RESEARCH ARTICLE

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Evaluation of Oxidative Stress, Anti-Oxidant, Vitamins and Co-Factor Elements in The Sera of Gastric Cancer in Iraqi Patients

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Abstract

Objective: The objective of this study is to analyze oxidative stress markers Total Oxidant Status (TOS) and total Antioxidant Status (TAS), assess antioxidant levels (vitamin C, E), and evaluate co-factor element profiles zinc (Zn), copper (Cu), iron (Fe) in the serum of Iraqi gastric cancer patients. By elucidating these relationships, the research aims to enhance knowledge on oxidative stress, dietary factors, and potential therapeutic approaches for managing nutritional imbalances in this cohort. **Methods:** The study included 60 gastric cancer patients and 60 matched controls. Blood samples were collected and serum was extracted for analysis of TOS, TAS, Vitamin C, Vitamin E, copper, zinc, and iron levels. Measurements were conducted using spectrophotometry and ELISA kits from various companies. Statistical analysis was performed with IBM SPSS 25.0, presenting results as means ± SD, and differences between groups were assessed via independent samples t-test at $p < 0.05$ and $p \leq 0.01$. **Results:** The study results indicated statistically significant differences between gastric cancer patients and controls in various biomarkers, with all comparisons showing p-values less than 0.001. This suggests strong evidence for the observed differences between the two groups in (TOS), (TAS), vitamins C and E, Cu, Zn, and Fe levels. These relationships underscore the intricate connections among biomarkers in gastric cancer pathophysiology. **Conclusion:** The study underscores the intricate relationship between oxidative stress, antioxidant depletion, and micronutrient imbalances in gastric cancer. These findings offer valuable insights into the disease's pathophysiology, indicating potential diagnostic biomarkers. Further research is warranted to unravel underlying mechanisms and explore clinical applications for early gastric cancer diagnosis.

Keywords: Gastric cancer- oxidative stress- antioxidant- cofactor minerals and vitamins

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Introduction

Gastric cancer ranks as the second major cause of cancer-related mortality globally, with its epidemiology undergoing significant changes in recent decades [1]. Although early detection and comprehensive therapies have improved, gastric cancer patients still have a low 5-year survival rate of 20%-30%. Surgery remains the only option. Curative therapy for localized gastric cancer. Unfortunately, 50%-90% of patients with advanced and localized gastric cancer have a poor surgical prognosis due to local recurrence or distant metastases [2].

Preoperative risk stratification can enhance clinical outcomes for this patient population by guiding complete therapy. Prognostic biomarkers that can be easily and inexpensively acquired in clinical practice have gained interest. Many physicians and a growing number of researchers have conducted [3, 4].

Oxidative stress leads to macromolecular damage, protein denaturation, DNA damage, and lipid peroxidation. It also causes disruptions in regular metabolic processes.

This activity can result in the development of cancer. Oxidative stress increases tumor growth, invasion, and metastasis. There is a rare link between the development of gastric cancer and oxidative stress markers [5, 6]. Reactive oxygen species (ROS) are the primary mediators of oxidative stress and contribute to cancer growth by inducing. DNA damage and genetic abnormalities can suppress apoptosis and promote tumor cell growth, invasion, and metastasis [7, 8].

Biomarkers indicating oxidative stress can aid in determining prognosis and risk stratification for gastric cancer patients. The total oxidant status (TOS) assesses the body's overall oxidation, whereas the total antioxidant status (TAS) measures its entire antioxidant status [9, 10]. The oxidative stress index (OSI), calculated as the ratio

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of TOS to TAS, is a more accurate indicator of oxidative stress. OSI measures TAS and TOS to identify oxidation-antioxidant imbalances [11].

Gentile F et al. [12] proposed Oxidative stress levels have been presented as helpful markers for monitoring the beginning and progression of cancer.

Antioxidants are substances that hinder the process of oxidation, even at low levels, and therefore play various important roles in the body's physiology [13]. Antioxidants can divide into enzymatic and non-enzymatic antioxidants. Enzymatic antioxidants containing Catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD) are functionally interconnected because the product of the reaction catalyzed by SOD [14] and GSH. Vitamins A, C, and E are frequently consumed as dietary supplements for overall health benefits. These supplements are classified as non-enzymatic antioxidants. Due to their low risk and probable association with reduced cancer risk, they are an appealing choice as preventative anti-cancer drugs [15].

