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Study the effect some of antioxidant in polycystic ovary syndrome women

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Abstract---This study was conducted at the Women and Children's Hospital in Al-Qadisiyah from 1/10/2021 to 2/1/2022, and 50 patients were followed up for women suffering from polycystic ovaries on the third day of the menstrual cycle, and compared to the control group, which included 50 normal cases, which were confirmed to be free. Of the chronic diseases such as heart disease, thyroid, diabetes and blood pressure, the concentration of antioxidants was measured for both infected and non-infected women, including SOD, UA and MDA. A significant increase in antioxidants and decrease GSH was observed in women with PCOS compared to the control group. The concentration of copper, zinc, Cu and Zn elements was also measured, as we showed a high concentration of copper and a decrease in zinc in women with polycystic ovary syndrome compared to the control group.

Keywords---antioxidant, oxidative marker, oxidative stress, polycystic ovary syndrome, reactive oxygen species.

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders of women at reproductive age and the major cause of an ovulatory infertility¹ [1]. It was first described as the change of ovarian morphology by Cherauin 1844², and the diagnostic criteria were established by the European Society for Human Reproduction and Embryology (ESHRE) and American Society for Reproductive Medicine (ASRM) in 2003 based on the extensive studies during the last decades, which is the so-called Rotterdam Consensus Criteria³. PCOS is a disease with high heterogeneity, and its clinical features mainly include menstrual disorder,

secondary amenorrhea, serum hormone abnormality, hairiness, acne, obesity, and infertility⁴.

Polycystic ovary syndrome is often coupled with insulin resistance (IR), hyperandrogenemia, and other chronic systemic diseases rather than a simple local condition. However, oxidative stress (OS) and chronic inflammation. The mechanism of pathogenesis is unknown⁵. A lot of investigations have revealed that OS level is significantly increased in patients with PCOS compared with the normal, when oxidative status is evaluated by circulating markers, such as malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx)⁶.

However, OS level is also observed to be significantly correlated with obesity, insulin resistance, hyperandrogenemia, and chronic inflammation⁷. Though OS is considered as a potential inducement of PCOS pathogenesis, it is still undetermined whether the abnormal OS levels of patients with PCOS derive from PCOS itself or if they are related to the potential complications⁸. Antioxidants scavenge excess ROS to counteract potential for significant cell damage by excess ROS. Antioxidants help create a balance between beneficial oxidant generation (frequently act as cell signaling molecules) and damaging oxidative stress. There are two categories of antioxidants: enzymatic and non-enzymatic. Enzymatic antioxidants include SOD, catalase, and GPx. Non-enzymatic antioxidants include GSH, α -tocopherol (vitamin E), β -carotene, ascorbate (vitamin C), taurine, L-carnitine, coenzyme Q10, etc⁹. There are three SOD isoforms in eukaryotes: manganese SOD (Mn-SOD), copper/zinc SOD (Cu/Zn-SOD), and extracellular SOD (EC-SOD)¹⁰.

Antioxidants that prevent or restrict the harmful effects of oxygen radicals have been linked to the female reproductive system and the pathogenesis of infertility in women. In individuals with idiopathic infertility, tubal fertility problems, and endometriosis, changes in antioxidant concentrations in serum and peritoneal fluid have been examined¹¹. The findings suggest that studying antioxidant concentrations in PCOS patients is worthwhile. Several studies have looked at antioxidant markers to see if they might link OS and PCOS to metabolic syndrome symptoms like diabetes, obesity, and cardiovascular disease¹².

ROS are free radicals with oxygen centers. An unpaired electron in the outermost shell is an extremely unstable configuration, and free radicals quickly react with other molecules or radicals to achieve the stable configuration of pairs of electrons in their outermost shells [101]. Several basic cellular processes lead to the production of ROS within a cell. Cellular respiration involves the reduction of molecular oxygen (O_2) to water in the electron transport chain. This reduction occurs through a series of reactions: (i) $O_2 + e^- \longrightarrow O_2^{\cdot -}$, (ii) $O_2^{\cdot -} + 2H_2O \longrightarrow 2H_2O_2$, (iii) $H_2O_2 + OH^{\cdot} \longrightarrow OH^- + O_2^{\cdot}$. As mentioned earlier, the superoxide anion radical ($O_2^{\cdot -}$), hydrogen peroxide (H_2O_2), and the hydroxyl radical (OH^{\cdot}) are three major species of ROS.

