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Oxidative Stress and Antioxidant Status in Women with Polycystic Ovary Syndrome (PCOS): Stres Oksidatif dan Status Antioksidan pada Wanita dengan Sindrom Ovarium Polikistik (PCOS)

Masar Hadi Ismail	Department of Biotechnology, College of Science, Diyala University, Diyala
Naseer Hafedh Ibrahim	Department of Biology, College of Science,University of Diyala,Diyala
Huda Abdul Hameed Abdulrahman	Department of Biology, College of Science,University of Diyala,Diyala
Osama A. Mohsein	Main Laboratory Unit, Al Habbobi Teaching Hospital, Thi-Qar Health Directorate, Thi-Qar

General Background: Polycystic Ovary Syndrome (PCOS) is a prevalent endocrine disorder linked to metabolic and reproductive disturbances, where oxidative stress has been increasingly implicated. **Specific Background:** Evidence suggests that an imbalance between reactive oxygen species (ROS) and antioxidant defenses may contribute to the pathophysiology of PCOS, but inconsistencies in findings highlight the need for further clarification. **Knowledge Gap:** Despite recognition of oxidative stress in PCOS, limited studies in Middle Eastern populations have comprehensively assessed both oxidative markers and antioxidant status in relation to clinical features. **Aim:** This study aimed to evaluate oxidative stress levels and antioxidant defenses in Iraqi women with PCOS compared to healthy controls, and to investigate correlations with clinical and biochemical parameters. **Results:** Findings revealed significantly elevated oxidative stress markers (MDA, NO, AOPP) and reduced antioxidant levels (SOD, GPx, CAT, TAC) in PCOS patients, with strong correlations between redox imbalance and BMI, LH/FSH ratio, hirsutism, and acne severity. **Novelty:** This study provides region-specific evidence of impaired antioxidant defense in PCOS, highlighting oxidative stress as a critical mediator of symptom severity. **Implications:** These results underscore the potential for antioxidant-based interventions as adjunct therapies in managing metabolic and reproductive complications of PCOS.
Highlight :

- PCOS women show increased oxidative stress and reduced antioxidants.
- Oxidative stress links with BMI, hormones, and clinical symptoms.
- Antioxidant imbalance plays a role in PCOS pathogenesis

Keywords : Polycystic Ovary Syndrome (PCOS), Oxidative Stress, Antioxidant Status, Reactive Oxygen Species (ROS), Inflammation

Introduction

Polycystic Ovary Syndrome (PCOS) is one of the most prevalent endocrine disorders in women of reproductive age, with a diverse array of symptoms such as hyperandrogenism, oligo- or anovulation, and polycystic ovarian morphology [1]. It is believed to occur in 6-15% of women worldwide according to the diagnostic criteria of and populations in which the studies were conducted [2]. Apart from its reproductive manifestations, PCOS is related to a range of metabolic abnormalities including insulin resistance, obesity, dyslipidemia and even increases the risk of both type 2 diabetes mellitus (T2DM) and cardiovascular disease [3]. Although much is now known about PCOS, the exact pathophysiology of PCOS is still incompletely understood, with new evidence implicating an important role for oxidative stress and defective antioxidant responses.

Oxidative stress is characterized as a disproportion between the generation of reactive oxygen species (ROS) and the capacity of the biological system to detoxify these reactive intermediates relatively or to repair the damage that are produced [4]. ROS are chemically reactive molecules that contain oxygen such as the free radicals superoxide anion and hydroxyl radical as well as non-radical species like H2O2. ROS play important functions in cell signaling, host defense, and homeostasis under normal physiological condition. However, if ROS is produced in surplus amounts, it results in attack on lipids, proteins, and DNA, which impairs cellular activities and facilitates inflammation and apoptosis [5,6].