Microminerals such as zinc (Zn), copper (Cu), and iron (Fe) play vital roles in enhancing and preserving the effectiveness of these antioxidants. The essential cofactors linked to SOD are copper and zinc, so it is referred to as Cu/Zn SOD. Zinc suppresses the activity of RNA polymerase and diminishes the reproduction of viruses [16].

The purpose of this study is to give significant insights into the oxidative stress state (TOS, TAS), antioxidant levels as vitamin (C, E) concentrations, and co-factor (Zn, Cu, Fe) element profiles in the sera of Iraqi gastric cancer patients. The findings may help to improve our understanding of the impact of oxidative stress and dietary variables in gastric cancer development and progression. Furthermore, the study's findings might have implications for possible treatment strategies addressing oxidative stress and nutritional imbalances in this patient group.

Materials and Methods

The Study Population

The study's participants were separated into two groups: patients and controls. The patient group comprised 60 gastric cancer patients (40 females and 20 males, ages 30-60 years). Individuals with gastric cancer were checked by a doctor at the "Oncology Teaching Hospital" in Medical City, Baghdad, Iraq. The control group consisted of 60 healthy individuals who were precisely matched in age and gender to the sick group. Between September and December 2023, all trial volunteers provided informed written permission before participating, and the patients completed a questionnaire. All of the patients in the research had no history of smoking, alcohol intake, or pregnancy. Furthermore, those with additional medical disorders including diabetes, hypertension, and hyperthyroidism were expressly excluded from the study, which focused entirely on patients with gastric cancer.

Sample Collection

Five-milliliter venous blood samples were obtained from gastric cancer patients and controls, placed in a gel tube, and left at room temperature (25°C) for 30 minutes to separate the clot, before being centrifuged at 4000 rpm for 5 minutes to separate serum. The obtained serum was tested for oxidative and antioxidant parameters (TOS, TAS, vitamin C, E, copper, zinc, and iron).

Sample analysis

Serum levels of TOS and TAS in the blood were measured using a spectrophotometer microplate reader using the colorimetric method described by the protocol by Rel assay diagnostic (generation total antioxidant status, total oxidant status) for MEGA TIP, Türkiye [17]. Serum vitamin C, vitamin E determination by Kinesisdx, a human vitamin C ELISA kit, and a human vitamin E ELISA by Kinesisdx company in California, USA. Based on sandwich enzyme-linked immunosorbent assay (ELISA) technology [18]. Serum levels of iron determination by the iron direct method kit, company, Biolabo sas, Maizy [19], France based on the auto method. Serum levels of zinc and copper were measured using the zinc assay kit and the copper assay kit by Gcell Company China [20].

Statistical analysis

The analysis utilized version 25.0 of the IBM SPSS Statistics software (IBM Corporation, New York, United States). Descriptive statistics were employed for data analysis, and the results are presented as means ± standard deviation (SD). An independent samples t-test was applied to evaluate mean differences between the patient and control groups. Statistical significance was considered at $p < 0.05$ and highly significant at $p \leq 0.01$.

Results

Table 1 shows the results of this study, which compared gastric cancer patients to the control group. The average age of gastric cancer patients was 52 years with a standard deviation of 9.3, whereas the mean age of the control group was 50 years with a standard deviation of 10.3.

The p-value associated with this comparison was non-significant. For the parameter "BMI, Kg/m^2", the mean BMI of gastric cancer patients was 23.5 kg/m2 with a standard deviation of 3.7, while the control group had a mean BMI of 24.1 kg/m^2 with a standard deviation of 4.1. The p-value associated with this comparison was non-significant as well. The results showed that there is no statistically significant difference in age or BMI between gastric cancer patients and the control group. These findings gave a valuable chance to do a comparative

Table 1.Analysis of Age and BMI between Control and Gastric Cancer Patients

The studied Parameters	Mean ±SD Patients with gastric cancer	Mean ±SD for control	p-value
Age (years)	52±9.3	50±10.3	0.571NS
BMI (Kg/m^2)	23.5±3.7	24.1±4.1	0.684 NS