Methods

A total of 100 subjects, healthy controls (n = 50) (G1), and 50 women with PCOS (G2) were included in this study. The mean age of the control group (45.12 ± 11.9 years), the age of the G2 patient groups (45.12 ± 14.7 years, 54.33 ± 8.7) were selected in the period from 1-10-2021 to 2-1-2022. This study, including blood samples and experiment protocols, was approved by the Ethical Committee of Women's and Children's Hospital in Al-Qadisiyah Governorate. In addition to. Additionally, obtain informed consent from all study participants prior to sample collection. 5 ml of blood was collected in gel tubes, and then the plasma was separated by centrifugation (4000 rpm, $0.894 \times g$) (Gottingen, Germany) at room temperature for 10 min. Study samples were divided into Eppendorf tubes. Measurement of plasma levels of SOD, GSH, and MDA by ELISA kits (Elabscience, China).

Statistical Analysis

All values were expressed as mean \pm standard deviation for normally distributed data and as median (inter quartile range) for skewed data. Differences between the two groups were analyzed using Mann-Whitney U test. A p-value less than 0.05 was considered as statistically significant. Statistical analysis was done by using Microsoft excel spread sheets and SPSS for windows version 11.5 (SPSS, Inc; Chicago IL).

Results and Discussion

Table(1): show the concentration of GSH and SOD, URIC ACID in PCOS

Groups	GSH mean \pm SD	p-value	SOD mean \pm SD	P-value	URIC ACID mean \pm SD	p-value
G1	17.79 \pm 3.74	<0.05	2160.76 \pm 745.54	<0.05	2.74 \pm 1.34	<0.05
G2	7.04 \pm 2.47	<0.05	527.36 \pm 169.29	<0.05	5.80 \pm 1.30	<0.05

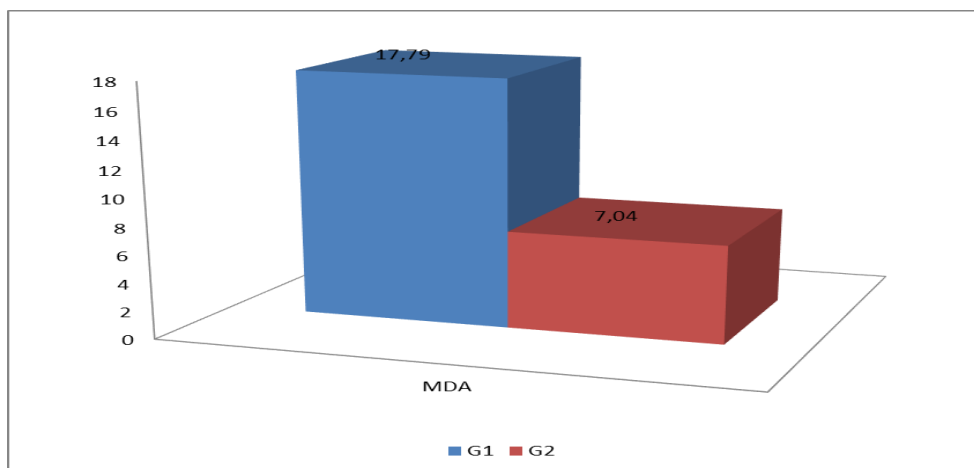


Figure (1) Mean values for GSH in PCOS patients and control group

Show the Table (1) a significant and Figure (1) decrease ($p < 0.05$) in the concentration of serum GSH in the POC of the women with in comparison with the control group. These results are compatible with the results of the studies of ⁵, However there are no significant difference

