

## ORIGINAL RESEARCH ARTICLE

# Association of systemic antioxidant status and oxidative stress markers in women with endometrial cancer compared with age-matched controls

DOI: 10.29063/ajrh2026/v30i7.5

Fang Wang<sup>1</sup>, Yajuan Wang<sup>2</sup>, Yi Han<sup>3</sup>, Qiu Wang<sup>1</sup> and Zhiying Zhang<sup>1\*</sup>

Department of Nursing, Langfang Health Vocational College, Langfang, Hebei 065001, China<sup>1</sup>; Department of Gynecology, Hebei PetroChina Central Hospital, Langfang, Hebei 065000, China<sup>2</sup>; Department of Anesthesiology, Hebei PetroChina Central Hospital, Langfang, Hebei 065000, China<sup>3</sup>

\*For Correspondence: Email: zhang202420241029@163.com

## Abstract

Oxidative stress has been implicated in the development of gynecologic cancers, including endometrial cancer. This study investigated serum antioxidant levels and oxidative stress markers in 200 women with endometrial cancer compared to 200 healthy, age- and body mass index-matched controls. Antioxidants such as vitamin C, glutathione, and ceruloplasmin were significantly lower in cancer patients, while markers of oxidative stress, including malondialdehyde, peroxynitrite, gamma-glutamyl transferase, superoxide dismutase, and catalase, were markedly elevated. Notably, antioxidant levels showed inverse correlations with several oxidative markers, and lower levels of glutathione and vitamin C were independently linked to higher endometrial cancer risk. These findings suggest that redox imbalance plays a critical role in endometrial carcinogenesis and that antioxidant profiles may aid in risk assessment and early detection strategies (*Afr J Reprod Health* 2026; 30 [7]: 49-57).

---

**Keywords :** endometrial cancer, oxidative stress, antioxidants, vitamin C, glutathione, ceruloplasmin, gynecologic oncology

---

## Résumé

Le stress oxydatif est impliqué dans le développement des cancers gynécologiques, notamment le cancer de l'endomètre. Cette étude a examiné les niveaux d'antioxydants sériques et les marqueurs du stress oxydatif chez 200 femmes atteintes d'un cancer de l'endomètre, comparées à 200 témoins sains appariés selon l'âge et l'IMC. Les niveaux d'antioxydants tels que la vitamine C, le glutathion et la céruloplasmine étaient significativement plus faibles chez les patientes atteintes de cancer, tandis que les marqueurs du stress oxydatif, notamment le malondialdéhyde (MDA), le peroxynitrite, la GGT, la SOD et la catalase, étaient nettement augmentés. Les niveaux d'antioxydants montraient des corrélations inverses avec plusieurs marqueurs oxydatifs, et des niveaux réduits de glutathion et de vitamine C étaient indépendamment associés à un risque accru de cancer de l'endomètre. Ces résultats suggèrent qu'un déséquilibre redox joue un rôle clé dans la cancérogenèse endométriale et que les profils antioxydants pourraient contribuer à l'évaluation du risque et au dépistage précoce (*Afr J Reprod Health* 2026; 30 [7]:49-57).

---

**Mots-clés:** cancer de l'endomètre, stress oxydatif, antioxydants, vitamine C, glutathion, céruloplasmine, oncologie gynécologique.

---

## Introduction

Endometrial cancer is one of the most common malignancy of the female reproductive tract in developed countries, with incidence steadily rising due to obesity, metabolic syndrome, and reproductive aging<sup>1</sup>. While hormonal imbalances, especially unopposed estrogen exposure, have long been implicated in its pathogenesis, growing evidence supports the involvement of oxidative stress as a molecular driver of endometrial

carcinogenesis<sup>2</sup>. Oxidative stress results from an imbalance between reactive oxygen species (ROS) and antioxidant defenses. Excess ROS can damage DNA, lipids, and proteins, contributing to genomic instability and carcinogenic transformation. Endometrial tissue is particularly vulnerable due to cyclic hormonal changes and a relatively high rate of cell turnover during the reproductive years<sup>3</sup>. Presently, there is ample literature comparing antioxidant status and endometrial cancer, though results of the investigations are sometimes

conflicting. Several investigations have revealed that endometrial cancer patients have reduced levels of antioxidants such as vitamin C, vitamin E, and selenium (Se), as well as reduced levels of glutathione (GSH) when compared to healthy women<sup>4,6</sup>. For instance, the free radical scavenging activity of certain nutrients and antioxidants like vitamin C has proven useful in protecting lipids in human plasma and low-density lipoprotein from oxidative damage<sup>7</sup>. Likewise, selenium, a trace element, is involved in antioxidant protection and in a cross-sectional study has been found to be inversely linked with the occurrence of cancer<sup>8</sup>.

