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Oxidative stress level among females with Type 2 Diabetes Mellitus with & without Polycystic Ovarian Syndrome.

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Abstract

Background: The present study aimed to evaluate the level of oxidative stress by measuring the plasma concentration of oxidants in Type 2 Diabetes Mellitus (T2DM) patients with and without Polycystic Ovarian Syndrome (PCOs).

Methodology: A total of 500 diabetic patients between 25 to 45 years of age were divided into two groups; group 1 included 250 T2DM patients with PCOs, and 250 T2DM patients without PCOs were included in group 2. In addition to the demographic and clinical parameters, antioxidants include Superoxide Dismutase (SOD), Malondialdehyde (MDA), Catalase (CAT), Total antioxidant capacity analyte (TAC), and Glutathione Peroxidase (GSH) was also measured.

Results: No significant difference in the level of antioxidants; SOD and MDA was observed between the diabetic females with and without PCOs ($p>0.05$). However, Glutathione Peroxidase (GSH-Px) was significantly low in T2DM patients with PCOs as compared to those without PCOs ($p<0.05$). Surprisingly, the mean catalase levels were significantly high among T2DM females with PCOs (3.6 ± 0 .5 U/g of Hb) than those without PCOs (3.4 ± 0.7 U/g of Hb; $p<0.001$).

Conclusion: It is suggested that both T2DM and PCOs are linked to a high level of oxidative stress status, but the high catalase level among diabetic PCOs females is alarming and needs to be further studied. Thus, these changes accentuate the need for lifestyle modifications.

Keywords

Type 2 Diabetes Mellitus, Oxidative Stress, Polycystic Ovarian Syndrome, Antioxidants.

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Introduction

For decades researchers have been observing diabetes mellitus patterns concerning disease variation, incidence, and prevalence. The burden of diabetes is increasing every second worldwide; it is the most frequent chronic disorder and also among the leading causes of death in the urbanized areas of society. It has been characterized as complex and multifactorial metabolic syndrome, and it has been evolving from metabolic disorder to an inflammatory condition[1]. Moreover, in the pathogenesis of diabetes-related complications, the role of oxidative stress has been widely studied[2].

Evidently, PCOs women display higher oxidative stress levels. In the Pakistani population, the polycystic ovarian syndrome rate is up to 52%[3]. It is one of the most common causes of anovulatory insufficiency associated with long-term effects such as Type 2 Diabetes Mellitus (T2DM), hyperinsulinemia, glucose intolerance, coronary heart disease, and hyperplasia of endometrium wall[4]. Several factors like insulin resistance and hypothalamic-pituitary-ovarian dysregulation play a vital role in its pathogenesis[5]; it also directly relates to dietary habits[6].

It has been seen that mitochondrial dysfunction and cellular alteration are also propagated by oxidative stress[7]. Oxidative stress strongly relates to women's infertility, and it also weakens insulin action[8], as seen in T2DM[2]. Numerous studies demonstrate a high prevalence of T2DM among people of Pakistan and revealed a significant relationship between diabetes and oxidative stress[9-11]. Furthermore, Archibong and his colleagues revealed that PCOs pathophysiology had involvement of oxidative stress. Abnormal oxidative stress markers are observed among PCOs women. Although the relationship between oxidative stress and PCOs isn't completely understood and explained in the literature yet. But few studies suggest that oxidative stress alters steroidogenesis and leads to high androgen levels disturbing the follicular development[12].

The existing polycystic ovarian syndrome criteria suggest the presence of anovulation with symptoms of hyperandrogenism and ultrasonography for the confirmation of polycystic ovaries measuring up to 9 to 10 mm in diameter with 12 particle numbers[13]. High glucose levels promote free radical production[14], and the weakened immune system cannot fight off the improved reactive oxygen species [ROS] synthesis. Its imbalance leads to the dominance of oxidative pressure[15]. This chemical imbalance leads to the production of excess concentrations of ROS, which harms vital organs of the body through different forms of production of high levels of active oxygen[16]. Therefore, it is essential to evaluate the oxidative stress level; hence, the present study aimed to evaluate the level of oxidative stress by measuring the plasma concentration of oxidants in T2DM females with and without PCOs.

Methodology

In this cross-sectional study, a total of 500 T2DM female patients presenting at the Government College Women University, Faisalabad-Pakistan during May 2019 to June 2020 were enrolled and divided equally into two groups, group 1 (T2DM patients with PCOs) and group 2 (T2DM patients without PCOs). All the non-consenting patients and those with other comorbidities were excluded from the study sample.

Whole blood samples of 10 ml were collected both in fasting and postprandial condition. Fasting and postprandial glucose, glycated hemoglobin, serum fasting, and postprandial insulin were measured using an automation enzymatic assay. SOD, MDA, CAT, TAC, and GSH was measured through automation enzymatic /substrate assay.

Institutional ethical approval was obtained before study commencement [Reference: Biochem/21/30/09; Dated 11-08-2020]. The study was explained to each participant, and written informed consent was obtained. The statistical analysis was performed on SPSS version 20.0. Quantitative data were represented as mean ± SD, and the comparative analysis was performed using

the Independent sample T-test, a $p < 0.05$ was considered significant.