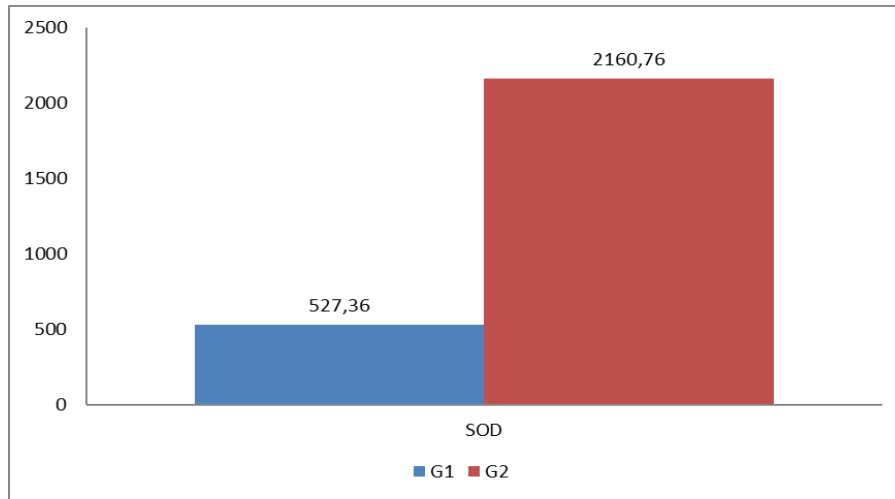


Figure (2) Mean values for SOD in PCOS patients and control group

Show the Table (1) a significant and Figure (2) higher ($p < 0.05$) in the concentration of serum SOD in the POC of the women with in comparison with the control group These results are compatible with the results of the studies of¹³ SOD is an enzyme and an important antioxidant defense that eliminates superoxide anions (O_2^-), as a major oxygen radical, by catalyzes of them to H_2O_2 and final by GPx converted to water¹⁴. Several common forms of SOD exist depending on the metal cofactor and the protein fold such as the Cu/Zn type, Fe and Mn types, and the Ni type ¹⁵.

SOD activity in PCOS reported in several studies. Sabuncu *et al.* determined antioxidant status in women with PCOS evaluated blood SOD level in PCOS patients compared with healthy controls. They showed that women with PCOS had higher SOD levels than normal subjects¹⁶. Moreover, Zhang *et al.* showed that the serum SOD level in PCOS patients was significantly lower than the control group¹⁷.

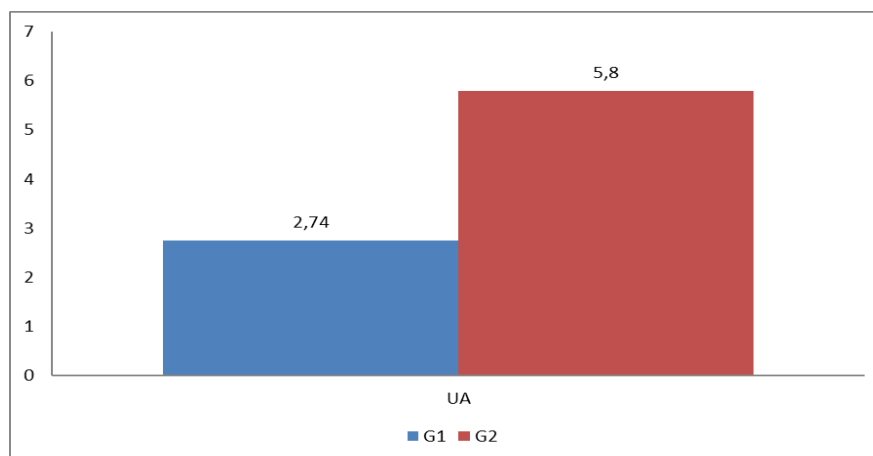


Figure (3) Mean values for UA in PCOS patients and control group

Show the Table (1) a significant and Figure (3) higher ($p < 0.05$) in the concentration of serum UA in the POC of the women with in comparison with the control group. Uric acid is the main antioxidant in human blood serum. Its elevated concentration correlates with obesity, insulin resistance, high blood pressure, heart diseases, and stroke. In humans, it is formed as a result of the degradation of purines. Because humans no longer have urate oxidase activity, uric acid is not transformed into allantoin, as occurs in other mammals. As a result of the inhibitory activity of estrogens, uric acid levels are usually lower in women, amounting to 200–400 μM . Unfortunately, elevated levels increase the risk of hyperuricemia and gout. Uric acid removes singlet oxygen, the peroxy radical (RO_2), the hydroxyl radical (HO), and peroxy nitrite, but it does not eliminate the superoxide radical¹⁸.