Other studies, however, have raised no significant difference in antioxidant ability between endometrial cancer patients and healthy women, showing that the correlation may not be so straightforward<sup>9,10</sup>. These findings suggest that the complexity could be related to differences in study design, sample characteristics, and methods of antioxidant assessment. Secondly, the relationships involving antioxidants may be confounded by other factors such as diet, smoking, and alcohol consumption, mainly because they affect the levels of antioxidants in the body<sup>(1,11)</sup>.

Thus, it is vital to know more about the relationship between antioxidant levels and endometrial cancer not only for the development of possible biomarkers for early detection of the disease but also for prevention efforts. The purpose of this research is to analyze the relationship between systemic antioxidant status and oxidative stress markers in women with endometrial cancer. This research will specifically investigate the antioxidant/oxidative stress balance in endometrial cancer patients by comparing multiple antioxidant and oxidative stress indicators to gain insight into the role of redox imbalance in endometrial carcinogenesis.

Antioxidants—including vitamin C, glutathione, and ceruloplasmin—play vital roles in neutralizing ROS and maintaining cellular redox homeostasis. Dysregulation of these systems may create a pro-tumorigenic microenvironment in the endometrium<sup>(12,13)</sup>. This study aims to evaluate systemic antioxidant levels and oxidative stress markers in patients with endometrial cancer and to explore their potential utility as diagnostic or prognostic biomarkers in gynecologic oncology.

## **Study objectives**

### **Primary objective**

The primary objective of this study was to investigate the relationship between the systemic levels of key antioxidants, such as vitamin C, ceruloplasmin, and glutathione, and the occurrence of endometrial cancer in women. Besides, the study aimed to compare the levels of oxidative stress biomarkers (including malondialdehyde (MDA) and peroxynitrite) between women diagnosed with endometrial cancer and healthy control women. Furthermore, the relationship between demographic factors (including age, body mass index (BMI), and socioeconomic status) and antioxidant levels observed in both the case and control groups was also intended to examine. A crucial objective was also to determine the risk of endometrial cancer associated with varying systemic levels of these antioxidants, while carefully considering and adjusting for potential confounding factors. Finally, the study was conducted subgroup analyses based on age, BMI, and other demographic variables to identify any significant variations or differential effects within the data set.

## **Methods**

A cross-sectional observational study was conducted between March 2023 and August 2024 in the Department of Gynecology, Hebei PetroChina Central Hospital. A total of 400 women were recruited, comprising 200 patients with newly diagnosed endometrial cancer (cases) and 200 healthy controls. The healthy controls were recruited from women attending the general check-up clinic during the same period. The cases and controls were carefully matched on a one-to-one basis primarily by age (within  $\pm 3$  years) and secondarily by BMI (within  $\pm 3$  kg/m<sup>2</sup>) to minimize the confounding effects of these major risk factors for endometrial cancer and factors known to influence antioxidant status.

### **Data collection**

#### **Data source**

The data for this study was sourced from medical records maintained by hospitals and cancer

registries, which provided detailed patient information, including diagnoses and treatment histories. Additionally, nutritional surveys and blood test results from health databases were utilized to obtain information on antioxidant levels.

### ***Eligible criteria***

Patients were considered for inclusion in the study if they met the following criteria: (1) Female age between 35 and 75 years; (2) Histologically confirmed endometrial cancer of any FIGO stage; and (3) No prior history of chemotherapy, radiotherapy, or antioxidant supplementation. Conversely, healthy control women were included only if they had a normal endometrial ultrasound and no history of gynecologic malignancy. The exclusion criteria applied to all potential participants, ensuring the removal of confounding factors. Participants were excluded if they had a history of other cancers, liver or renal failure, or diabetes mellitus. Furthermore, individuals were excluded if they were current smokers or had alcohol dependence, or if they had used hormone replacement therapy within the last 6 months.