Many factors contribute to increased oxidative stress in PCOS. The most of PCOS patients have hyperinsulinemia and insulin resistance, both of which contribute to the elevated mitochondrial ROS generation, resulting in oxidative damage [7]. Obesity, which is often seen in PCOS, also worsens oxidative stress by inducing inflammation in adipose tissues and disordering the expressions of adipokines, which in turn disturbs insulin signaling and metabolic homeostasis [8]. In addition, the hyperandrogenism per se may also activate oxidative pathways, worsening the redox imbalance [9]. These interconnected pathways form a vicious circle in which oxidative stress is an important component in the metabolic and reproductive disturbances observed in PCOS.

Avariety of biomarkers have been used to evaluate the status of OSI in PCOS and include malondialdehyde (MDA), the end product of lipid peroxidation, nitric oxide (NO), which is a reactive nitrogen species, functionally beneficial in regulating vasculature under normal; but deleterious in the presence of excess and advanced oxidation protein products (AOPP), reflecting the level of protein oxidative damage [10]. Meanwhile, the antioxidant defense system, including enzymatic antioxidants (superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT)) and non-enzymatic antioxidants and total antioxidant capacity (TAC), exerts an important function to scavenge these ROS, and hence protect the cells from oxidative damage [11,12].

The analysis of the redox status in PCOS has great clinical relevance. Oxidative stress does not only lead to the ovarian damage in the form of the follicular cells and the oocytes but also serves as a proinflammatory and pro-atherogenic factor thus participating in the increase of the cardiovascular risk [13]. In addition, defective antioxidant activity might restrict the ability of the body to cope with ROS-induced damage and this, in turn, could lead to an exacerbation of the symptoms and related comorbidities of PCOS. Therefore, antioxidant therapies in the form of lifestyle modifications, dietary supplements as well as pharmaceuticals have been the subject of interest as adjuvant therapies in the management of metabolic and reproductive disturbances found in PCOS [14,15].

Although there is increasing evidence of the association between oxidative stress and PCOS, discrepancies persist regarding magnitude and the type of biochemical pathways affected, in part attributable to the variability in study population, diagnostic criteria, and methods of measurement. Accordingly, additional studies are necessary to better understand the specific contribution of oxidative stress and antioxidant status in PCOS development and to explore personalized strategies [16].

This study aims to evaluate oxidative stress markers and antioxidant status in women with PCOS

compared to healthy controls, investigating their associations with clinical and biochemical parameters, thereby contributing to the understanding of redox imbalance in PCOS and its potential as a therapeutic target.

Methodology

This case-control study was conducted from January to June 2025, at Al-Habboubi Teaching Hospital, Nasiriyah, Iraq. The study involved 100 women diagnosed with Polycystic Ovary Syndrome (PCOS) based on the Rotterdam criteria and 50 age-matched healthy women as controls. Inclusion criteria were women aged 18–40 years, confirmed PCOS diagnosis, and no hormonal therapy or antioxidant supplements for at least three months prior to participation. Exclusion criteria included pregnancy, lactation, diabetes, thyroid or endocrine disorders, chronic illnesses, smoking, or use of interfering medications. After overnight fasting, 5 mL of venous blood was collected from each participant, allowed to clot at room temperature, and centrifuged at 3000 rpm for 10 minutes to separate the serum, which was stored at –20°C until analysis. Oxidative stress markers including Malondialdehyde (MDA), Nitric Oxide (NO), and Advanced Oxidation Protein Products (AOPP) were measured using the TBARS method, Griess reagent assay, and spectrophotometric methods, respectively. Antioxidant markers including Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), Catalase (CAT), and Total Antioxidant Capacity (TAC) were assessed using standard biochemical assays and commercial kits.

Statistical analysis:

Statistical analysis was carried out using SPSS version 26, with results expressed as mean ± SD. Student’s t-test, Mann-Whitney U test, and Pearson’s correlation were used as appropriate, and a p-value of less than 0.05 was considered statistically significant.

