The North African Journal of Scientific Publishing (NAJSP)
مجلة شمال إفريقيا للنشر العلمي (NAJSP)
E-ISSN: 2959-4820
Volume 4, Issue 2, 2026
Page No: 423-431
Website: https://najsp.com/index.php/home/index
SJIFactor 2024: 5.49 0.69 :2025 (AIF) معامل التأثير العربي ISI 2024: 0.696

Molecular Crosstalk between Redox Enzymes, Oxidative Stress, Hormonal Dysregulation, and Pregnancy Loss in Polycystic Ovary Syndrome

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التداخل الجزيئي بين إنزيمات الأكسدة والاختزال والإجهاد التأكسدي واضطراب الهورمونات وفقدان الحمل في متلازمة تكيس المبايض

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Received: April 05, 2026	Accepted: May 20, 2026	Published: June 04, 2026

Abstract:

Background: Polycystic ovary syndrome (PCOS) is a heterogeneous disorder that influences both reproductive and metabolic health in women and is widely recognized as a major contributor to female infertility. Oxidative stress develops when the generation of reactive oxygen species exceeds the capacity of antioxidant defense systems to maintain cellular balance. In pregnancy, the placenta is considered one of the primary sources of oxidative activity, whereas antioxidant mechanisms increase as a protective physiological response against cellular injury. **Objectives:** The study aims to determine the molecular interaction between oxidation-reduction enzymes and oxidative stress by measuring methionine sulfoxide reductase A, catalase, glutathione S-transferase, xanthine oxidase, myeloperoxidase, methionine adenosyl transferase, and aminoacylase-3 and their relationship to hormonal disorders and miscarriages in patients with polycystic ovary syndrome. **Methods:** The research was performed in Mosul and included serum specimens obtained from 60 women with polycystic ovary syndrome together with 50 healthy control subjects. **Results:** These data indicate that PCOS is underpinned by a shared metabolic etiology, defined by chronic oxidative stress and a marked redox imbalance. These findings reinforce the classification of PCOS within a continuum of metabolic pathologies intrinsically linked to insulin resistance and systemic inflammation. **Conclusion:** PCOS exhibits a complex pathophysiology characterized by the partial, yet insufficient, upregulation of antioxidant defenses, a failure to mitigate persistent oxidative damage. This study underscores the critical influence of the hormonal milieu in modulating these enzymatic and biochemical profiles. Furthermore, the correlation between oxidative imbalance and adverse clinical outcomes, such as miscarriage, highlights the potential of these markers as prognostic indicators for disease progression and long-term complications.

Keywords: Polycystic Ovary Syndrome, Miscarriage, Change of Hormones, Methionine Sulfoxide Reductase A, Catalase, Antioxidants.

الملخص:
الخلفية: متلازمة تكيس المبايض اضطرابٌ غير متجانس يؤثر على الصحة الإنجابية والأيضية لدى النساء، ويُعرف على نطاق واسع بأنه عامل رئيسي في عقم النساء. ينشأ الإجهاد التأكسدي عندما يتجاوز إنتاج أنواع الأكسجين التفاعلية قدرة أنظمة الدفاع المضادة للأكسدة على الحفاظ على التوازن الخلوي. خلال فترة الحمل، تُعتبر المشيمة أحد المصادر الرئيسية للنشاط التأكسدي، بينما تزداد آليات مضادات الأكسدة كاستجابة فسيولوجية وقائية ضد تلف الخلايا. **الأهداف:** تهدف الدراسة الى معرفة التداخل الجزيئي بين إنزيمات الأكسدة والاختزال والإجهاد التأكسدي من خلال قياس مستويات إنزيمات ميثيونين سلفوكساید ردكتيز A والكتاليز وكلوتاثايون S-ترانسفيريز، وزانثين أوكسيديز، ومايلوبيروكسيديز، وميثيونين أدينوسيل ترانسفيريز وأمينوأسيليز-3 علاقتهم مع حالات اضطراب الهورمونات والإجهاض لدى مريضات متلازمة تكيس المبايض. **طريقة العمل:** أُجري البحث في الموصل، وشمل عينات مصل مأخوذة من 60 امرأة مصابة بمتلازمة تكيس المبايض، بالإضافة إلى 50 امرأة سليمة كمجموعة سيطرة. **النتائج:** تشير النتائج بقوة أن متلازمة تكيس المبايض تشترك في أساس أيضي مشترك يتميز بالإجهاد التأكسدي المزمن واختلال واضح في التوازن بين المؤكسدات ومضادات الأكسدة، مما يدعم فكرة أن هذه الحالات تمثل سلسلة متصلة من الاضطرابات الأيضية المرتبطة بمقاومة الأنسولين والالتهاب. **الخلاصة:** تُظهر متلازمة تكيس المبايض نمطًا أكثر تعقيدًا مع زيادة جزئية في تنظيم بعض أنظمة مضادات الأكسدة (مثل ميثيونين سلفوكساید ردكتيز A وميثيونين أدينوسيل ترانسفيريز في بعض الحالات)، مما يشير إلى استجابة تعويضية للإجهاد التأكسدي لا تزال غير كافية لموازنة الضرر التأكسدي المستمر. تلعب التقلبات الهرمونية دورًا تنظيميًا حاسمًا في تعديل الإجهاد التأكسدي، مما يُغير بشكل كبير من الملامح الإنزيمية والكيميائية الحيوية في كلتا الحالتين، ويُبرز أهمية البيئة الهرمونية في تشكيل أعراض المرض وشدته. ترتبط عوامل سريرية مثل الإجهاض بدرجة اختلال التوازن التأكسدي، مما يشير إلى فائدتها المحتملة كمؤشرات تنبؤية لتطور المرض ومضاعفاته.