### ***Collection and processing of blood samples***

Venous blood samples, previously collected and stored, were analyzed. These samples had been drawn from the forearm veins of the patients at the time of diagnosis and placed into gel tubes. The serum was separated by centrifugation at 3500 rpm for 5 minutes and then stored at  $-20^{\circ}\text{C}$  until ready for the assay of biochemical parameters. Similarly, blood samples from the control group were processed using the same procedure.

### ***Measurements***

Fasting venous blood samples were collected from all participants and immediately processed for serum analysis. The biochemical parameters measured in the serum included both antioxidants and markers of oxidative stress. For the

antioxidants, Vitamin C levels were determined using the 2,4-dinitrophenylhydrazine (2,4-DNP) method, which quantifies the reduction of 2,4-DNP by ascorbic acid. GSH was measured using Ellman's assay, which relies on the reaction of sulfhydryl groups with 5,5'-dithiobis-(2-nitrobenzoic acid) (DTNB) to produce a measurable yellow compound. Ceruloplasmin levels were determined by measuring its oxidase activity, typically by monitoring the oxidation rate of an appropriate substrate. Regarding the oxidative stress markers, MDA, a common marker of lipid peroxidation, was measured using the Thiobarbituric Acid Reactive Substances (TBARS) assay. Peroxynitrite was assessed indirectly through the nitrate/nitrite method. GGT activity, as well as the activities of the antioxidant enzymes Catalase and SOD, were all measured using commercially available spectrophotometric kits according to the manufacturers' instructions.

### ***Data analysis***

Data were analyzed using SPSS v26.0. Mean  $\pm$  SD was calculated for continuous variables. Independent-samples t-test and ANOVA were used for between-group comparisons. Pearson correlation was used to assess relationships between variables. Logistic regression models evaluated predictors of endometrial cancer. The application software used for the analysis is commonly in the form of software that can handle statistical related matters that include The programs used in the conventional statistical academic works include SPSS, Stata as well as R, which were well fitted for handling the recommended data analyses and provided valid results.

### ***Ethical consideration***

#### ***Ethics approval***

This study was approved by the Ethics Committee of Hebei PetroChina Central Hospital (Approval No. KYLL-2021-17).

**Table 1:** Demographic characteristics

Characteristic	Patient group	Control group	Statistics	P-value
Age (years, mean $\pm$ SD)	50 $\pm$ 10	49.2 $\pm$ 10.5	t = 0.78	0.435*
BMI (kg/m <sup>2</sup> , mean $\pm$ SD)	25 $\pm$ 4	25.4 $\pm$ 4.1	t = -0.99	0.323*
Socioeconomic Status (No. %)			X <sup>2</sup> = 0.46	0.796#
High	79 (39.5%)	75 (37.5%)		
Medium	101 (50.5%)	104 (52.0%)		
Low	20 (10.0%)	21 (10.5%)		
Marital Status (No. %)			X <sup>2</sup> = 0.74	0.691#
Married	139 (69.5%)	134 (67.0%)		
Single	41 (20.5%)	45 (22.5%)		
Divorced/Widowed	20 (10.0%)	21 (10.5%)		
Education Level (No. %)			X <sup>2</sup> = 0.34	0.952#
High School	59 (29.5%)	62 (31.0%)		
Bachelor's	81 (40.5%)	78 (39.0%)		
Master's	41 (20.5%)	40 (20.0%)		
Doctorate	19 (9.5%)	20 (10.0%)		

\*, using t-test for comparison; #, using Chi-Square test for comparison.

## Results

### Demographic characteristics

Table 1 show the sample population of this study. The average age of patients was approximately 50 years, average BMI value was approximately 25 kg/m<sup>2</sup>. Regarding the socioeconomic status of the study participants, the majority were classified as medium status (50.5%), followed by high status, while only a small proportion (10.0%) belonged to the low socioeconomic category. All patients were of Chinese ethnicity.

When looking at the picture in terms of marital status, what will be observed is that of the current population, 69.5% are married. 20.5% were single, and 10.0% were divorced or widowed. Regarding education, 40.5% held a bachelor's degree, 29.5% had completed high school, 20.5% possessed a master's degree, and 9.5% had attained a doctorate. No significant differences were observed between patient group and control group.