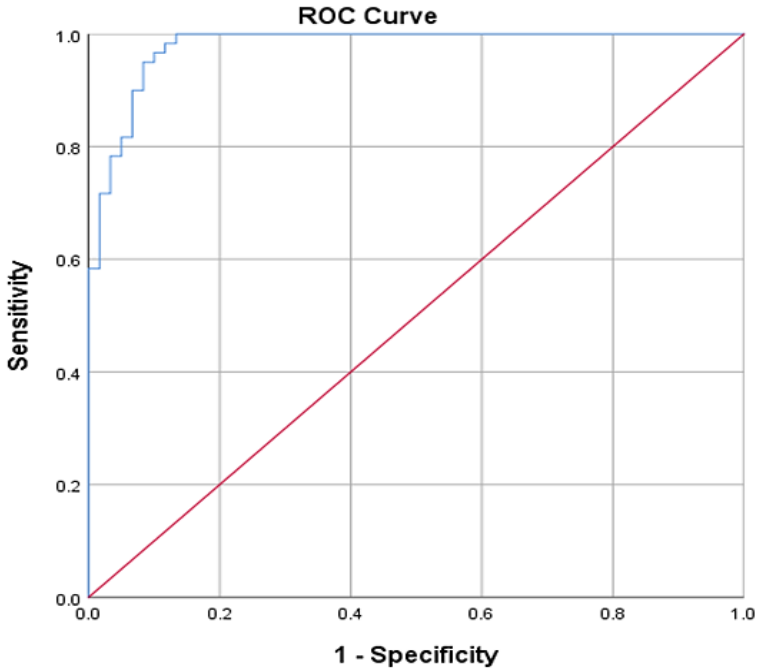

Figure 1. Roc Analysis for Oxidative Stress Used in This Study for TOS.

Table 2. Analysis of TOS, TAS between Control and Gastric Cancer Patients

The studied parameters	Mean ±SD For patients with gastric cancer	Mean ±SD for control	p-value
TOS	91.9±10.3	68.0±8.58	<0.001**
TAS	1.41 ± 0.187	1.74±0.11	<0.001**

study between patients and control.

The findings in this study indicated the mean values and standard deviations (SD) for two parameters, TOS (Total Oxidant Status) and TAS (Total Antioxidant Status), in patients with gastric cancer vs a control group, as shown in Table 2. The mean±SD of TOS value in gastric cancer patients was 91.9±10.3, whereas in the control group, it was 68.0±8.58. The p-value of <0.001 indicated a significant difference in TOS between the two groups. Gastric cancer patients had a mean TAS value of 1.41±0.187, whereas the control group had 1.74±0.11. A p-value of less than < 0.001 indicated a significant

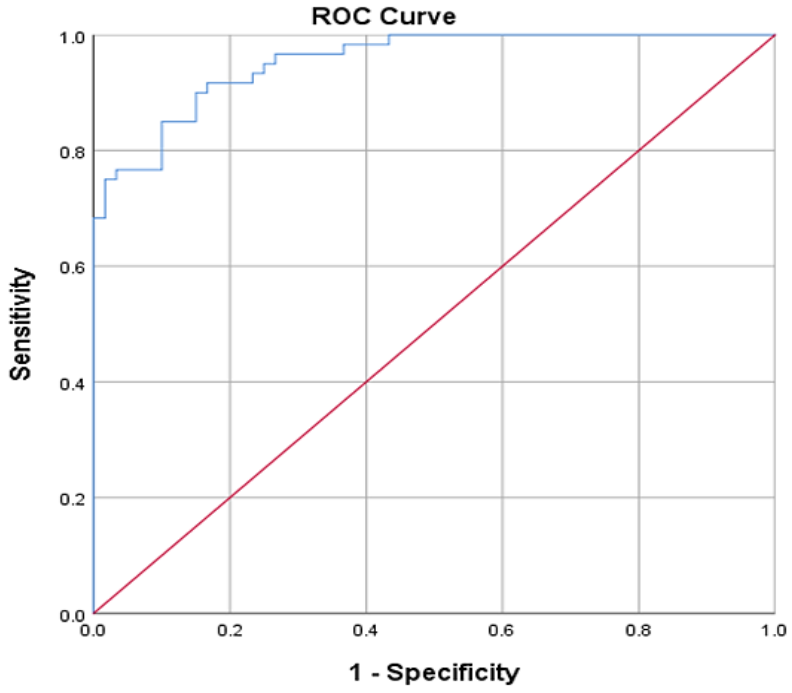

Figure 2. Roc Analysis for Oxidative Stress Used in This Study for TAC.