الكلمات المفتاحية: متلازمة تكيس المبايض، الإجهاض، تغير الهورمونات، ميثيونين سلفوكساید ردكتيز A، الكتاليز، مضادات الأكسدة.

Introduction:

Polycystic ovary syndrome (PCOS) is recognized as a complex condition that adversely affects both reproductive and metabolic functions in women. It is also regarded as one of the major contributors to female infertility. Women with PCOS who achieve pregnancy may still face a higher likelihood of complications during gestation, including gestational diabetes mellitus (GDM) and preterm delivery... etc. [2]. Among women who underwent a comprehensive clinical assessment for PCOS, the syndrome was identified in 165 out of 1134 cases, representing 14.5% of the studied cohort. Diagnostic classification was established according to the clinical manifestations observed during evaluation. [3]. PCOS, particularly in women exhibiting hyperandrogenism, has been linked to multiple cardiometabolic disturbances such as obesity, dyslipidemia, hypertension, and impaired glucose metabolism including prediabetes and type 2 diabetes mellitus [4]. Furthermore, affected characteristics, women also commonly present with infertility, complications of pregnancy, obesity, insulin resistance, hirsutism, acne, androgenic alopecia, and mood disorders.

An imbalance between reactive oxygen species (ROS) generation and antioxidant defense mechanisms results in a condition referred to as oxidative stress. This process promotes excessive ROS formation and oxidation of cellular macromolecules, ultimately contributing to tissue and cellular injury [5]. Under certain pathological or physiological conditions, antioxidant capacity may become weakened or depleted, leading to elevated ROS accumulation and enhanced oxidative stress. Excessive ROS production can disturb normal metabolic pathways and trigger cell death. Moreover, ROS readily interact with biomolecules such as DNA, proteins, lipids, and carbohydrates, causing oxidative damage, disruption of cellular homeostasis, and eventual cellular loss [6]. Pregnancy itself is considered a state associated with increased oxidative stress and elevated circulating ROS levels, with the placenta representing the principal source of ROS during gestation. In response, antioxidant synthesis is enhanced to counterbalance oxidative damage and maintain physiological stability [7]. Multiple hormonal disturbances have been identified in women with PCOS. Hormones including insulin, growth hormone, ghrelin, LEAP-2, gonadotropin-releasing hormone, the luteinizing hormone/follicle-stimulating hormone (LH/FSH) ratio, and sex steroids such as androgens and estrogens exhibit abnormal regulation in affected patients. These endocrine alterations are closely associated with metabolic complications including diabetes mellitus, insulin resistance, obesity, infertility, and irregular menstrual function in women with PCOS [8].

