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IJPBS |Volume 5| Issue 3|JUL-SEPT|2015|01-07

Research Article
Biological Sciences

A COMPARATIVE STUDY OF OXIDATIVE STRESS AND ANTIOXIDANT STATUSIN TYPE 2 DIABETES MELLITUS WITH AND WITHOUT PCOS IN AND AROUND THE INDORE REGION

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ABSTRACT

***Background**: Diabetes Mellitus is known to be associated with increased oxidative stress; polycystic ovarian syndrome (PCOS) is one of the most common endocrine diseases of women. **Aim**: The aim of the study iscomparison of oxidative stress and antioxidant status in T2DM patients with and without polycystic ovary syndrome. **Methods:** Three hundred T2DM (Type 2 Diabetes Mellitus) with and without PCOs patients attending the Medicine & Gynecology outpatients Departments at SAIMS Indore. 150 T2DM with PCOS patients, 150 T2DM without PCOS patients. The change in MDA, SOD, CATALASE, TAC were measured in all patients.*

***Results:** TAC, Catalse was found to be statistically significant (P<0.001) . SOD, MDA was found to be not significant (P>0.005) using independent sample 't' test. **Conclusion:** The result of our study revealed that T2DM, PCOS is associated with imbalanced oxidative/ antioxidative status.*

KEY WORDS

Type 2 Diabetes Mellitus (T2DM), Polycystic ovarian syndrome (PCOS), Oxidative stress, Antioxidant Status, MDA, SOD.

INTRODUCTION

Diabetes mellitus (DM) is one of the most frequent chronic diseases worldwide, being among the top five main causes of death in developed countries. This endocrine disease is also becoming epidemic in developing countries[1].The prevalence of diabetes is rising all over the world duetopopulationgrowth, aging, urbanisation, and the increaseofobesity due to physical inactivity. Asper estimate of the International Diabetes Federation (IDF),the total number of people in India with diabetes which wasaround 50.8million in 2010 would be 87.0million by 2030[2].

Polycystic ovary syndrome (PCOS) is one of the most common and heterogeneous endocrine disorders among women of reproductive age. The prevalence is estimated at 5-10% (knochenhauer et al 1998, Azziz et al 2004,Goldenbery N et al 2008)[3]. It is a heterogeneous disorder of chronic anovulation and hyperandrogensim and it is often associated with obesity and insulin resistance[4]. It is one of the most common causes of anovulatoryinfertility associated with long-term

consequences such as type 2 diabetes mellitus, endometrial hyperplasia, and coronary arterydisease[5]. The new definition of PCOS suggested that the diagnosis of PCOS must be based on the presence of two of the three following criteria: (i) oligo- and/or anovulation, (ii) clinical and/or biochemical signs of hyperandrogenism, and (iii) polycystic ovaries on ultrasonography and exclusion of related disorders[6,].The ultrasound criteria for polycystic ovaries is defined as the presence of 12 or more follicles measuring 2 to 9 mm in diameter and /or an increased ovarian volume > 10 cm3 on transvaginal ultrasound scanning.PCOS is diagnosed even when only one polycystic ovary is present [7].

Oxidative stress plays a pivotal role in cellular injury fromhyperglycemia. High glucose level can stimulate free radicalproduction. Weak defence system of the body becomesunable to counteract the enhanced ROS generation and as aresult condition of imbalance between ROS and their protectionoccurs which leads to domination of the condition ofoxidative stress[8]. However overand/or uncontrolled production of ROS is deleterious.Due tooxidative stress the metabolic abnormalities of diabetes causemitochondrial superoxide overproduction in endothelialcells of both large and small vessels, as well as in the myocardium[9].

Oxidative stress is commonly referred as the imbalancebetween oxidants and antioxidants. When the imbalance favorsoxidants, generation of excessive amounts of reactiveoxygen species harm our body in various waysthroughthe generation of excessive amounts of reactive oxygen species[10]. Oxidative stress is also known to independently contribute to endothelial dysfunction.

The aim of our study was comparison of oxidative stress and antioxidant status in T2DM patients with and without polycystic ovary syndrome.