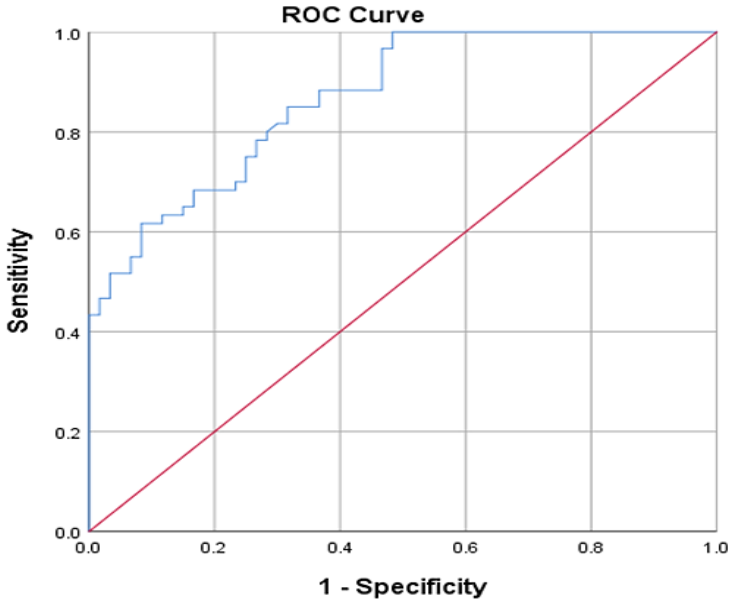

Figure 3. Rock Analysis for Anti-Oxidants Used in This Study for Vitamin C

Table 3. Analysis of Vit-C, and Vit-E between Control and Gastric Cancer Patients

The studied parameters	Mean ±SD Patients with gastric cancer	Mean ±SD for control	p-value
Vit-C	1.03±0.2	1.35±0.182	<0.001**
Vit-E	8.31±1.37	13.05±1.65	<0.001**

difference between the two groups.

Table 3 shows the vitamin C and E levels in gastric cancer patients compared to controls. The mean SD for the patients group was 1.03±0.2, whereas the control group was 1.35±0.182. The p-value was less than 0.001, indicating a statistically significant difference in vitamin C levels between the two groups. In patients with gastric cancer, the mean±SD value of Vitamin E was 8.31±1.37, whereas the control group had 13.05±1.65. The p-value was less than 0.001, indicating a statistically significant difference between the two groups.

Table 4 shows that patients with gastric cancer have a mean copper level of 82.4 ± 11.03 units, compared to 115 ± 10.8 units in the control group. The difference in copper levels between the two groups is statistically significant, as evidenced by a p-value less than 0.001. Zinc levels in