Miscarriage represents one of the most frequently reported complications of pregnancy and may occur as either an isolated or recurrent event [9]. The World Health Organization (WHO) defines recurrent miscarriage (RM) as the occurrence of three or more consecutive pregnancy losses before the twentieth week of gestation [10]. Primary RM refers to women with no history of live birth, whereas secondary RM describes patients who have experienced at least one previous live birth [11]. Recent

investigations have increasingly focused on the relationship between PCOS and recurrent miscarriage. A higher prevalence of PCOS has been documented among women with RM, and several PCOS-related features, including hyperandrogenism, insulin resistance, hyperinsulinemia, obesity, elevated plasminogen activator inhibitor-1 (PAI-1), and hyperhomocysteinemia, have been linked to an increased risk of recurrent miscarriage [12].

This study aims to investigate the molecular interaction between oxidation-reduction enzymes and oxidative stress by measuring methionine sulfoxide reductase A(MsrA), catalase (CAT), glutathione S-transferase (GST), xanthine oxidase (XO), myeloperoxidase (MPO), methionine adenosyltransferase (MAT), and aminoacylase-3(ACY3), and evaluation hormonal imbalances and pregnancy loss in patients with PCOS.

Materials and methods:

Blood sample collection:

Where collected from women have PCOS (n=60) and control healthy (n=50) from Albatool Teaching hospitals and AlMosul general hospitals under the supervision of doctors who specialize whose ages ranged between (15-40) years, in Mosul city in period between from 16 February 2025 to October 2025 filled the questionnaire. A questionnaire was utilized to gather the medical history and personal information of each participant.

Diagnosis of PCOS:

PCOS was diagnosed according to the Rotterdam, 2003 criteria [13], requiring at least two of the following: oligo/anovulation, hyperandrogenism, or polycystic ovarian morphology on ultrasound.

Hormonal Classification:

PCOS patients were classified as having hormonal changes if at least one reproductive hormone was outside the normal reference range, and as having no hormonal changes if all measured hormones were within the normal range.

Study Design:

This study was designed as a case-control study. A total of 110 women were recruited, including 60 patients diagnosed with PCOS as the case group and 50 healthy women as the control group. Redox enzymes were compared between cases and controls, and subgroup analyses were performed according to hormonal status and miscarriage history:

Group I: Healthy Control Group:

- Healthy women (n = 50).

Group II: PCOS Patients Group:

- **Women diagnosed with Polycystic Ovary Syndrome (PCOS) (n = 60).**

The PCOS group was further subdivided according to hormonal status into:

- PCOS patients with hormonal changes (n = 30)
- PCOS patients without hormonal changes (n = 30)

Additionally, according to miscarriage history, the PCOS group was classified into:

- PCOS patients without recurrent/higher miscarriage (n = 20)
- PCOS patients with recurrent/higher miscarriage (n = 40)

Blood sample preparation:

Every participant in this trial had five millilitres of venous blood drawn, and her whole medical history was gathered. The blood samples were immediately placed into plain tubes, centrifuged at 3000xg for 15 minutes, and then placed in a water bath at 37°C for 10 minutes to finish the blood serum separation process.

Exclusion Criteria:

The study excluded women with history of using drugs, hyperprolactinemia, tumors, smoking, hypertension, diabetes mellitus, individuals with chronic or acute inflammatory diseases, and cardiovascular disease, to minimize confounding.

Methods for determination of enzymes variables:

Manual methods were also used to measure the levels of enzymatic parameters, **as follows:**

Dithiothreitol (DTT), which contains two sulfhydryl (SH) groups in its structure, functions as a thioredoxin-like reducing agent for MsrA. In this assay, 5,5′-dithio-bis (2-nitrobenzoic acid) (DTNB) reacts readily with reduced DTT in proportion to the concentration of MsrA, producing a yellow-colored compound that was detected spectrophotometrically at 412 nm [14].

Catalase (CAT) activity was evaluated according to the standard procedure described in reference [15], based on the oxidation of ammonium molybdate by hydrogen peroxide. Residual hydrogen peroxide remaining after the CAT enzymatic reaction formed a colored product, and its absorbance was measured at 410 nm.

GST activity depends on the conjugation of compounds containing electron-attracting groups, especially aromatic substrates such as 1-chloro-2,4-dinitrobenzene, with the thiol (-SH) group of

reduced glutathione (GSH). This reaction generates dinitrophenyl thioether along with chloride ions [16]. The absorbance of the final reaction mixture was subsequently determined spectrophotometrically at a wavelength of 340 nm.

