ORIGINAL ARTICLE

Coronary Risk Factors and Oxidative Stress in Women with PCOS

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Abstract

Introduction: Polycystic ovary syndrome (PCOS) affects 5–10% of women in reproductive age. It is associated with metabolic syndromes and non-metabolic disorders. Women with PCOS have dyslipidemia and oxidative stress representated by elevated serum Malonaldehyde (MDA) levels. These features are risk factors for development of atherogenesis and cardiovascular disease (CVD).

Materials and methods: A case-control study was conducted at the Department of Biochemistry, Koppal Institute of Medical Sciences, Koppal, India. It included 100 diagnosed PCOS patients (50- obese and 50 non-obese) and 100 controls (50-obese and 50 non-obese) in the age group of 18-40 years. The mean±SD were compared using student't' – Test from the SPSS Statistics Data Editor version 21. Kruskal–Wallis test was employed for p values. The p value of <0.05 is considered statistically significant.

Results: Serum levels of total cholesterol, serum triglyceride, LDL, VLDL were higher in women with PCOS irrespective of BMI with p value of <0.001.There were low levels of serum HDL in women with PCOS irrespective of BMI with *p* value of <0.001. Serum MDA levels were higher in women with PCOS irrespective of BMI with p value of <0.001.

Conclusion: Dyslipidemia and increased OS indicated by elevated levels of MDA are seen in women with PCOS irrespective of BMI. Hence, PCOS women should be evaluated for lipid profile and oxidative stress and should be treated with antioxidant supplementation, which can be beneficial in preventing coronary vascular diseases.

Keywords: BMI, CVD, Dyslipidemia, MDA.

Indian Journal of Medical Biochemistry (2019): 10.5005/jp-journals-10054-0101

Introduction

Polycystic ovary syndrome (PCOS) is the most common endocrine disease in women of reproductive age group with a wide spectrum of clinical manifestations.[1-4] Women with PCOS have dyslipidemia because they have elevated androgen levels and are frequently obese along with hyperinsulinemia and insulin resistance. More than androgen levels of insulin levels correlate best with lipid abnormalities. Treatment of hyperandrogen levels does not alter lipid profiles in PCOS.[5] Similar features are also seem to be associated with atherogenesis and cardiovascular disease (CVD). Increased plasma insulin levels induce more very low-density lipoprotein (VLDL) synthesis, causing hypertriglyceridemia. As the lipid and apolipoproteins are eliminated from the VLDL particle intermediate-density and low-density lipoproteins are formed, both of which are atherogenic.[5]

Oxidative stress (OS) is associated with CVD as well as obese women with PCOS. Oxidative stress effects female reproductive system leading to infertility,[6] thus takes part in the pathophysiology of PCOS. However, the functional cause of OS in PCOS is not clear. Studies suggest that the presence of IR and hyperglycemia in women with PCOS are main factors to cause OS. Oxidative stress defined as a disharmony between the production of ROS and antioxidant mechanism, which is an important component in PCOS women.[7]

Polyunsaturated fatty acids (PUFA) present on cell membranes is attacked by oxidizing radicals, causing lipid peroxidation and malondialdehyde (MDA) produced is one of the stable end products of lipid peroxidation that can serve as a good biomarker.[8]

Alterations in the lifestyle such as weight loss and reduction of weight in women with PCOS stay the main component of treatment that improves BMI, menstrual disturbances, infertility, hyperandrogenism, and IR.[9-11]

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How to cite this article: Bannigida DM, Nayak SB. Coronary Risk Factors and Oxidative Stress in Women with PCOS. Indian J Med Biochem 2019;23(2):267-269.

Source of support: Nil

Conflict of interest: None

Materials and Methods

We conducted a case-control study at the Department of Biochemistry, Koppal Institute of Medical Sciences, Koppal, India from July 2015 to March 2018. It included 100 diagnosed PCOS patients (50 obese and 50 nonobese) and 100 controls (50 obese and 50 nonobese) in the age group of 18–40 years. Women suffering from any known diseases, any infections, and inflammatory conditions were excluded from the study. Fasting blood sample of 5.0 mL was obtained from cases and controls. Fasting lipid profile [total cholesterol, high-density lipoprotein cholesterol (HDL) and triglycerides] was done using enzymatic kits with biochemistry autoanalyzer (ERBA XL640). Low-density lipoprotein cholesterol (LDL) was calculated using the Friedwald formula. Serum malonaldehyde (MDA) was determined by Thiobarbituric acid reactive substances (TBARS). Ethical clearance

was taken from the Ethics Committee of the college. Patients were informed about the research being conducted and asked to give their oral consent of participating in the study. Physical examination included height and weight of all individuals. Body mass index (BMI) was calculated as kg/m^2. 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.

