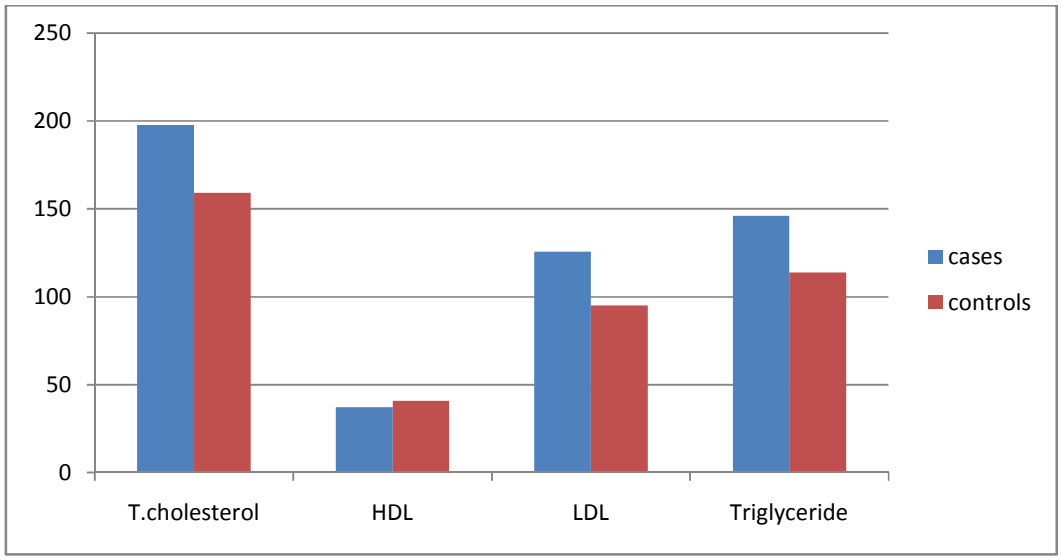
RESULTS: TABLE 1: Mean Total Cholesterol, HDL, LDL, TG Levels In Control Group & Study Group

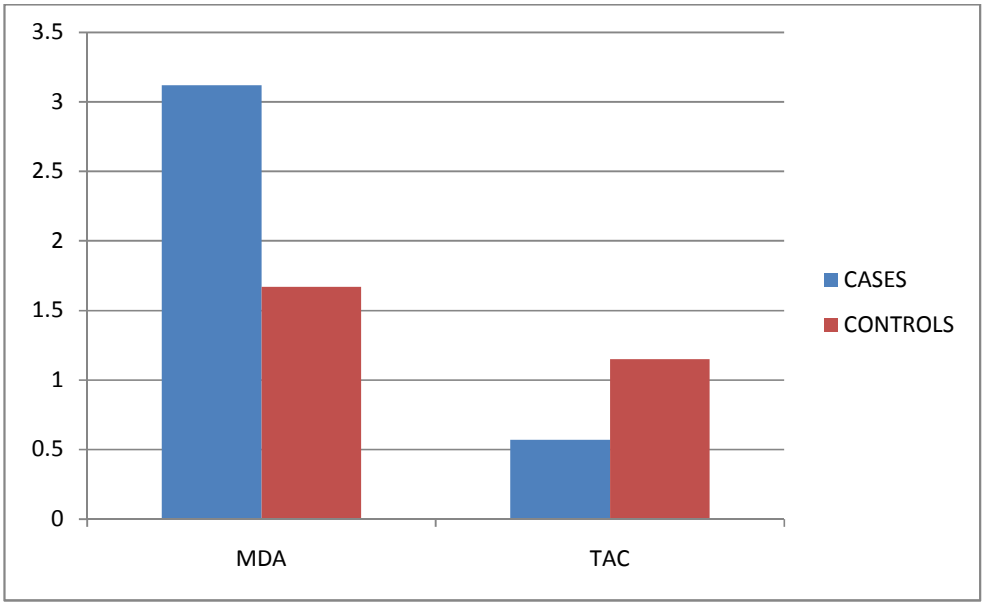
PARAMETERS (mg/dl)	Control group		Study group		P value
	Mean	Std.Dev	Mean	Std.Dev	
T.Cholesterol	159.16	12.87	197.81	37.94	<0.0003
HDL	40.87	3.58	37.13	5.02	<0.0013
LDL	95.13	14.16	125.52	41.29	<0.0003
Triglyceride	113.71	38.36	146.19	57.77	<0.0115



Graph- 1

TABLE 2: Mean MDA &TAC Levels In Control & Study Group

PARAMETERS	Control group		Study group		
	Mean	Std.Dev	Mean	Std.Dev	P value
MDA(nmol/ml)	1.67	0.53	3.12	1.16	<0.0001
TAC(umol/ml)	1.15	0.33	0.57	0.25	<0.0001



Graph -2

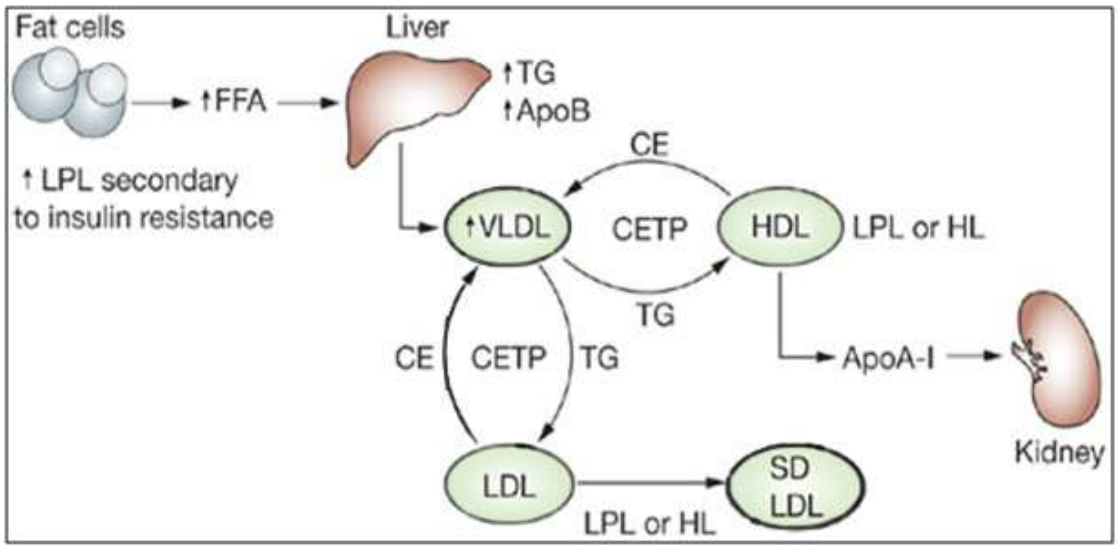


FIG.1:The role of insulin resistance in dyslipidemia