Xanthine oxidase (XO) activity was assessed according to the method reported by previous investigators [17] through spectrophotometric measurement of uric acid formation at 293 nm, based on the enzymatic oxidation of hypoxanthine. Myeloperoxidase (MPO) activity was evaluated through its ability to oxidize hydrogen peroxide in the presence of orthodianisidine substrate, leading to the formation of a colored product. The absorbance of the resulting solution was measured at 450 nm [18].

Methionine adenosyltransferase (MAT), in the presence of ATP as a donor of the adenosyl group, catalyzes the conversion of methionine into S-adenosylmethionine (SAM). At the completion of the reaction, inorganic phosphate released from the process was identified using malachite green reagent at a wavelength of 620 nm [19].

L-methionine +ATP + H_2O →SAM + PPi + Pi:

For ACY3: involves the enzymatic hydrolysis (Deacetylation) of a synthetic N-acetylated substrate, typically an N-acetyl-aromatic amino acid or a mercapturic acid derivative. The reaction releases an L-amino acid and an acetate group, and the activity is commonly quantified by measuring the increase in free primary amines (the released amino acid) [20].

Each one of the samples was conducted in duplicate, and seven-point standard curve has been used to create the calibration curve.

Statistical Analysis:

SPSS version 21 was employed for statistical analysis to calculate the mean values and standard deviations (SD). Comparisons between two variables were performed using the independent t-test. Statistical significance was considered when the p-value was equal to or less than 0.05, whereas *p*-values greater than 0.05 were regarded as non-significant [21].

Results and Discussion:

1. Study of Enzymes Associated with Oxidative Stress–Related Enzymes in Women with PCOS Compared with Healthy Controls:

That shown in Table 1: MsrA, CAT, GST, XO, MPO and ACY3 showed significant increased, **while MAT significant decreased:**

In PCOS, the decrease is tightly linked to insulin resistance and follicular health. MsrA is vital for protecting mitochondrial proteins. Ovarian mitochondrial dysfunction is a hallmark of PCOS pathophysiology, frequently linked to the deficiency of MsrA. The resulting accumulation of damaged proteins appears to disrupt critical physiological processes, specifically oocyte maturation and steroidogenesis [22]. This cellular damage is likely compounded by hyperandrogenism, which elevates oxidative strain and further overwhelms the MsrA repair system, thereby perpetuating the systemic metabolic dysregulation observed in this patient population [23].

Table (1): Enzymes Associated with Oxidative Stress–Related Enzymes in Women with PCOS Compared with Healthy Controls

Enzyme Activities (U/L)	Normal Women n=50		PCOS Patients n=60		*p*-value
	mean	SD	mean	SD	
MsrA	660.2	39.3	781.2	45.7	0.034*
CAT	71.076	3.09	86.41	5.47	0.042*
GST	313.67	6.12	498.62	59.53	0.015*
XO	628.19	34.79	691.25	41.74	0.047*
MPO	92.45	6.15	129.34	11.051	0.023*
MAT	95.2	2.4	58.1	3.24	0.008*
ACY3	4.56	0.27	13.93	4.72	0.001*

*Significant at ($p \leq 0.05$)**.**

Research into catalase (CAT) modulation has gained significant traction in the context of PCOS, primarily due to its role as a critical antioxidant defense against the oxidative stress implicated in the syndrome's metabolic and reproductive sequelae [24]. By facilitating the decomposition of hydrogen peroxide into water and oxygen, CAT acts as a sentinel enzyme in maintaining cellular integrity [25]. In PCOS, the interplay between hyperandrogenism and obesity drives elevated ROS, which inflict cumulative damage on DNA, proteins, and lipids [24]. This oxidative burden within the ovarian microenvironment is strongly correlated with impaired oocyte quality and follicular arrest, both of which are significant drivers of PCOS-related infertility [26].

Enhancing CAT activity offers a potential therapeutic strategy to mitigate the oxidative load that interferes with insulin receptor signaling [27]. Clinical observations indicate that PCOS patients with co-morbid insulin resistance typically display diminished CAT activity compared to their insulin-sensitive counterparts, with similar reductions observed in infertile cohorts [27]. Given that CAT is essential for protecting the ovarian microenvironment from oxidative-mediated damage [28], experimental interventions—such as the administration of aqueous garlic extract or chlorogenic acid—have demonstrated the efficacy of upregulating endogenous catalase. These interventions aid in restoring redox homeostasis and, consequently, improving ovulatory function and hormonal profiles [29].