Ethical approval:

This study was approved by the Human Ethics Committee of Al-Habboubi Teaching Hospital, Nasiriyah, Iraq. Informed consent was obtained from all participants after providing a detailed explanation of the study’s purpose and procedures. Participants were assured of the confidentiality and privacy of their personal information

Results

A. Socio-Demographic Characteristics of PCOS and Control Groups

The results of the statistical analysis of sociodemographic characteristics showed no significant difference in the mean age between women with PCOS (27.6 ± 4.5 years) and the control group (26.9 ± 4.2 years) (P = 0.312). In contrast, a significant increase in the mean body mass index (BMI) was observed in the patient group (29.8 ± 3.6 kg/m²) compared to the control group (23.7 ± 2.9 kg/m²), and this difference was highly statistically significant (P < 0.001). No significant differences were recorded in marital status, with 72% of married women in the patient group and 68% in the control group (P = 0.627). There was also no significant difference in the percentage of smokers between the two groups, with 18% of women with PCOS compared to 8% in the control group (P = 0.091). Also, no significant difference was found in employment status, with 46% of working women in the patient group compared to 56% in the control group (P = 0.263).

Variable	PCOS Group (n=100)	Control Group (n=50)	P-value
Age (years, Mean ± SD)	27.6 ± 4.5	26.9 ± 4.2	0.312
BMI (kg/m², Mean ± SD)	29.8 ± 3.6	23.7 ± 2.9	<0.001**
Marital Status (Married %)	72 (72%)	34 (68%)	0.627
Smoking Status (Yes %)	18 (18%)	4 (8%)	0.091

Employment (Employed %)	46 (46%)	28 (56%)	0.263

Table 1. *Comparison of age, BMI, marital status, smoking, and employment between women with PCOS and healthy controls*

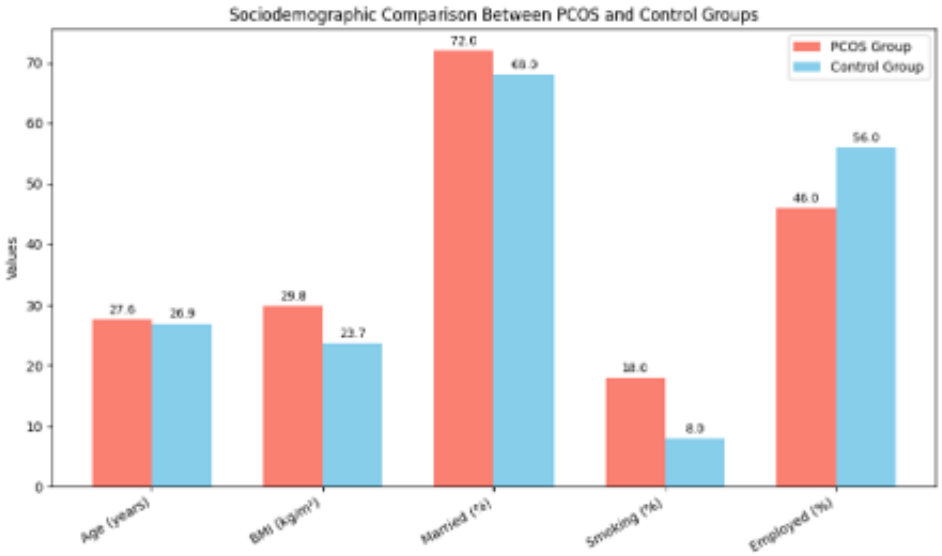

Figure 1. *Socio-Demographic Characteristics of PCOS and Control Groups*

B. Comparison of Oxidative Stress Markers Between PCOS Patients and Healthy Controls

The results showed a significant increase in oxidative stress indicators in women with PCOS compared to the control group. The mean malondialdehyde (MDA) concentration in the patient group was 4.82 ± 1.13 µmol/L, compared to 2.67 ± 0.89 µmol/L in the control group ($P < 0.001$). A significant increase in nitric oxide (NO) levels was also recorded in patients with PCOS, with a mean of 45.6 ± 10.3 µmol/L compared to 30.4 ± 8.2 µmol/L in healthy controls ($P < 0.001$). Also, advanced oxidation-related protein (AOPP) levels were significantly higher in the patient group (78.2 ± 15.7 µmol/L) compared to the control group (52.3 ± 12.6 µmol/L), with a high statistical significance value ($P < 0.001$). These results indicate a clear increase in oxidative stress in women with PCOS.