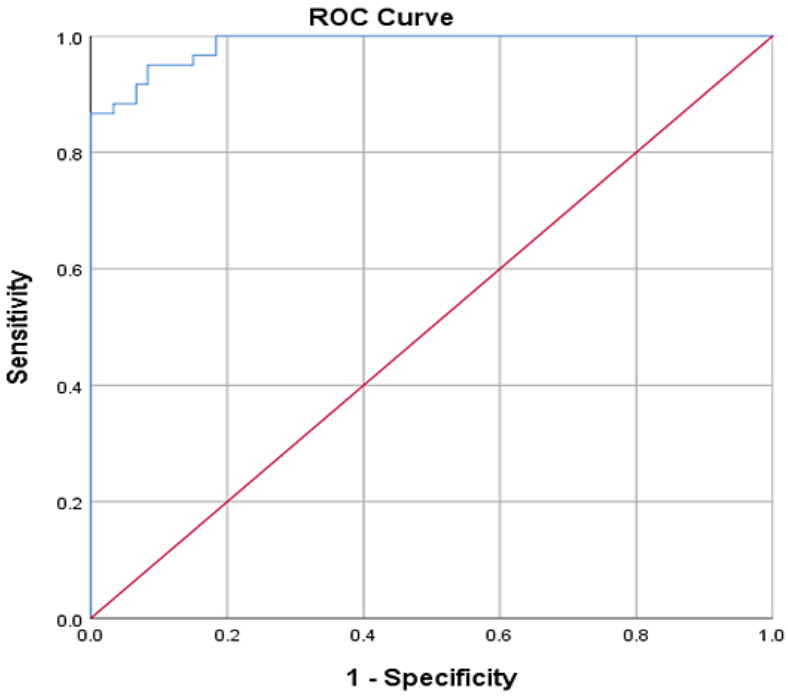

Figure 4. Rock Analysis for Anti-Oxidants Used in This Study for Vitamin E.

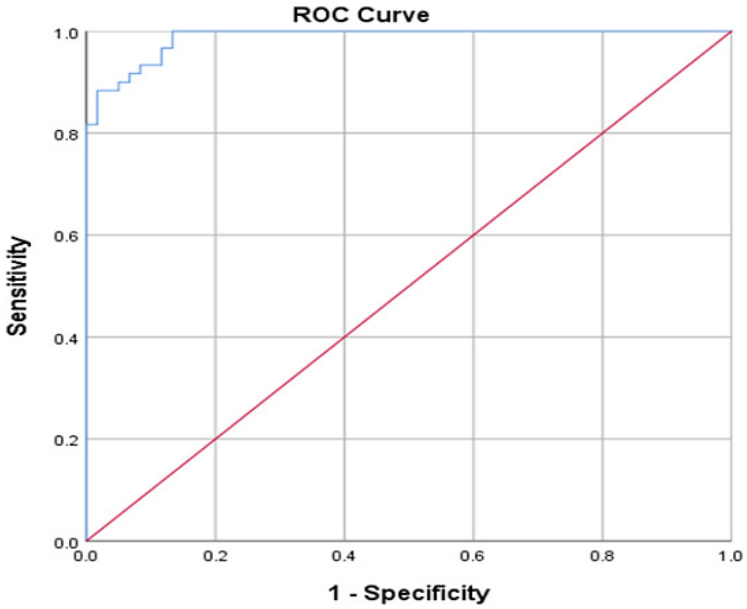

Figure 5. Rock Analysis for Co-Factor Minerals Used in This Study for Copper.

Table 4. Analysis of (Copper, Zinc, and Iron) between Control and Gastric Cancer Patients

The studied parameters	Mean ±SD Patients with gastric cancer (N=60)	Mean ±SD for control (N=60)	p-value
Copper	82.4±11.03	115±10.8	<0.001**
zinc	78.8±11.9	104.7±9.3	<0.001**
Iron	50.68±16.7	118.5±19.6	<0.001**

gastric cancer patients were 78.8 ± 11.9 units, whereas the control group had 104.7 ± 9.3 units. In comparison to copper, the p-value is less than 0.001, indicating a statistically significant difference between the means of gastric cancer patients and the control group. The former has a mean of 50.68 ± 16.7 units, while the latter has a mean of 118.5 ± 19.6 units.

The results show that individuals with stomach cancer had significantly lower amounts of iron, zinc, and copper than the control group reported. These results suggest that changes in these mineral levels could be important for the onset or spread of stomach cancer.

The Pearson correlation analysis in Table 5 demonstrated significant relationships between the examined parameters in gastric cancer patients. Total oxidant status (TOS) had a significant negative connection