Furthermore, systemic inflammation in PCOS patients triggers the post-translational modification of Xanthine Dehydrogenase into Xanthine Oxidase (XO). Recent 2024 data suggest that elevated XO levels competitively inhibit Nitric Oxide (NO) binding sites. This competitive inhibition provides a mechanism for the increased incidence of hypertension and vascular dysfunction in this population; essentially, the upregulation of XO sequesters the environment intended for vasodilatory signaling molecules. The study confirmed significantly elevated levels of XO in PCOS patients, identifying this enzyme as a primary source of ROS, which serves to further compromise the follicular environment [30]. "Hyperhomocysteinemia is frequently documented in women with PCOS, serving as a consistent biochemical marker of the metabolic dysregulation associated with the syndrome. Because MAT is the "gatekeeper" of the methionine cycle, its activity increases to convert methionine into SAM, effectively trying to pull the cycle forward and reduce homocysteine build up [31] (Figure 1).

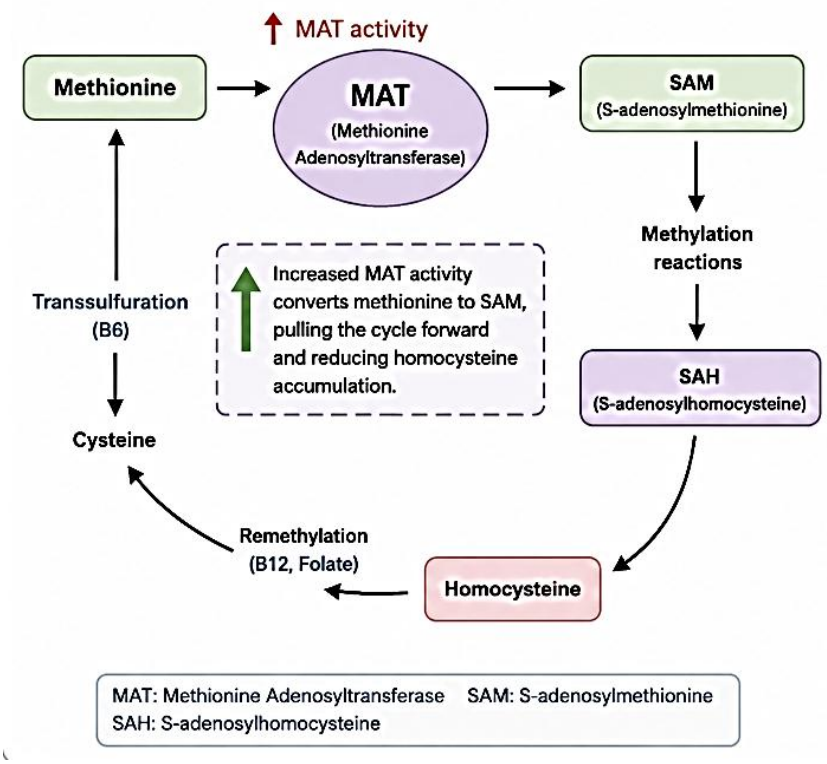

Figure (1): Illustrates the methionine cycle and increased MAT activity.

Elevated circulating MAT-related products and specific microRNAs (like miR-29a) that regulate these pathways can be observed early in pregnancy, serving as predictive markers for the eventual development of GDM [32]. Hyperandrogenism (excess testosterone) and hyperinsulinemia act synergistically to alter the expression of metabolic enzymes in the liver and ovaries. This hormonal environment can trigger an upregulation of MAT2A to facilitate the rapid cellular proliferation often seen in polycystic ovarian tissue [31].

The elevation of ACY3 activity may reflect the increased physiological demand for this enzyme in patients, particularly during the metabolism of N-acetylated amino acids produced through the degradation of intracellular N-terminally acetylated proteins as well as modified dietary proteins within the intestinal mucosa [33]. Scientific sources indicate that aminoacylase is an enzyme that catalyzes the hydrolysis of modified amino acids, specifically N-acyl-alpha-L-amino acids. Its primary function is to remove the acyl group from these acids, resulting in a free amino acid and an acyl group [34].