Marker	PCOS Group (Mean ± SD)	Control Group (Mean ± SD)	P-value
Malondialdehyde (MDA, µmol/L)	4.82 ± 1.13	2.67 ± 0.89	<0.001**
Nitric Oxide (NO, µmol/L)	45.6 ± 10.3	30.4 ± 8.2	<0.001**
Advanced Oxidation Protein Products (AOPP, µmol/L)	78.2 ± 15.7	52.3 ± 12.6	<0.001**

Table 2. *Levels of MDA, NO, and AOPP in serum samples of both groups*

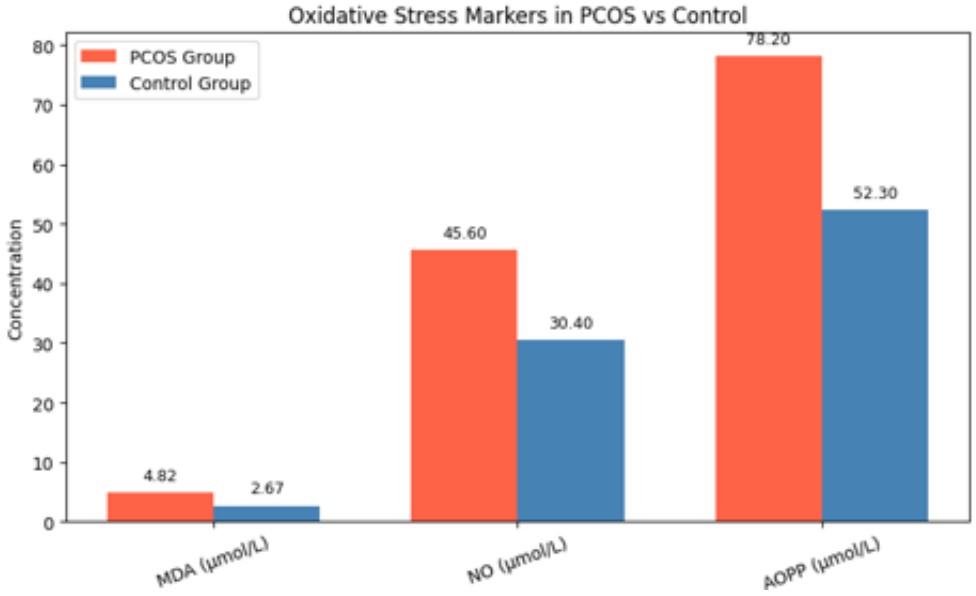

Figure 2. *Comparison of Oxidative Stress Markers Between PCOS Patients and Healthy Controls*

C. Serum Antioxidant Levels in Women with PCOS and Healthy Controls

The results showed a significant decrease in antioxidant levels in women with PCOS compared to the control group. Superoxide dismutase (SOD) concentrations were significantly lower in the patient group (82.4 ± 17.3 U/ml) compared to the control group (112.7 ± 19.5 U/ml) ($P < 0.001$). Glutathione peroxidase (GPx) levels were also significantly lower in patients (62.3 ± 11.4 U/L) compared to healthy controls (89.5 ± 13.1 U/L) ($P < 0.001$). A similar decrease in catalase (CAT) levels was observed in the PCOS group (26.1 ± 6.5 U/mg protein) compared to (39.3 ± 8.2 U/mg protein) in the control group ($P < 0.001$). The study also showed a significant decrease in total antioxidant capacity (TAC) in women with PCOS, with a mean of 0.92 ± 0.18 mmol/L, compared to 1.43 ± 0.25 mmol/L in the control group ($P < 0.001$). These results confirm a clear impairment of the antioxidant system in women with PCOS, reinforcing the hypothesis of a disturbance in their oxidative balance.