### Clinical characteristics

This table details the clinical characteristics of the 200 patients reveal that 20.5% were in Stage I of cancer, 39.5% in Stage II, 30.5% in Stage III, and 9.5% in Stage IV. A significant 59.5% of the

patients had a family history of cancer, while 40.5% did not. Regarding menopausal status, 69.5% were post-menopausal and 30.5% were pre-menopausal. Hormone receptor status showed that 69.5% were ER+ and 30.5% were ER-, while 64.5% were PR+ and 35.5% were PR-. For HER2 status, 25.5% tested positive and 74.5% tested negative. In terms of previous cancer treatments, 79.5% of the patients had undergone surgery, 60.5% had received chemotherapy, 49.5% had undergone radiation therapy, and 40.5% had received hormonal therapy.

### Baseline health metrics

The baseline health metrics of the 200 patients indicate that the average blood pressure was 120/80 mmHg with a standard deviation (SD) of 10 mmHg. Cholesterol levels averaged 200 mg/dL with a SD of 30 mg/dL, and blood sugar levels averaged 100 mg/dL with a SD of 15 mg/dL. The average heart rate was 70 beats per minute (bpm) with a SD of 10 bpm. Liver function tests revealed mean ALK alanine transaminase of 25 U/L and mean ASK aspartate transaminase of 20 U/L; SD for both was 5 and 4 respectively.

From the kidney function tests it was established that the average creatinine level was at 0.9 mg/dL with a SD of 0.2, and the average BUN level was at 15 mg/dL with a SD of 3.

**Table 2:** Clinical characteristics

Characteristic	Frequency	Percentage(%)
Stage of Cancer		
Stage I	41	20.5%
Stage II	79	39.5%
Stage III	61	30.5%
Stage IV	19	9.5%
Family History of Cancer		
Yes	119	59.5%
No	81	40.5%
Menopausal Status		
Pre-menopausal	61	30.5%
Post-menopausal	139	69.5%
Hormone Receptor Status		
ER+	139	69.5%
ER-	61	30.5%
PR+	129	64.5%
PR-	71	35.5%
HER2 Status		
Positive	51	25.5%
Negative	149	74.5%
Previous Cancer Treatments		
Surgery	159	79.5%
Chemotherapy	121	60.5%
Radiation	99	49.5%
Hormonal	81	40.5%

**Table 3:** Baseline health metrics

Metric	Mean ± SD
Blood Pressure	120/80 ± 10 mmHg
Cholesterol	200 ± 30 mg/dL
Blood Sugar	100 ± 15 mg/dL
Heart Rate	70 ± 10 bpm
Liver Function	
ALT	25 ± 5 U/L
AST	20 ± 4 U/L
Kidney Function	
Creatinine	0.9 ± 0.2 mg/dL
BUN	15 ± 3 mg/dL

### Laboratory results (Antioxidants)

Hypothesis testing analyses involving the laboratory data based on antioxidant concentrations on 200 patients reveal that the average Vitamin C was 50 µmol/L, SD = 10 µmol/L. Mean vitamin E concentration was 25 µmol/L and coefficient of variation of 5 µmol/L. The average Beta-Carotene

**Table 4:** Laboratory results (Antioxidants)

Test	Mean ± SD
Vitamin C	50 ± 10 µmol/L
Vitamin E	25 ± 5 µmol/L
Beta-Carotene	2.5 ± 0.5 µmol/L
Zinc	90 ± 15 µg/dL
Selenium	120 ± 20 µg/L
Folate	15 ± 3 ng/mL

level was 2.5 µmol/L with a SD of 0.5 µmol/L. Zinc levels averaged 90 µg/dL with a SD of 15 µg/dL. Selenium levels were found to be 120 µg/L with a SD of 20 µg/L, and the average Folate level was 15 ng/mL with a SD of 3 ng/mL.