MATERIALS AND METHODS

The present study conducted in the Department Of Biochemistry in collaboration with Departments of Gynecology, obstetrics, & Medicine, SAIMS MEDICAL COLLEGE & PG INSTITUTE, Indore.Three hundred women, were included in the study. Consent was taken from all subjects and the institutional review board, that looks into ethical aspects of human experimentation approved the study. In this study individuals were aged between 20-60 years, according to the world Health Organisation (WHO) definition.

Laboratory evaluation.

Patients with acute and chronic inflammatory conditions were excluded from the study. 8 ml of venous blood sample was collected in fasting condition processed and preserved for the analysis of various parameters: age, anthropometric, hemodynamic parameters, fasting glucose was estimated by standard diagnostic laboratory methods. SOD was estimated by Marklund and Marklundmethod. MDA was estimated by Jean C.D. method.Catalase (CAT) was estimated byAebi.H method. Total antioxidant capacity(TAC)was estimated by D.Koracevic et.al method.

PCOS diagnosed according to the Rotterdam criteria[6]. 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 (>10 ml).

Statistical analysis:

The statistical analysis were performed SPSS for windows version 20 program. All data were reported as mean ± standard deviation (SD).The variables showed normal distrubition(P,<0.05). So, independent sample 't' test was used for comparison of variables between the groups. Statistical significance was defined as p<0.05.

RESULTS

Table No: 1 Fig No:1 shows the baseline characteristics in the both groups. Both groups were similar in terms of BMI, systolic blood pressure (SBP) and diastolic blood pressure (DBP).

Comparison of biochemical parameter between both groups age and fasting glucose was found to be statistically significant (P<0.001) .

BMI and SBP, DBP was found to be statistically not significant (P>0.005) using independent sample 't' test.

Table No:1 CHARACTERISTICS OF STUDY GROUPS (T2DM WITH PCOS VS T2DM)

	T2DM with PCOS (n=150)	T2DM (n=150)	t	P
AGE	33.9±5	45.4±7.9	-14.317	.000
BMI	27.52±2.2	27.20±2.3	1.219	.224
SBP	125±7	128±8	-1.130	.259
DBP	81±5	81±6	.049	.961
FASTING GLUCOSE	140±17	179±34	-12.622	.000