Antioxidant Marker	PCOS Group (Mean ± SD)	Control Group (Mean ± SD)	P-value
Superoxide Dismutase (SOD, U/mL)	82.4 ± 17.3	112.7 ± 19.5	<0.001**
Glutathione Peroxidase (GPx, U/L)	62.3 ± 11.4	89.5 ± 13.1	<0.001**
Catalase (CAT, U/mg protein)	26.1 ± 6.5	39.3 ± 8.2	<0.001**
Total Antioxidant Capacity (TAC, mmol/L)	0.92 ± 0.18	1.43 ± 0.25	<0.001**

Table 3. *Comparison of enzymatic and non-enzymatic antioxidant markers between the two groups*

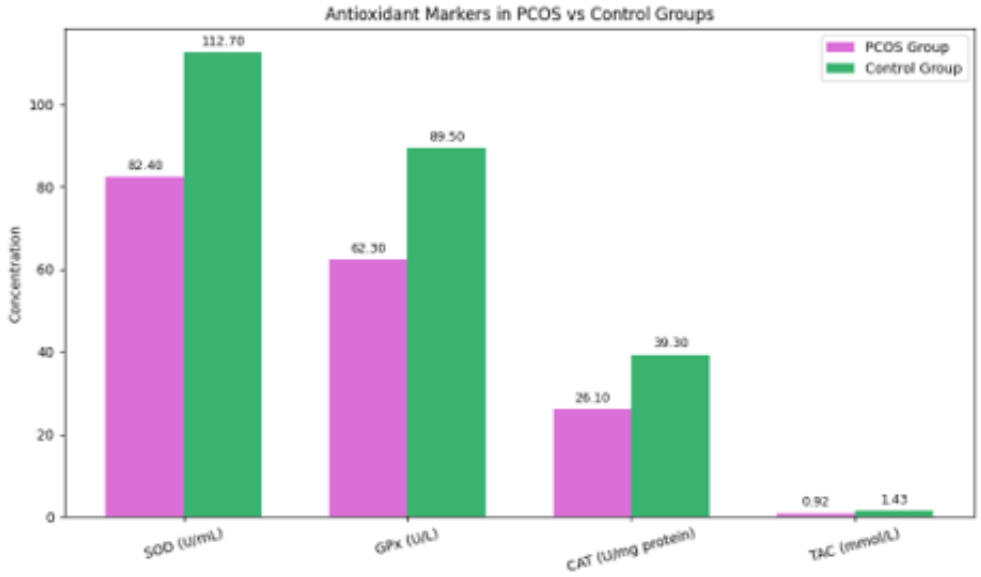

Figure 3. *Comparison of enzymatic and non-enzymatic antioxidant markers*

D. Correlation Between Oxidative Stress Markers and Clinical Parameters in Women with PCOS

Statistical correlation results showed a strong positive relationship between oxidative stress indicators and clinical parameters in women with PCOS. Moderate to strong positive correlations were found between body mass index (BMI) and malondialdehyde (MDA) ($r = +0.56$), nitric oxide (NO) ($r = +0.49$), and advanced oxidation products of protein (AOPP) ($r = +0.52$), all of which were highly statistically significant ($P < 0.001$). A positive correlation was also found between the LH/FSH ratio and MDA ($r = +0.43$), NO ($r = +0.38$), and AOPP ($r = +0.41$), all of which were statistically significant ($P < 0.01$). A strong significant correlation was also found between the degree of hirsutism and the concentrations of MDA ($r = +0.61$), NO ($r = +0.47$), and AOPP ($r = +0.59$) ($P < 0.001$). Acne severity showed a weak to moderate positive correlation with the three oxidative stress markers, with r values ranging from +0.29 to +0.37 and were significant ($P < 0.05$). These results suggest that the increased severity of clinical manifestations in PCOS patients is associated with increased levels of oxidative stress.