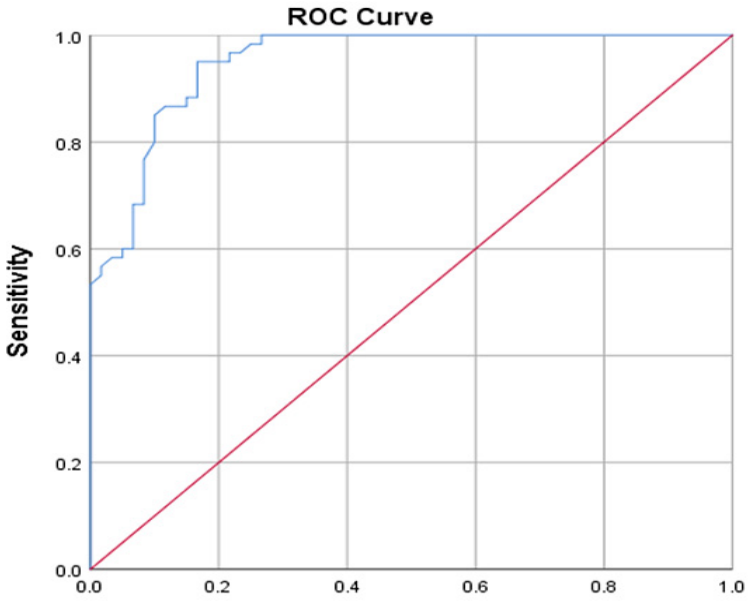

Figure 6. Rock Analysis for Co-Factor Minerals Used in This Study for Zinc.

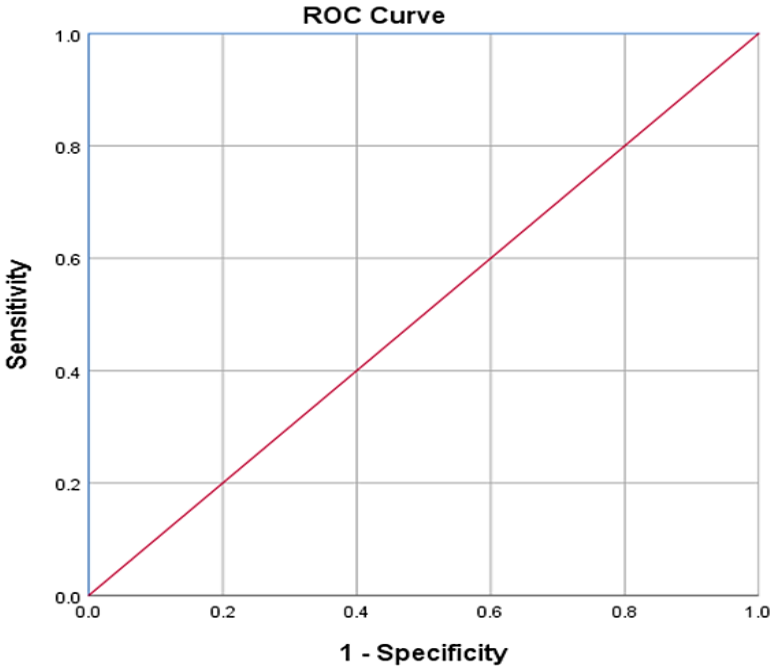

Figure 7. Rock Analysis for Co-Factor Minerals Used in This Study for Iron.

Table 5. Pearson Correlation between the Studied Parameters for the Patients

Variables		TOS	TAS	VIT-C	VIT-E	Copper	Zinc	Iron
TOS	r	-	-0.563**	-0.482**	-0.719**	-0.624**	-0.576**	-0.717**
	P		0.001	0.001	0.001	0.001	0.001	0.001
TAS	r	-0.563**	-	0.386**	0.560**	0.580**	0.503**	0.686**
	P	0.001		0.001	0.001	0.001	0.001	0.001
VIT-C	r	-0.482**	0.386**	-	0.540**	0.606**	0.465**	0.556**
	P	0.001	0.001		0.001	0.001	0.001	0.001
VET-E	r	-0.719**	0.560**	0.540**	-	0.689**	0.715**	0.749**
	P	0.001	0.001	0.001		0.001	0.001	0.001
Copper	r	-0.624**	0.580**	0.606**	0.689**	-	0.635**	0.744**
	P	0.001	0.001	0.001	0.001		0.001	0.001
Zinc	r	-0.576**	0.503**	0.465**	0.715**	0.635**	-	0.653**
	P	0.001	0.001	0.001	0.001	0.001		0.001
Iron	r	-0.717**	0.686**	0.556**	0.749**	0.744**	0.653**	-
	P	0.001	0.001	0.001	0.001	0.001	0.001	

with total antioxidant status (TAS), vitamins C, and E, demonstrating that oxidative stress is associated with reduced antioxidant levels. Similarly, TOS and TAS showed significant negative associations with copper, zinc, and iron levels, indicating a link between oxidative state and these trace metals. Furthermore, TAS was shown to have good associations with vitamins C and E, as well as copper, zinc, and iron levels, showing its antioxidant

