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Oxidative Stress Status Indicated By Serum MDA Levels And Lipid Profile In Obese And Non Obese Women With PCOS.

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ABSTRACT

Polycystic Ovary Syndrome (PCOS) is a multifactorial reproductive healthcare problem affecting 4-12% of women and a leading cause of female infertility worldwide. Over the past decade emerging evidence has shown that Oxidative Stress (OS) indicated by increased MDA (Malondialdehyde) levels, decreased antioxidant status and dyslipidemia are often linked with PCOS. Our study determines lipid profile and OS indicated by MDA were measured in serum of obese and non obese PCOS subjects and age matched controls in women from South India. Case-control study was carried out at the Biochemistry Department, Koppal Institute of Medical Sciences, Koppal, India from July 2015 to March 2018. It included 100 women with PCOS (50- obese and 50 normal) and 100 control subjects (50- obese and 50 normal), aged 18 to 40 years. Fasting lipid profile (cholesterol, high density lipoprotein cholesterol (HDL) and triglycerides) were determined using enzymatic method. Very low density lipoprotein cholesterol (VLDL) value was estimated using the Friedwald formula. Malonaldehyde (MDA) were determined as Thiobarbituric acid reactive substances (TBARS). LDL, VLDL and HDL showed statistical significance between all the groups. However, LDL and VLDL were increased compared to controls and HDL was decreased. In triglyceride all the groups showed statistical significance except between control normal and PCOS normal. In Total cholesterol there was showed statistical significance except between PCOS normal and PCOS obese and control obese and PCOS obese. MDA levels were increased in women with PCOS irrespective of BMI compared to their respective controls with a p value of <0.001, suggesting a significant inverse correlation between PON1 activity and MDA concentrations in women with PCOS irrespective of BMI. Our results revealed that PCOS is associated with dyslipidemia and increased oxidative status indicated by serum MDA levels.

Keywords: Polycystic ovarian syndrome, Lipid profile and MDA

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INTRODUCTION

Polycystic Ovarian Syndrome (PCOS) is an endocrine disorder affecting 5–10% of women in reproductive age, associated with; metabolic syndromes (IR, obesity, hypertension, dyslipidaemia [1, 2], non-metabolic disorders [3]; Cardiovascular Diseases psychological mentality (anxiety, depression, quality of life) and reproductive organs (infertility, hyperandrogenism, hirsutism) [4].

Women with PCOS can be predicted to have dyslipidaemia because they have elevated androgen levels and are frequently obese along with hyperinsulinemic and 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 [5].

Oxidative stress (OS) which plays a key role in the pathogenesis of cardiovascular disease (CVD) has been documented in obese PCOS women. Oxidative stress may influence not only on cardiovascular system but also on female reproductive system leading to infertility [6]. Thus, playing a key role in the pathophysiology of PCOS but the exact cause of OS in PCOS is not completely understood. Studies suggests that the presence of IR and hyperglycemia seen in PCOS women are profound factors to increase the oxidative stress. Oxidative stress defined as an imbalance between the production of ROS and antioxidant defense system is an important component in PCOS women [7].

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. Total antioxidant capacity is the ability of serum to quench free radical production, protecting the cell structure from molecular damage [8].

The lifestyle of women with PCOS presents the corner stone for an optimal treatment and has shown to improve body composition, hyperandrogenism and IR in women with PCOS [9, 10]. Modifications such as weight reduction and exercise have been found to improve menstrual disturbance and infertility in obese PCOS women. A reduction in central fat and improved IR sensitivity has also improved their reproductive systems [11].

MATERIALS AND METHODS

A Case-control study was conducted on 100 PCOS patients (50- obese and 50 non-obese) and 100 (50-obese and 50 non-obese) controls in the age group of 18-40 years. Women under the age of 18 years and women suffering from any known diseases were excluded from the study. Fasting blood sample of 5.0 ml was obtained from each subject who participated in the study. Fasting lipid profile [total cholesterol, high density lipoprotein cholesterol (HDL) and triglycerides] was done using enzymatic kits with biochemistry autoanalyser [ERBA XL640]. Low density lipoprotein cholesterol and VLDL values have long been estimated using the Friedwald formula. Malonaldehyde (MDA) is determined as Thiobarbituric acid reactive substances (TBARS) Ethical approval was obtained from the Ethics Committee at the college for research to be conducted. Obese and non-obese women with and without PCOS between the ages of 18-35 years were included. Physical examination of each subject was carried out. The height and weight of all individuals were measured. Body mass index (BMI) was measured as kg/m2. Diagnosis of PCOS was done according to the Rotterdam ESHRE revised consensus 2003. Subjects included in the study were never on any hormonal contraceptives, aspirin, statins, vitamin supplements or any other significant drug therapy.

Women under the age of 18 years, over the age of 40 years and women suffering from any known diseases, any infections and inflammatory conditions, congenital adrenal hyperplasia, hyperprolactinemia, Cushing's syndrome were excluded from the study.

The ethics committee approval was obtained from the institutional ethics committee. Patients were informed about the research being conducted and asked to give their consent to participate in the study. The mean ± SE were then compared by one way ANOVA with Student Newman Keul's multiple

comparison test. The p value of <0.05 is considered statistically significant and <0.001 as highly significant.