Parameter	MDA (r)	NO (r)	AOPP (r)	P-value
BMI	+0.56	+0.49	+0.52	<0.001
LH/FSH Ratio	+0.43	+0.38	+0.41	<0.01
Hirsutism Score	+0.61	+0.47	+0.59	<0.001
Acne Severity	+0.34	+0.29	+0.37	<0.05

Table 4. *Association of MDA, NO, and AOPP with BMI, LH/FSH ratio, hirsutism, and acne severity*

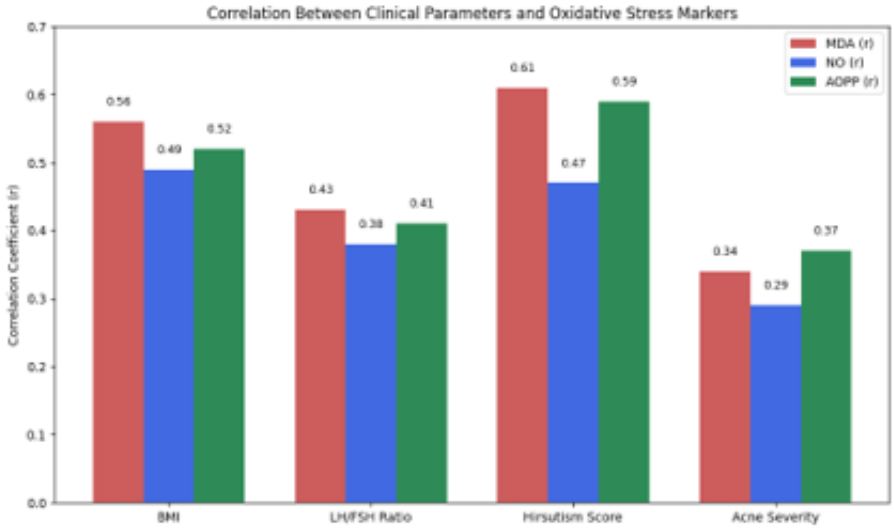

Figure 4. *Association of MDA, NO, and AOPP with BMI, LH/FSH ratio, hirsutism, and acne severity*

E. Correlation Between Antioxidant Markers and Oxidative Stress Indicators in Women with PCOS

The study results showed a statistically significant inverse relationship between oxidative stress markers and antioxidant levels in women with PCOS. Superoxide dismutase (SOD) was negatively correlated with malondialdehyde (MDA) (r = -0.51), nitric oxide (NO) (r = -0.43), and advanced protein oxidation products (AOPP) (r = -0.49), all of which were highly statistically significant (P < 0.001). A similar negative correlation was observed with glutathione peroxidase (GPx) with MDA (r = -0.47), NO (r = -0.38), and AOPP (r = -0.44), all of which were significant (P < 0.01). In addition, total antioxidant capacity (TAC) had the highest inverse correlation, with correlations of -0.58 with MDA, -0.46 with NO, and -0.54 with AOPP, and these correlations were highly significant (P < 0.001). These findings reflect the impaired ability of the antioxidant system to counter oxidative stress in women with PCOS.

Antioxidant Marker	MDA (r)	NO (r)	AOPP (r)	P-value
SOD	-0.51	-0.43	-0.49	<0.001
GPx	-0.47	-0.38	-0.44	<0.01
TAC	-0.58	-0.46	-0.54	<0.001