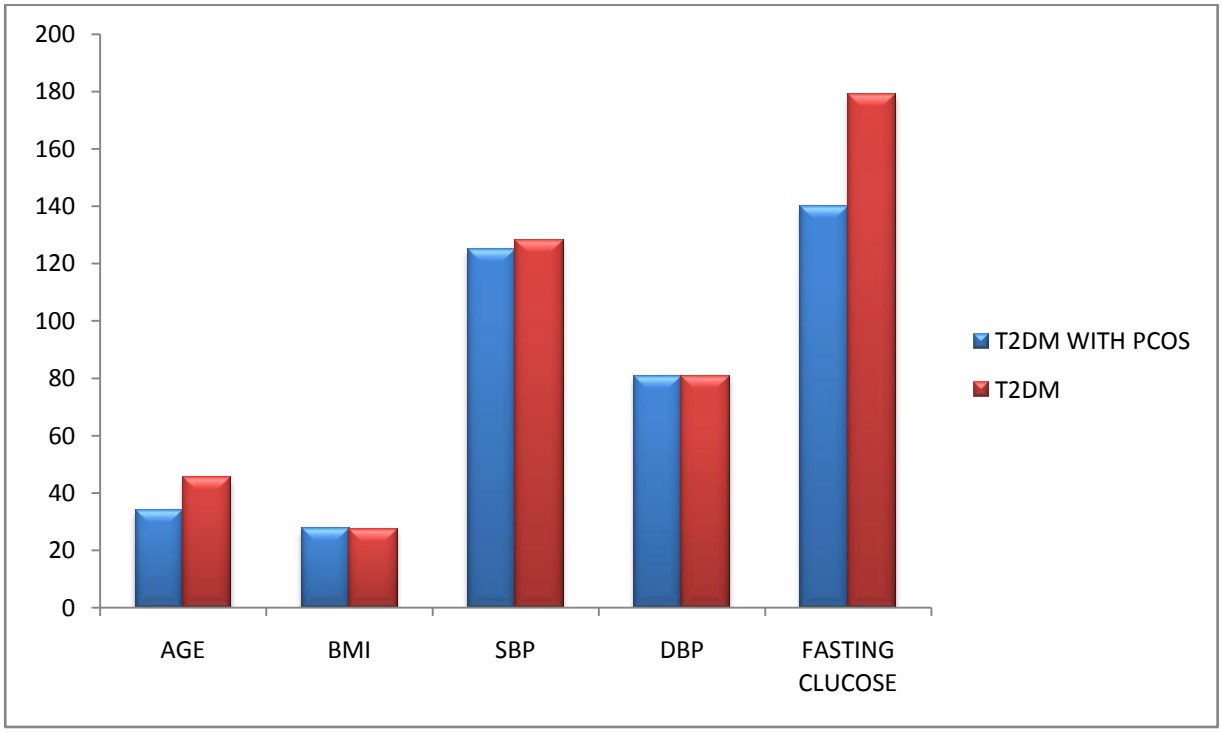

Fig No:1 CHARACTERISTICS OF STUDY GROUPS (T2DM WITH PCOS VS T2DM.

Table No : 2 COMPARISON OF ANTIOXIDENTS VARIABLES BETWEEN T2DM WITH PCOS AND T2DM

ANTI OXIDENTS VARIABLES	T2DM with PCOS (n=150)	T2DM (n=150)	T	P
	Mean ± SD	Mean Standard Deviation		
SOD (U/g of Hb)	3.2 ± .5	3.2 ±.6	.129	.898
CATALASE (U/g of Hb)	3.6 ± .5	3.4 ± .7	3.320	.001
MDA (nmol/ml)	5.6 ± .6	5.6 ± 1.0	.286	.775
TAC (mmol/l)	.9 ± .2	1.0 ± .3	-2.190	.030

Table No: 2 Fig No:2 shows that comparison of ANTIOXIDENTS VARIABLES between both groups CATALASE, TAC was found to be statistically significant (P<0.001) .

SOD & MDA was found to be statistically not significant (P>0.005) using independent sample 't' test.

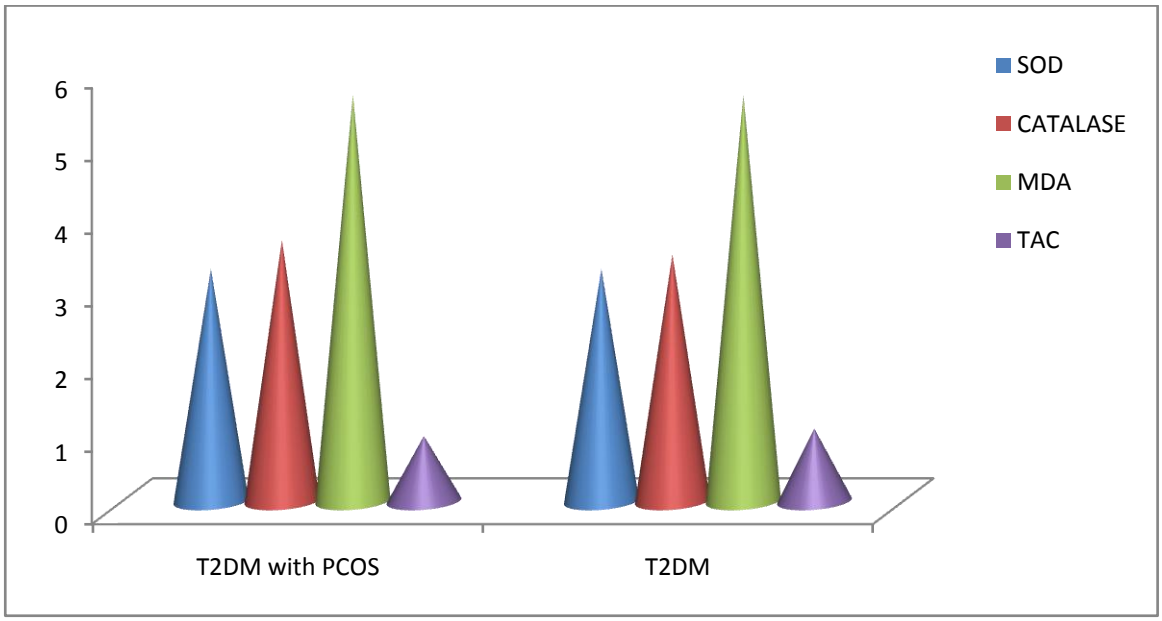

Fig No :2 COMPARISON OFANTIOXIDENTS VARIABLES BETWEEN T2DM WITH PCOS AND T2DM.