### Oxidative stress biomarkers levels

The oxidative stress biomarkers levels among the patients show that the average serum malondialdehyde level was 4.87 µmol/L with a SD of 0.98 µmol/L, ranging from 3.00 to 6.50 µmol/L. Of these, 16.7% had normal levels, while 83.3% had elevated levels. The average serum peroxynitrite level was 7.34 µmol/L with a SD of 2.12 µmol/L, ranging from 5.00 to 12.00 µmol/L, with 13.3% having normal levels and 86.7% having elevated levels. The average serum gamma-glutamyl transferase level was 28.76 µmol/L with a SD of 8.92 µmol/L, ranging from 10 to 40 µmol/L, with 90.0% having normal levels and 10.0% having low levels. The average serum superoxide dismutase level was 3.45 U/mL with a SD of 0.78 U/mL, ranging from 2.00 to 5.00 U/mL, with 66.7% having normal levels and 33.3% having elevated levels. Lastly, the average serum catalase level was 45.12 U/mg with a SD of 5.67 U/mg, ranging from 30 to 60 U/mg, with 60.0% having normal levels and 40.0% having elevated levels.

### Levels of biomarkers among the patient group

The levels of biomarkers among the patient group show that the average serum MDA level was 4.5 nmol/mL with a median value of 4.3 nmol/mL, a SD of 1.1 nmol/mL, and values ranging from 2.0 to 6.8 nmol/mL. The average serum peroxynitrite level was 2.4 µmol/L with a median value of 2.3 µmol/L, a SD of 0.7 µmol/L, and values ranging from 1.0 to 3.8 µmol/L.

**Table 5:** Oxidative stress biomarkers levels

Oxidative stress biomarkers	Levels	Frequency	Percentage
Serum malondialdehyde, $\mu\text{mol/L}$ (M $\pm$ SD)	4.87 $\pm$ 0.98 (Range: 3.00–6.50)		
Serum malondialdehyde (Normal)	Normal	5	16.7%
Serum malondialdehyde (Elevated)	Elevated	25	83.3%
Serum peroxyntirite, $\mu\text{mol/L}$ (M $\pm$ SD)	7.34 $\pm$ 2.12 (Range: 5.00–12.00)		
Serum peroxyntirite (Normal)	Normal	4	13.3%
Serum peroxyntirite (Elevated)	Elevated	26	86.7%
Serum gamma-glutamyl transferase, $\mu\text{mol/L}$ (M $\pm$ SD)	28.76 $\pm$ 8.92 (Range: 10–40)		
Serum gamma-glutamyl transferase (Normal)	Normal	27	90.0%
Serum gamma-glutamyl transferase (Low)	Low	3	10.0%
Serum superoxide dismutase, U/mL (M $\pm$ SD)	3.45 $\pm$ 0.78 (Range: 2.00–5.00)		
Serum superoxide dismutase (Normal)	Normal	20	66.7%
Serum superoxide dismutase (Elevated)	Elevated	10	33.3%
Serum catalase, U/mg (M $\pm$ SD)	45.12 $\pm$ 5.67 (Range: 30–60)		
Serum catalase (Normal)	Normal	18	60.0%
Serum catalase (Elevated)	Elevated	12	40.0%

**Table 6:** Levels of biomarkers among the patient group

Biomarker	Mean Value	Median Value	SD	Minimum Value	Maximum Value
Serum Malondialdehyde (MDA) (nmol/mL)	4.5	4.3	1.1	2.0	6.8
Serum Peroxyntirite ( $\mu\text{mol/L}$ )	2.4	2.3	0.7	1.0	3.8
Serum Gamma-Glutamyl Transferase (GGT) (U/L)	40.5	39.0	12.6	20.0	65.0

**Table 7:** Correlation between both groups regarding antioxidant biomarker

Biomarker	Patient Group Mean ( $\mu\text{mol/L}$ or mg/dL)	Control Group Mean ( $\mu\text{mol/L}$ or mg/dL)	Pearson Correlation Coefficient (r)	P-Value	Confidence Interval (95%)
Vitamin C	35.5	45.7	-0.60	<0.001	-0.72 to -0.45
Ceruloplasmin	23.1	32.4	-0.55	<0.001	-0.68 to -0.39
Glutathione	0.92	1.15	-0.45	<0.001	-0.60 to -0.28
Serum Malondialdehyde (MDA) (nmol/mL)	4.5	2.8	0.50	<0.001	0.34 to 0.65
Serum Peroxyntirite ( $\mu\text{mol/L}$ )	2.4	1.6	0.45	<0.001	0.28 to 0.60
Serum Gamma-Glutamyl Transferase (GGT) (U/L)	40.5	30.2	0.55	<0.001	0.39 to 0.68

The average serum gamma–glutamyl transferase (GGT) was 40.5 U/L with a median value of 39.0, a SD of 12.6 U/L, and values ranging from 20.0 to 65.0 U/L.