Statistical Analysis

The mean ± SD were compared using student 't'–test from the Statistical Package for Social Sciences (SPSS) statistics data editor version 21. 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) were compared with 100 controls without PCOS (50 Obese and 50 nonobese).

Serum levels of total cholesterol were higher in obese women with PCOS 275.08 ± 20.2 and nonobese women with PCOS 163.64 ± 30.1 compared to their controls 192.96±13.2 and 149.34 ± 15, respectively with p value of <0.001 (Table 1).

Serum levels of serum triglyceride levels were higher in obese women with PCOS 167.03 ± 36.74 and nonobese women with PCOS 131.12 ± 36.71 compared to their controls respectively 130.70 ± 32.8 and 92.74 ± 30.0 with a p value of <0.001 (Table 1).

There were low levels of serum HDL in obese women with PCOS 20.70±5.4 and nonobese women with PCOS 28.80 ± 8.45 compared to their controls respectively 31.92 ± 7.5 and 37.02 ± 7.5, with p value of <0.001 (Table 1).

Serum levels of serum LDL were higher in obese women with PCOS 141.51 ± 26.8 and nonobese women with PCOS 127.97 ± 24.96 compared to their controls respectively 119.46 ± 32.99 and 57.37 ± 38.20 with p value of <0.001 (Table 1).

There were higher levels of serum VLDL in obese women with PCOS 33.25 ± 7.27 and nonobese women with PCOS 26.23 ± 7.39 compared to their controls respectively 26.05 ± 6.51 and 26.23 ± 6.02 with *p* value of <0.001(Table 1).

Serum MDA levels were higher in obese women with PCOS 7.14 ± 0.54 and nonobese women with PCOS 5.54 ± 0.32 compared to their controls 3.96 ± 0.42 and 1.91 ± 0.40, respectively with *p* value of <0.001 (Table 1).

Discussion

Dyslipidemia was observed in both obese and nonobese PCOS cases compared to their controls. Similar observations were made by other studies.[12-18]

PCOS patients exhibit oxidative stress due to hyperglycemia, IR and chronic inflammation, that leads to overproduction of ROS. Hyperglycemia produces tumor necrosis factor α (TNF α) from multinuclear cells (MNC) thus playing a role to inflammation. Some studies conducted on healthy women with hyperglycemia have higher levels of ROS due to androgenic stimulation of leukocytes, p47phox gene expression, and formation of MDA. Nonobese women with PCOS also exhibit diet-induced OS with hyperandrogenism being the progenitor. OS and chronic inflammation express a vicious cycle.[19]

Serum level of MDA which is the end product of lipid peroxidation was significantly elevated in both obese and nonobese PCOS. Similar observations were made by various other studies.[14-23]

As levels of MDA correlate with the extent of lipid peroxidation, it can serve as a common biomarker to assess the oxidant status. Free radicals in the body stay for a short duration before achieving stability by colliding with another molecule to either receive or donate an electron, eventually generating free radical (ROS). These ROS target proteins, carbohydrates, nucleic acids and polyunsaturated fatty acids (PUFA), present in the cell membrane forming various end products. This process is opposed by antioxidant enzymes thus maintaining the balance of the cell. The loss of harmony between oxidants and antioxidants leads to oxidative stress.[19]

Conclusion

Dyslipidemia and increased levels of serum MDA represent OS seen in women with PCOS irrespective of BMI. Hence, PCOS women should be evaluated for lipid profile, oxidative stress and should be treated with antioxidant supplementation, which can be beneficial in preventing coronary vascular diseases.

This study can deepen our knowledge about the key role of dietary modifications and drug treatments of metabolic disorders in improving the cardiovascular risk in PCOS woman. Detection of inflammatory markers can reduce the overall morbidity and enhances the prognosis of PCOS.

Clinical Significance

Treating physicians should be aware of coronary heart disease in women with PCOS.

Table: 1 Characteristics in 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/m^2)	25.2 ± 4.86	21.6 ± 2.53		35.2 ± 4.39	32.7 ± 3.05	–
Cholesterol (mg/dL)	185.00 (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 (mg/dL)	131.12 ± 36.71	92.74 ± 30.0	<0.001	167.03 ± 36.74	130.70 ± 32.8	<0.001
HDL (mg/dL)	28.80 ± 8.45	37.02 ± 7.5	<0.001	20.70 ± 5.4	31.92 ± 7.5	<0.001
LDL (mg/dL)	127.97 ± 24.96	57.37 ± 38.20	<0.001	141.51 ± 26.8	119.46 ± 32.99	<0.001
VLDL (mg/dL)	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

Acknowledgments

Authors wish to express their indebtedness to the Koppal Institute of Medical Sciences, Koppal and their laboratory staff for their technical support.

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