DISCUSSION

In the current study SOD was found to be statistically not significant (P>0.005). SOD is the important antioxidant enzyme having an antitoxic effect against super oxide anion. The over expression of SOD might be an adaptive response and it results in increased dismutation of superoxide to hydrogen peroxide. This is in agreement with previous reports[11,12].On the other hand, the erythrocyte antioxidant enzymes i.e. SOD &GPx activities have been increased significantly in patients with PCOS compared to controls[13].However, a few other studies have found increase in oxidative stress even in lean PCOS women[11,12]. Kimura et al[14]suggested that extracellular superoxide dismutase (EC-SOD) levels could serve as a marker for vascular damage, possibly reflecting oxidative damage of vascular endothelium induced by hyperglycemia. Madhur Gupta et al[15]studied that level of SOD

were significantly decreased in diabetics with IHD when compared with the diabetic group without complications.

The present study reported that CATALASE was found to be statistically significant (P<0.001). Catalase is the enzyme, which protects the cells from the accumulation of hydrogen peroxide by dismutating it to form water and oxygen or by using it as an oxidant in which it works as a peroxidase [16]. Shankar Shetty et al[17]Serum Total antioxidants levels, antioxidant enzymes CAT were significantly decreased in type 2 diabetic subjects when compared to normal subject (p<0.05).A study reported that catalase activity were significantly lower in obese women with PCOS compared with healthy controls[3].In most of the studies TAOS was found to be decreased in PCOS women compared to controls [3,18,19].

This oxidative stress has also been implicated as a causal factor for hyperandrogenism in these women [20] .In the present study we found that MDA was statistically not significant (P>0.005) between both groups. On the other hand Erdogan et al. showed no statistically significant difference in mean MDA levels between PCOS patients and control group [21].Hisalkar et al diabetic complications are developed with increased activity of free radical – induced lipid peroxidation and accumulation of lipid peroxidation products[22]. However, in a study from Turkey, total antioxidant status was found to be increased in non-obese women with PCOS [23]. A study wasreported of elevated MDA levels have been reported in patients with PCOS (Yildirim B et alv2005)[11].KUSÇU et al [12]reportedthat MDA level is significantly higher in young, non-obese PCOS patients even in the absence of IR when compared with controls.

Rise in MDA could be due to increased generation of reactive oxygen species (ROS) due to the excessive oxidative damage generated in these patients. These oxygen species in turn can oxidize many other important bimolecular including membrane lipids. Similar reports of elevated MDA levels have been reported in patients with PCOS [24]. In the present study TAC was found to be statistically significant (P<0.001). JAFFAR et al[25]used the total antioxidant capacity (TAC) test and suggested that this approach can be useful to evaluate the impact of drugs or antioxidant treatments on delaying the onset of complications associated with OS. SARITA A SHINDE et al[26]proved that diabetic patients have significantly lower TAS levels as compared to normal controls.

However a few Studies showing oxidative stress in PCOS women have reported conflicting results. A few studies have reported increased oxidative stress in obese[18 , 27] as well as in lean PCOS women[11,12]. However, a recent study done in Chinese population reported increased oxidative stress only in obese PCOS women and not in lean PCOS women [28]. There is one study in Indian women with PCOS which was done in obese individuals [3].

CONCLUSION

Oxidative stress plays pivot role in progression and development of diabetes and its complication. The prevalence of diabetes is rising worldwide due to population growth, aging, urbanization, and increased of obesity due to physical inactivity. Imbalanced antioxidant status in women of both groups. The result of this study haveshowsdecreasedcatalase activity supports to oxidative stress in PCOS. The results of our study emphasize the need for initiating lifestyle measures early and in the overweight category itself.

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