Some studies have shown that UA can be directly used to induce the inflammatory response of fat cells. Furthermore, UA is an antioxidant, and UA can be transformed into a pro-oxidant and directly participate in the proliferation of fat cells and the oxidative stress response in the state of obesity, which is the main cause of obesity and IR¹⁹. Excessive androgen is one of the clinical features of PCOS and an important cause of infertility in women with PCOS²⁰. In these women with PCOS, excessive androgens are produced primarily by the ovaries and adrenal glands, leading to massive follicular atresia, which ultimately causes ovulation disorders²¹. Serum androgen levels have been shown to be an independent risk factor for MS in a study of girls with PCOS²². Some studies have shown that the androgen level of PCOS patients is positively correlated with IR, and hyperandrogenemia can induce IR by reducing insulin clearance and increasing triacylglycerol release and lipoprotein lipase activity²³. Androgen is a promoter of HUA in PCOS patients. By downregulating the expression of the hUAT gene, androgen promoted UA reabsorption in renal tubules and reduced UA secretion to accelerate the occurrence of HUA²⁴.

Table(2): show the concentration of MDA in PCOS

Groups	MDA mean± SD	p-value
Control	8.9±0.08	<0.05
POC	35.20±1.79	

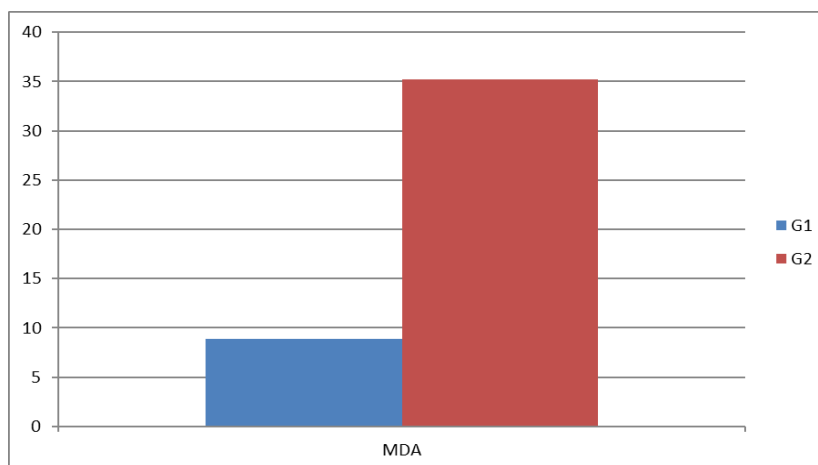


Figure (4) Mean values for MDA in PCOS patients and control group

Show the Table (2) a significant and Figure (4) higher ($p < 0.05$) in the concentration of serum UA in the POC of the women with in comparison with the control group. These results are similar to the results of [ofe²⁵](#). $p < 0.05$) in the concentration of serum MDA in the of woman in POCs comparison with control. These results are compatible with the studies of [f²⁶²⁷²⁸](#). MDA results from lipid peroxidation of polyunsaturated fatty acids²⁹ is stable and can serve as a good biomarker³⁰. MDA level in PCOS reported in several studies. One meta-analysis showed that circulating mean MDA concentrations according to the age and BMI were increased 47% in women with PCOS compared with controls⁷.

Kuscu *et al.* compared blood MDA level in PCOS patients with healthy controls. They showed the MDA level was significantly higher in the PCOS group but was independent of obesity.¹³ In another study, Zhang *et al.* demonstrated that serum MDA levels in PCOS patients were significantly higher than the control group, but BMI and age were not recorded¹⁸. In addition, Dursun *et al.* studied PCOS patients and found serum MDA levels in PCOS patients were similar to those of BMI and smoking status matched controls³¹. Palacio *et al.* compared PCOS patients with BMI and age matched controls. They demonstrated that higher levels of erythrocyte MDA were seen in PCOS patients compared with controls. These results also were found by Sabuncu *et al.*³².