RESULTS

Total of 100 women diagnosed as having PCOS (50- Obese and 50 non Obese) and 100 as being normal without PCOS (50- Obese and 50 non Obese) were included in the study. The mean age of obese with PCOS women were 25.4 ± 4.12 when compared to the mean age of obese women without PCOS 24.5 ± 2.11) with a p=0.11 which was good for comparison as there were no statistical difference. The mean age of non-obese with PCOS women were 23.0 ± 2.99 when compared to the mean age of non-obese women without PCOS 25.1 ± 3.44) with a p=0.11 which was also good for comparison as there were no statistical difference.

Serum levels of total cholesterol in obese women with PCOS 196.00 (184.00, 213.00) and non-obese women with PCOS 184.00 (151.00, 198.50) compared to their controls 185.00(156,193) and 108.50 (94.75, 128.00) respectively with a p value of <0.001

There were higher levels of serum triglyceride levels in obese women with PCOS (167.03±36.74) and non-obese women with PCOS(131.12±36.71) compared to their controls respectively (130.70±32.8 and 92.74±30.0), However all the four groups had triglyceride levels within the reference range with a p value of <0.01. There were low levels of serum HDL in obese women with PCOS (20.70±5.4) and non-obese women with PCOS (28.80±8.45) compared to their controls respectively (31.92±7.5and 37.02±7.5), However all the four groups had HDL levels within the reference range with a p value of <0.01. There were also higher levels of serum LDL in obese women with PCOS (141.51±26.8) and non-obese women with PCOS(127.97±24.96) compared to their controls respectively (119.46±32.99 and 57.37±38.20) with a p value of <0.01. There were higher levels of serum VLDL in obese women with PCOS (33.25±7.27) and non-obese women with PCOS (26.23±7.39) compared to their controls respectively (26.05±6.51 and 26.23±6.02) with a p value of 0.00.

Serum MDA levels in obese women with PCOS (7.14±0.54) and non-obese women with PCOS (5.54±0.32) compared to their controls (3.96±0.42) and (1.91±0.40) respectively with a p value of <0.001.

Table 1: Baseline characteristics in obese and non-obese women with PCOS and controls

	Non -Obese			Obese		
Characteristics	**Cases**	**Control**	**P Value**	**Cases**	**Control**	**P Value**
Age (Years)	23.0±2.99	25.2±3.44		25.4±4.12	24.5±2.11	
BMI (kg/m2)	25.2±4.86	21.6±2.53		35.2±4.39	32.7±3.05	
Cholesterol	185.0 (156,193)	108.50 (94.75, 128.00)	<0.001	196.00 (184.00, 213.00)	184.00 (151.00, 198.50)	<0.001
TGL	131.12±36.71	92.74±30.0	<0.001	167.03±36.74	130.70±32.8	<0.001
HDL	28.80±8.45	37.02±7.5	<0.001	20.70±5.4	31.92±7.5	<0.001
LDL	127.97±24.96	57.37±38.20	<0.001	141.51±26.8	119.46±32.99	<0.001
VLDL	26.23±6.02	18.56±7.39	<0.001	33.25±7.27	26.05±6.51	<0.001
MDA (nmol/ml)	5.54±0.32	1.91±0.40	<0.001	7.14±0.54	3.96±0.42	<0.001

DISCUSSION

In our study the lipid profile were significantly increased in both obese and non-obese PCOS cases compared to controls, Similar observations were made by Tao Zuo et al [12], Desai V et al [13], Karabulut AB et al [14], Valkenburg TO et al [15], Djuro Macut et al [16], Anuradha Kalra et al [17], Unni NC et al [18].

PCOS patients have demonstrated oxidative stress due to hyperglycemia, insulin resistance and chronic inflammation. OS is increased due to IR as hyperglycemia and higher levels of free fatty acid leads to excess production of ROS. Hyperglycemia also plays a role in inflammation by producing TNF α from MNC. Studies conducted in lean healthy reproductive age women having hyperglycemia suggest that excess androgen increases the generation of ROS from leukocytes, p47phox gene expression and formation of MDA. The presence of OS in absence of obesity could be due to diet induced OS and hyperandrogenism being the progenitor. OS increases chronic inflammation and vice versa [19].

Serum levels of malondialdehyde (MDA) which is the end product of lipid peroxidation and regarded as a marker of oxidative stress assessment are statistically elevation in both obese and non-obese PCOS (P= <0.005). Similar observatios were made by various other studies. Karabulut AB et al [14], Biplab Mandal et al [20], Zhang D et al [21], Palacio JR et al [22], and Fenkci V et al [23].

MDA is one of the most common biomarker to assess the oxidant status, as its levels correlates with the extent of lipid peroxidation. Free radicals in the body stay for a short duration before achieving stability by colliding with another molecule to either recieve or donate an electron, in the process they generate another free radical (ROS). These ROS targets proteins, carbohydrates, nucleic acids and Polyunsaturated fatty acids (PUFA), present in the cell membrane known as lipid peroxidation forming various end products among which malondialdehyde (MDA) is one of the important end products of this process.. This process is opposed by antioxidant enzymes thus redox balance of cell. The imbalance between oxidants and antioxidants leads to Oxidative Stress [19].

CONCLUSION

In the present study we found dyslipidaemia and increased oxidative stress indicated by elevated levels of MDA in obese and non-obese patients with polycystic ovary syndrome. These are the risk factors for CVD due in PCOS women. Hence PCOS women should be evaluated for status of serum lipids and oxidative stress.

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