Table 5. *Associations of SOD, GPx, and TAC with MDA, NO, and AOPP levels*

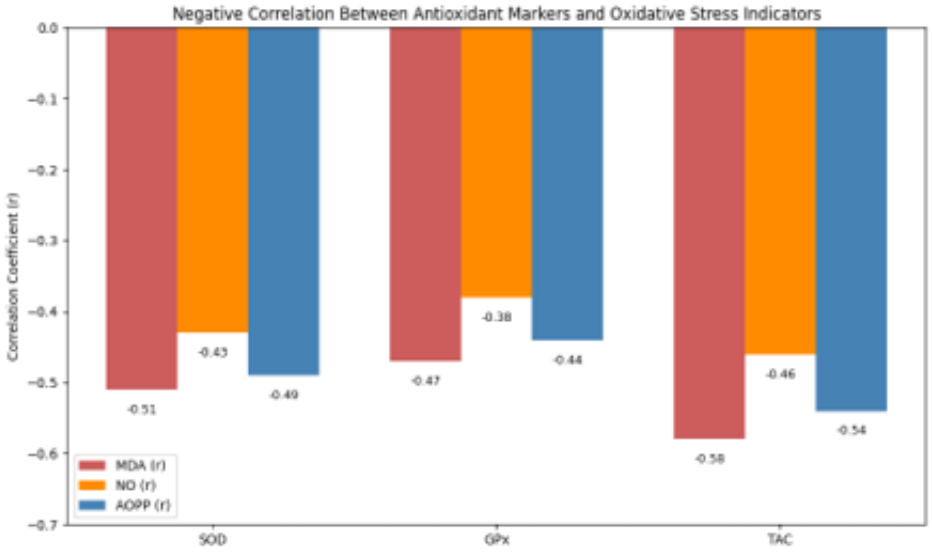

Figure 5. *Correlation Between Antioxidant Markers and Oxidative Stress Indicators in Women with PCOS*

Discussion

Results of the current study indicated that patients suffering from PCOS have higher amounts of OS markers such as MDA, NO, and AOPP compared with healthy women. Concurrently, antioxidant defense system was considerably decreased, including significantly lower level of SOD, GPx, CAT and TAC in PCOS group. These results indicate an unbalanced redox status in PCOS, that leads to an ultimately pro-oxidative condition.

These findings are supported by a number of previous studies, reporting elevated oxidative stress in PCOS patients. For instance, Sabuncu et al. 5 reported increased MDA and reduced antioxidant enzyme activity in PCOS women and further supported the fact that oxidative stress is involved in the pathophysiology of the disease [17]. Duleba and Dokras similarly described the association with hyperandrogenism, insulin resistance, and elevated oxidative stress in PCOS [18]. Moreover, [19], found reduced TAC and SOD levels in PCOS women, representing defective antioxidant defense system.

There were also significant positive associations between oxidative stress markers (MDA, NO, AOPP) and clinical indices including BMI, LH/FSH ratio, hirsutism and acne scores in our study. This is consistent with the idea that greater body mass and hormonal derangements in PCOS may further aggravate oxidative damage [20]. These relationships are consistent with the observations made by González et al., who claimed that the overproduction of insulin and obesity in patients with PCOS are responsible for oxidative stress [21].

In contrary, contradictory findings are observed in several studies. For example [22], found no difference in markers of oxidative stress in PCOS patients and controls among lean women, indicating that BMI may act as a mediator rather than PCOS [11]. These differences may be due to differences in the selection of the participants in terms of the BMI and insulin resistance status, because oxidative stress is affected by obesity and metabolic syndrome [23].

Furthermore, variability in sensitivity of assays, number of subjects examined and lack of data regarding confounding factors, including dietary pattern, physical activity, and smoking habits, may explain the conflicting results between studies. Although we adjusted for smoking and excluded individuals with chronic disease or supplement, not all previous studies had adjusted for these factors, which may affect oxidative marker levels [24].

The measured decline in antioxidant enzymes (SOD, GPx and CAT) and TAC may also be attributed to increased generation of ROS in PCOS, persistent overgeneration which exceeds the antioxidant defense [25]. Oxidative stress appears to be the culprit that can be detrimental for the ovarian function leading to damaged oocytes, folliculogenesis alteration and insulin resistance as observed in PCOS [26].

Conclusion

In conclusion, the results of this study indicated a significant oxidative stress to antioxidant balance disturbance in PCOS women in general and in those with more severe clinical and/or higher BMI values. This oxidative stress load might be involved in the aetiology and pathophysiology of reproductive and metabolic complications in PCOS. Additional research is needed to determine whether antioxidants may be beneficial for preventing or reducing these effects.

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