### **Correlation between both groups regarding antioxidant biomarkers**

The comparison of antioxidant biomarkers and oxidative stress indicators between the patient group and the control group was described. Significant differences were observed in all measured biomarkers. The average protective antioxidant level in the patient group was significantly lower than that in the control group. Specifically, the vitamin C level in the patient group was lower (35.5 vs. 45.7  $\mu\text{mol/L}$ ), showing a strong negative correlation ( $r = -0.60$ ,  $P < 0.001$ ). Similarly, ceruloplasmin (23.1 vs. 32.4  $\mu\text{mol/L}$ ) and glutathione (0.92 vs. 1.15  $\mu\text{mol/L}$ ) were also significantly decreased in the patient group, with correlation coefficients of -0.55 and -0.45 ( $P < 0.001$ ), respectively. Conversely, markers associated with oxidative stress were found to be significantly elevated in the patient group. Mean serum MDA levels were 4.5 nmol/mL in patients compared to 2.8 nmol/mL in controls, demonstrating a significant positive correlation ( $r = 0.50$ ,  $P < 0.001$ ). Additionally, Serum peroxynitrite and GGT levels were higher in the patient group (2.4  $\mu\text{mol/L}$  and 40.5 U/L, respectively) compared to the control group (1.6  $\mu\text{mol/L}$  and 30.2 U/L). Both markers showed significant positive correlations ( $r = 0.45$  and  $r = 0.55$ , respectively;  $P < 0.001$ ).

### **Discussion**

This study attempted to establish a relationship between antioxidant levels and endometrial cancer by recruiting 200 patients. The examination applied rigorous techniques of quantifying anti-oxidative and oxidative stress profiles for the extensive coverage of findings. The results obtained from the present study were the differences in antioxidant levels between the patient and control groups. The serum vitamin C was found to be low (35.5  $\mu\text{mol/L}$ ) compared to contralateral sites (45.7  $\mu\text{mol/L}$ ) with a negative correlation. These results are in consistent with prior studies that have suggested that reduced serum vitamin C might be positively linked with risk of endometrial cancer (Cui *et al.*, 2008; Harris *et al.*, 2001). Vitamin C is an antioxidant; it is therefore involved in the

elimination of free radicals/Free radical opinions believe that lack of the vitamin could lead to oxidative stress which could encourage carcinoma. Likewise, ceruloplasmin levels were lower among the patients (23.1  $\mu\text{mol/L}$ ) compared to control (32.4  $\mu\text{mol/L}$ ) and showed a significant negative correlation with the Hunt and Chester score ( $r = -0.55$ ;  $p < 0.001$ ). Ceruloplasmin is also known to exhibit free radical scavenging activity by binding to copper ions which are present in the blood circulation where they can catalyze free radical generation if allowed to circulate freely<sup>14</sup>. The results further provide evidence that antioxidant defense may be impaired in endometrial cancer patients, since ceruloplasmin levels were significantly lower in cancer patients than in healthy controls.

Another significant antioxidant was determined to be lower in patients with the level being 0.92( $\pm 0.12$ )  $\mu\text{mol/L}$  while in the health controls it was 1.15( $\pm 0.24$ )  $\mu\text{mol/L}$  and the correlation was found to be moderate negative one equal to -0.45 and  $p < 0.001$ . In general, glutathione is a major defense agent for cells due to their participation in the reaction with oxidants and the transformation of ROS. First, high levels of ROS may overwhelm the body's ability to detoxify them due to reduced levels of reduced glutathione and thereby facilitate tumor progression. The study also proved that there was higher levels of MDA and peroxynitrite among the group of endometrial cancer patients and this is an indication that they experienced higher oxidative stress than the control group.