2. Study of Enzymes Associated with Oxidative Stress in Patients with PCOS Do Not Have Hormonal Changes Compared with Have.

In **Table 2** showed: XO, MPO and MAT increasing significantly but GST and ACY3 decreasing significantly and others MsrA and CAT non-significant:

Table (2): PCOS Patients Do Not Have Hormonal Changes Compared with Have.

Enzyme Activities (U/L)	PCOS Patients Do Not Have Hormonal Changes N=30		PCOS Patients Have Hormonal Change N=30		*p*-value
	mean	SD	mean	SD	
MsrA	770.8	54.7	786.8	26.8	.990
CAT	86.86	9.55	87.38	3.84	.0980
GST	445.62	125.27	325.37	86.96	.041*0
XO	512.88	19.31	879.31	37.91	.001*0
MPO	102.33	23.09	153.09	9.11	.001*0
MAT	47.2	3.91	69.9	4.71	.001*0
ACY3	17.044	2.024	10.576	3.77	.03*0

*Significant at ($p \leq 0.05$)**.**

The biochemical landscape of PCOS is fundamentally driven by a dysregulated "hormonal-metabolic axis." Hyperinsulinemia and hyperandrogenism create a persistent pro-oxidative environment, significantly escalating the demand for the neutralization of ROS. This chronic physiological strain exhausts endogenous antioxidant defenses; specifically, the rapid depletion of glutathione (GSH) and GST compromises the cellular capacity to mitigate lipid peroxidation and prevent DNA damage [35]. Simultaneously, the excessive production of hydrogen peroxide overwhelms the catalytic efficiency of catalase (CAT) [36], while the persistent inflammatory milieu inhibits methionine sulfoxide reductase A (MsrA) activity. This inhibition leaves cellular proteins vulnerable to permanent structural degradation [37].

This hormonal shift triggers distinct pathways that propagate oxidative injury, as evidenced by the elevation of specific biochemical damage markers. Malondialdehyde (MDA) levels rise as a direct consequence of androgen-stimulated lipid peroxidation, which targets polyunsaturated fatty acids within the cell membrane, leaving a distinct footprint of cellular destruction [37]. Furthermore, the pro-inflammatory environment characteristic of PCOS induces the overproduction of myeloperoxidase (MPO) in leukocytes, a process that significantly exacerbates vascular pathology [38]. Furthermore, XO activity is upregulated during tissue hypoxia, accelerating purine degradation into uric acid and superoxide radicals [36].

ACY3 activity is also altered due to changes in the metabolism of mercapturic acids and the detoxification of N-acetylated amino acids under high oxidative pressure [39]. The distinction between patients presenting with significant hormonal aberrations, such as elevated androgens, high LH/FSH ratios, and low SHBG, and those with more stable hormonal profiles is primarily determined by the severity of insulin resistance and the resulting "oxidative-nitrosative blast.

Hormonal imbalances, particularly Hyperinsulinemia and hyperandrogenism escalate the metabolic demand for reactive oxygen species (ROS) neutralization, leading to the rapid consumption of glutathione (GSH) and the associated enzyme Glutathione-S-transferase (GST), which are essential for detoxifying lipid peroxides and protecting DNA from oxidative damage [35]. Elevation of Oxidative Damage Markers (MPO, XO) The hormonal shift in PCOS triggers pathways that directly generate harmful byproducts. Myeloperoxidase (MPO), an enzyme typically found in white blood cells, rises because the hormonal environment in these conditions is "pro-inflammatory," causing immune cells to overproduce MPO and contribute to vascular damage [38]. Furthermore, XO activity is upregulated during tissue hypoxia and insulin resistance, accelerating the breakdown of purines into uric acid and superoxide radicals [35].

3. A study of enzymes associated with Oxidative Stress–Related Enzymes in Women with PCOS who experienced miscarriage compared with those who did not:

In **Table 3** showed: GST, XO and MPO significant decreased and MsrA significant increased, while others enzymes (CAT, MAT, ACY3) non-significant.

Following an abortion, there is often a transient but sharp increase in markers of oxidative damage. The sudden cessation of placental blood flow and the subsequent tissue remodeling trigger the activation of XO and MPO. These enzymes facilitate an "oxidative burst" as immune cells clear residual tissue, leading to the peroxidation of polyunsaturated fatty acids and a measurable rise in MDA [40].