Table(3): show the concentration of Zn and Cu in PCOS

Groups	Zn mean± SD	p-value	Cu mean± SD	p-value
Control	57.42±14.59	<0.05	155.85±60.66	<0.05

POC	31.03±9.46	<0.05	237.85±58.45	
				<0.05

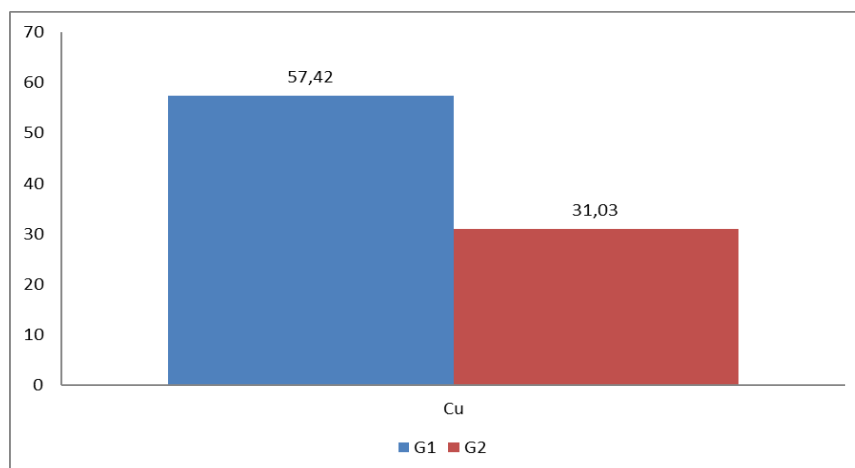


Figure (5) Mean values for CU in PCOS patients and control group

Show the Table (3) a significant and Figure (5) higher ($p < 0.05$) in the concentration of serum Cu in the POC of the women with in comparison with the control group. This result matched with the results of the studies of ^{33,34}. The survey conducted by Celik on copper, homocysteine, and early vascular disease in lean women with PCOS showed high copper levels in PCOS patients ³⁵. Previous study has shown that patients with PCOS copper is involved in the metabolism of oxygen and plays an important role in free radical reactions. Moreover, a significant higher copper level in women with PCOS was reported by ³⁶. Physiologically, copper is considered as prooxidant and oxidant metal³⁷. A low copper level can lead to decreased activity of superoxide dismutase and sequentially increases superoxide radical generations and increases oxidative stress ³⁸. On the other hand, a high copper level can lead to generation of reactive oxygen.

High copper concentrations can contribute to the release of LH and adrenocorticotrophic hormone by affecting the pituitary gland, which affects ovulation. Previous research has shown that copper and zinc may cause oxidative stress to act on PCOS by affecting the hormone levels ¹⁷.

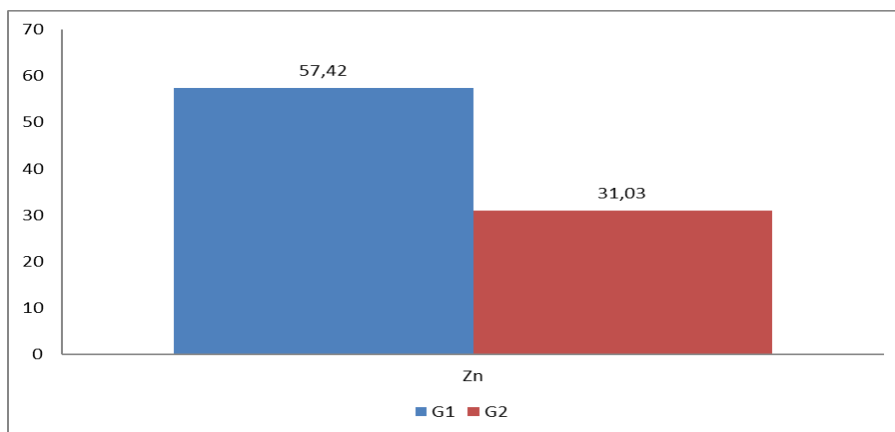


Figure (6) Mean values for Zn in PCOS patients and control group

Show the Table (3) a significant and Figure (6) higher ($p < 0.05$) in the concentration of serum Zn in the POC of the women with in comparison with the control group. These results are compatible with the results of the studies of³⁹. Our study indicated that circulating zinc levels in women with PCOS were significantly lower than those in healthy controls when detailed analysis is conducted. Biochemical role Zinc (Zn), one of the most important trace elements, is essential for more than 300 different cellular processes. Zn also is a basic element for many vital functions including homeostasis, immune responses, oxidative stress, and apoptosis and in other words, for health, either physically or mentally. Zinc also is involved in fertility and reproduction³⁸. Besides, zinc is important for insulin synthesis and action in both, normal and diabetes mellitus condition⁴⁰.

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