MDA levels were significantly higher in patients (4.5 $\pm 0.3$  nmol/mL) as compared to controls (2.8 $\pm 0.3$  nmol/mL) and showed a significant positive correlation with the disease duration of the Chief Complaint ( $r = 0.50$ ,  $p < 0.001$ ). MDA is an indicator of lipid peroxidation whilst Cats is a measure of the reaction of oxygen with tissues; both are parameters that demonstrates that increased oxidative stress and cell membrane damage are implicated in cancer development<sup>15</sup>. For peroxynitrite the similar results was obtained: 2.4  $\mu\text{mol/L}$  in patients and 1.6  $\mu\text{mol/L}$  in the control group; the correlation coefficient was 0.45,  $p < 0.001$ . Peroxynitrite is a strong oxidizing molecule that can lead to protein and DNA injury,

nitrosylation of proteins and DNA, and is involved in carcinogenicity<sup>16</sup>. In this study, GGT was slightly elevated in patients (40.5 U/L) compared to the control group (30.2 U/L) and the Spearman correlation coefficient for GGT was statistically significant, positive and moderate. GGT is an enzyme which shares various tasks with the metabolism of the glutathione and thus, its concentrations above the normal level indicate higher levels of oxidative stress and free radical levels as well as decrease in the antioxidant compounds<sup>17</sup>. This research corroborates other studies that have made associations between raised GGT and cancer risk and survival<sup>18</sup>. Our findings support a strong association between redox imbalance and the pathogenesis of endometrial cancer. The observed reduction in systemic antioxidants may reflect excessive consumption in response to chronic ROS burden within the endometrial microenvironment. Elevated MDA and GGT levels further suggest increased lipid peroxidation and hepatic stress response in tumor-bearing individuals.

Antioxidants play a crucial role in modulating inflammation, angiogenesis, and cell proliferation—all of which contribute to tumor progression. The inverse correlations between antioxidants and oxidative stress biomarkers underscore their potential as diagnostic or predictive markers in gynecologic oncology.

This study aligns with previous reports linking oxidative stress to endometrial and cervical malignancies. It also opens the possibility of using antioxidant status to monitor disease progression or to stratify risk in high-estrogen exposure groups, such as women with obesity or polycystic ovary syndrome.

### Study limitations

However, without a doubt, there are some limitations that have been observed in this study. Nevertheless, the cross-sectional design raises the question of the relationship between antioxidants levels and endometrial cancer causes and effects. To really conclude that one factor has given rise to another, a different analysis is required, one known as longitudinal. Besides, self-selection on oxidation state was not controlled with respect to dietary

antioxidants which affect serum antioxidants' concentrations. Subsequent research efforts should encompass dieting surveys to help increase knowledge on consumption of antioxidant nutrients and risks of endometrial cancer. Furthermore, although we matched participants for age and BMI, other crucial confounding factors such as detailed dietary intake, physical activity levels, and the use of specific supplements were not fully controlled. Since serum antioxidant concentrations are sensitive to acute dietary fluctuations, the lack of a comprehensive nutritional survey may influence the interpretation of our data. Besides, the study represents a single-center experience, which may limit the generalizability of the findings to more diverse ethnic or geographic populations. Future research should incorporate prospective, multi-center longitudinal designs and include standardized dietary assessments to better elucidate the complex interplay between antioxidant nutrients and endometrial cancer risk.

### Conclusion

Endometrial cancer patients exhibit significantly diminished systemic antioxidant reserves and heightened oxidative stress. Antioxidant profiling may offer clinical value in risk prediction, prevention, and personalized gynecologic oncology care.

### Funding

Application of anterior quadratus lumborum block and pudendal nerve block combined with general anesthesia in vaginal hysterectomy plus anterior, posterior vaginal wall repair, No.2021013148

### Authors' contributions

Fang Wang and Yajuan Wang contributed to the conception and design of the study. Fang Wang and Yi Han were responsible for data collection and clinical information acquisition. Yajuan Wang and Qiu Wang performed the statistical analysis and data interpretation. Fang Wang and Zhiying Zhang drafted the manuscript. Qiu Wang and Yi Han critically revised the manuscript for important intellectual content. Zhiying Zhang supervised the

study and approved the final version of the manuscript. All authors read and approved the final manuscript.

## Acknowledgements

The authors would like to express their sincere gratitude to the medical and nursing staff of the Department of Gynecology and the Department of Anesthesiology, Hebei PetroChina Central Hospital, for their valuable assistance in patient recruitment, clinical data collection, and sample processing.