This process is particularly pronounced in cases of spontaneous abortion, where pre-existing oxidative stress is often a causative factor for the pregnancy loss itself [41].

Table (3): Enzymes associated with Oxidative Stress–Related Enzymes in Women with PCOS who experienced miscarriage compared with those who did not.

Enzyme Activities (U/L)	PCOS with Higher Miscarriage N=40		PCOS without Higher Miscarriage N=20		*p*-value
	mean	SD	mean	SD	
MsrA	630.2	36.5	825.31	58.91	.025*0
CAT	86.28	6.78	88.47	5.83	.890
GST	445.83	43.35	291.70	29.30	.001*0
XO	797.33	62.18	563.11	22.88	0.037*
MPO	152.56	32.23	111.47	9.85	.028*0
MAT	49.6	3.02	50.3	3.56	.5060
ACY3	12.39	2.8	13.262	5.10	.370

*Significant at ($p \leq 0.05$).

The physiological trauma and inflammatory response associated with abortion lead to the rapid consumption of the body's primary antioxidant defences. GSH and GST are heavily utilized to neutralize the surge of ROS generated during the termination process, often leaving the patient in a state of "antioxidant debt" [42]. Similarly, the activity of CAT and MsrA typically declines as these enzymes are overwhelmed by the sudden influx of hydrogen peroxide and oxidized proteins during the acute inflammatory phase following the procedure or event [40].

This highly reactive molecule causes nitrosative damage to cellular proteins and lipids, further complicating the recovery of the vascular endothelium [40]; while it initially acts as an antioxidant, its rise can reflect increased purine breakdown from tissue turnover [42], while ACY3 levels are affected by the altered mercapturic acid metabolism required to detoxify the metabolic byproducts of pregnancy termination [40].

The difference in these markers between PCOS patients without abortion and PCOS patients with abortion highlights a state of redox resilience. In successful pregnancies (no abortion), the body maintains high levels of repair enzymes and antioxidants to neutralize the "Aggressors" that would otherwise cause placental or embryonic failure. MsrA: This is the "protein repairman." It reverses oxidative damage (methionine sulfoxidation) on critical proteins. High MsrA levels in the "no abortion" group ensure that the proteins involved in implantation and early placental the decrease in GST in the "no abortion" group might seem counterintuitive, **but it actually reflects Reduced Demand:**

- **In the abortion group**, GST spikes as a "last-ditch effort" to clear massive toxic loads.
- **In the successful pregnancy group**, elevated GSH levels and reduced concentrations of harmful oxidative agents suggest that the antioxidant defense system remains effective, allowing normal cellular and placental functions to continue properly [37]. XO and MPO are considered major enzymatic sources of free radicals, and their lower activity reflects a more controlled inflammatory environment. In particular, increased MPO activity has been linked to vascular and placental tissue injury; therefore, maintaining lower MPO levels may contribute to pregnancy stability and fetal development3] 5[.

Conclusions:

PCOS appears to involve a more complicated oxidative stress profile, characterized by partial activation of certain antioxidant mechanisms, including MsrA and MAT in some patients. This response may represent an adaptive attempt to limit oxidative injury, although it does not fully prevent ongoing cellular damage. Hormonal disturbances also seem to influence oxidative balance by altering enzymatic and biochemical activities in both conditions. Furthermore, the severity of oxidative imbalance may correlate with clinical manifestations such as miscarriage, suggesting that these biomarkers could have value in predicting disease progression and related complications.

Suggest future research avenues:

Future research should focus on the gene expression of ACY3 using RT-PCR to understand the molecular mechanisms behind enzyme elevation in insulin-resistant states. Beside of, further investigation is needed into the effect of metformin and antioxidant supplementation on restoring the balance of CAT and GST activities in diabetic and PCOS populations.

Acknowledgements:

The authors would like to thank the staff of the Albatool Teaching Hospitals, AL Mosul General Hospital for their cooperation and assistance during sample collection.

Funding Statement: No

Conflict of Interest:

The authors declare no conflict of interest.

Ethical clearance:

On August 25, 2025, the University of Mosul, College of Science, Ethical Committee accepted the study's protocol (Ref:5175), and each one of the participants provided a written consent.

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