Results

The mean age of the T2DM patients with PCOs was 41.2 ± 6.1 years, while 51.4 ± 8.0 years of those without PCOs. A significant difference was observed in the mean Fasting Blood Glucose (FBG), Random Blood Sugar (RBS), hemoglobin A1c (HbA1C), and Homeostatic model assessment for Insulin Resistance (HOMA-IR) levels in both study groups ($p<0.01$), as shown in table 1. Moreover, there was no significant difference in fasting and random insulin levels (FI and RI) in both study groups.

Table 2 shows the level of antioxidants in T2DM patients with and without PCOs. Our results suggest that there was no significant difference in the level of antioxidants; SOD and MDA, in both groups ($p>0.05$). However, Glutathione Peroxidase (GSH-Px) and CAT were significantly low in T2DM patients with PCOs as compared to those without PCOs ($p<0.05$).

Table 1: Demographic & clinical parameters of T2DM patients with and without PCOs.

Parameters	T2DM patients with PCOs	T2DM patients without PCOs	p-value
	Mean±SD		
Age	41.2±6.1	51.4±8.0	<0.01*
BMI	28.52±3.0	27.50±2.5	0.148
SBP	128±8.0	130±9.0	0.201
DBP	80±5.0	81±6.0	0.852
FBG	150±18.0	189±44.0	<0.01*
RBS	170±19.0	200±40.0	<0.01*
HbA1C	9.5±0.60	8.1±0.59	<0.01*
HOMA-IR	2.7±1.5	2.1±1.2	<0.01*
FI	15.1±4.1	14.4±1.9	<0.01*
RI	16.2±5.2	15.1±4.1	<0.01*

Body Mass Index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Fasting Blood Glucose (FBG), Random Blood Sugar (RBS), Hemoglobin A1c (HbA1C), and Homeostatic model assessment for Insulin Resistance (HOMA-IR), Fasting Insulin (FI), Random Insulin (RI).
*p<0.05 is considered significant.

Table 2: Comparison of antioxidants levels among T2DM patients with and without PCOs.

Antioxidant	T2DM patients with PCOs	T2DM patients without PCOs	p-value
	Mean±SD		
SOD (U/g of Hb)	3.2±0.5	3.2±0.6	0.898
CAT (U/g of Hb)	3.6±0.5	3.4±0.7	<0.001*
MDA (nmol/ml)	5.6±0.6	5.6±1.0	0.775
TAC (mmol/l)	0.9±0.2	1.0±0.3	0.002*
GSH-Px	0.35±0.30	0.48±0.41	<0.001*

Superoxide Dismutase (SOD), Catalase (CAT), Malondialdehyde (MDA), Total antioxidant capacity analyte (TAC), Glutathione Peroxidase (GSH-Px)
*p<0.05 is considered significant.

Discussion

The current study was conducted to evaluate the level of oxidative stress in T2DM with and without PCOs. It was observed that there was no statistically significant difference in the level of SOD, CAT, and MDA in both study groups. Studies in the past suggest that erythrocyte antioxidant enzymes, including SOD & GSH-Px activities, are significantly increased in T2DM patients diagnosed with the polycystic ovarian syndrome as compared to controls. However, these are the vital enzyme acting as an antitoxin against anion of super oxide16. Similarly, in a few studies, it was also found that elevation of oxidative pressure was observed even in obese females with PCOs[17]. Literature in the past suggests that the concentration of extracellular SOD increases after a vascular injury that significantly leads to vascular endothelium tissue damage[18].

Though a significant difference in the level of CAT in T2DM patients with PCOs was observed compared to counterparts ($p<0.05$), studies suggest that CAT tends to protect the cells from accumulation of H_2O_2 by converting it into water and oxygen. Moreover, it is also used as an oxidant that acts as peroxidase[19]. We had observed that the mean catalase levels were higher among T2DM females with PCOs, which is in contrast to the existing knowledge on the catalase activity in both the disease conditions. As known hereditary catalase deficiencies promote diabetes risk, and the PCOS females are frequently observed with lower catalase activity[20-22].

The TAC levels in T2DM patients with PCOs were found low as compared to those in T2DM patients without PCOs. It is suggested that the reduced level of TAC in females with polycystic ovarian syndrome causes oxidative stress that could lead to an increase in the serum level of androgen in females with T2DM and PCOs[21]. Consistent with this, our results also indicate that TAC has a significant role and is altered in the co-occurring disease conditions (T2DM and PCOs). Furthermore, no significant change in MDA level was observed in both study groups ($p>0.05$). Baryam et al., in their study, also reported in support, they also suggested that most of the diabetic complications related to vital organs are due to elevated levels of running oxidative pressure of ROS[19]. However, few studies have shown contrasting results[23].

In addition, a significantly low GSH level was observed in T2DM patients with PCOs (0.35 ± 0.30 mol/mol Hb) compared to T2DM patients without PCOS (0.48 ± 0.41 mol/mol Hb). Ziech et al. in 2011 also found similar results[24]. Moreover, Lagman et al., in their study, concluded that Glutathione level was significantly reduced in the females with PCOs as compared to the females in the control group ($p<0.001$)[3]. Such a low concentration of Glutathione might be partly associated with insulin resistance. In addition to this imbalance levels of reactive oxygen species, H_2O_2 also causes the reduction of Glutathione depletion[25].

Conclusion

It is concluded that there is an abnormal status of antioxidants in women diagnosed with T2DM and PCOs. Although the catalase sufficiency observed in the present study contrasts the existing theory on the reduced catalase activity among diabetic and PCOs females, which needs further experimental validation as catalase plays a therapeutic role.

Conflicts of Interest

The authors have declared that no competing interests exist.

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