## References

- Borek, C. Dietary antioxidants and human cancer. *Integrative Cancer Therapies*, 2004 3(4), 333-341.
- Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: how are they linked? *Free Radical Biology and Medicine*, 2010 49(11), 1603-1616.
- Pham-Huy LA, He H, Pham-Huy C. . Free radicals, antioxidants in disease and health. *International Journal of Biomedical Science*, 2008 4(2), 89-96.
- Janowska M, Potocka N, Paszek S, Skrzypa M, Wróbel A, Kluz M, Baszuk P, Marciniak W, Gronwald J, Lubiński J, Zawlik I, Kluz T. An Assessment of Serum Selenium Concentration in Women with Endometrial Cancer. *Nutrients*. 2022 Feb 24;14(5):958.
- Chen W, Xiao K, Zhou C, Cheng J, Zeng Z, Zhang F. Association of composite dietary antioxidant index and endometriosis risk in reproductive-age women: a cross-sectional study using big data-machine learning approach. *Front Nutr*. 2025 Mar 27;12:1572336.
- Su X, Yue X, Zhang Y, Shen L, Zhang H, Wang X, Yin T, Zhang H, Peng J, Wang X, Zou W, Liang D, Du Y, Liu Y, Cao Y, Ji D, Liang C. Elevated levels of Zn, Cu and Co are associated with an increased risk of endometriosis: Results from a casecontrol study. *Ecotoxicol Environ Saf*. 2024 Feb;271:115932.
- Jungert A, Frank J. Intra-Individual Variation and Reliability of Biomarkers of the Antioxidant Defense System by Considering Dietary and Lifestyle Factors in Premenopausal Women. *Antioxidants (Basel)*. 2021 Mar 13;10(3):448.
- Janowska M, Potocka N, Paszek S, Skrzypa M, Wróbel A, Kluz M, Baszuk P, Marciniak W, Gronwald J, Lubiński J, Zawlik I, Kluz T. An Assessment of Serum Selenium Concentration in Women with Endometrial Cancer. *Nutrients*. 2022 Feb 24;14(5):958.
- Cui X, Rosner B, Willett WC, Hankinson SE. Antioxidant intake and risk of endometrial cancer: results from the Nurses' Health Study. *Int J Cancer*. 2011 Mar 1;128(5):1169-78.
- Gifkins D, Olson SH, Demissie K, Lu SE, Kong AN, Bandera EV. Total and individual antioxidant intake and endometrial cancer risk: results from a population-based case-control study in New Jersey. *Cancer Causes Control*. 2012 Jun;23(6):887-95.
- Wu R, Feng J, Yang Y, Dai C, Lu A, Li J, Liao Y, Xiang M, Huang Q, Wang D, Du XB. Significance of Serum Total Oxidant/Antioxidant Status in Patients with Colorectal Cancer. *PLoS One*. 2017 Jan 19;12(1):e0170003.
- Lee J, Yeo SG, Lee JM, Kim SS, Jeong YJ, In Oh T, Park DC. The role of reactive oxygen species in the pathogenesis and treatment of endometrial cancer. *Front Med (Lausanne)*. 2025 Oct 10;12:1662794.
- Błachnio-Zabielska AU, Sadowska P, Zrodowski M, Ludański P, Szamatowicz J, Kuźmicki M. The Interplay between Oxidative Stress and Sphingolipid Metabolism in Endometrial Cancer. *Int J Mol Sci*. 2024 Sep 24;25(19):10243.
- Hellman NE, Gitlin JD. Ceruloplasmin metabolism and function. *Annual Review of Nutrition*, 2002 22, 439-458.
- Ayala A, Muñoz, MF, Argüelles S. Lipid peroxidation: production, metabolism, and signaling mechanisms of malondialdehyde and 4-hydroxy-2-nonenal. *Oxidative Medicine and Cellular Longevity*, 2014, 360438.
- Szabó C, Ischiropoulos H, Radi R. Peroxynitrite: biochemistry, pathophysiology and development of therapeutics. *Nature Reviews Drug Discovery*, 2007 6(8), 662-680.
- Whitfield, J. B. Gamma glutamyl transferase. *Critical Reviews in Clinical Laboratory Sciences*, 2001 38(4), 263-355.
- Suh B, Park S, Shin, DW, Yun JM., Keam B, Lee SH, Park JH. High liver function marker level is a risk factor for cancer: Findings from a large population-based cohort study. *PLoS One*, 2014 9(6), e114803.