Table 6. ROC شnalysis (Specificity and Sensitivity) for the Studied Parameters

Parameter	AUC	SE	p-value	Cut-off value	Sensitivity	Specificity
TOS	0.978	0.011	<0.001	79.8	95%	92.50%
TAS	0.954	0.016	<0.001	1.61	90%	85%
VIT-C	0.876	0.031	<0.001	1.21	75%	75%
VIT-E	0.986	0.007	<0.001	10.34	95%	92%
Copper	0.987	0.007	<0.001	98.5	90%	95%
Zinc	0.95	0.018	<0.001	91.5	95%	83%
Iron	1	0	<0.001	84.03	100%	100%

effects. These findings highlight the complicated interactions between oxidative stress indicators and antioxidant defenses, as well as their relationships with trace element levels in gastric cancer patients.

The results in Table 6 show the area under the curve (AUC), standard error (SE), p-value, cut-off value, sensitivity, and specificity of each parameter. Total Oxidant Status (TOS) had excellent discriminating power, with an AUC of 0.978, showing that it can successfully distinguish between the two groups. Figure 1 shows that TOS is highly accurate in detecting persons with gastric cancer, with a sensitivity of 95% and specificity of 92.5%. Similarly, Total Antioxidant Status (TAS) has significant discriminating power, with an AUC of 0.954. TAS has a sensitivity of 90% and a specificity of 85% at a cut-off value of 1.61, demonstrating its usefulness as a diagnostic marker, as illustrated in Figure 2.

Vitamins C and E have strong discriminating power, with AUC values of 0.876 and 0.986, respectively. Figures 3 and 4 reveal that Vitamin C has a sensitivity and specificity of 75%, but Vitamin E has a sensitivity of 95% and a specificity of 92%. Both copper and zinc have significant discriminatory power, with AUC values of 0.987 and 0.950, respectively. Figures 5 and 6 demonstrate that these characteristics have high sensitivity and specificity values, indicating that they might be useful diagnostic indicators for gastric cancer. Iron appeared as the most potent diagnostic marker, with an AUC value of 1.000, indicating complete discriminatory power. Figure 7 shows that iron has a sensitivity and specificity of 100% in detecting gastric cancer patients.

Discussion

In this study, we examined the intricate interplay between oxidative stress markers, antioxidant defenses, and the status of essential vitamins and co-factor elements in gastric cancer patients. As well as the investigation sheds light on the underlying mechanisms driving gastric carcinogenesis and highlights potential avenues for therapeutic intervention and diagnostic refinement. The results indicate that patients with gastric cancer exhibit higher levels of total oxidant status (TOS), lower levels of total antioxidant status (TAS), as well as decreased concentrations of Vitamin C and Vitamin E compared to the control group. These outcomes imply that gastric cancer patients experience heightened oxidative stress and potential deficiencies in their antioxidant defense mechanisms. Additionally, the study demonstrates significant variations in the levels of copper, zinc, and iron among gastric cancer patients in comparison to the control group. These findings suggest that imbalances in the metabolism of trace elements may be associated with the development or progression of gastric cancer.

The stomach is a fragile organ responsible for metabolizing, and the presence of oxidative stress plays an important role in the development of different disorders, including stomach cancer [21]. Oxidative stress arises from the excessive production of reactive oxygen species (ROS) or a decline in antioxidant defenses, resulting in the pathogenesis of gastric inflammation and ulcerogenic [22, 23]. Further, it can damage DNA in stomach epithelial cells, supporting its association with gastric carcinogenesis [24]. ROS also widely participates in human tumorigenesis by affecting major intracellular signaling pathways, such as MAP kinase and PI3K/Akt pathways [25, 26] .It has been revealed that several biomarkers directly reflecting oxidative stress status were significantly associated with cancer, such as TOS, TAS, OSI, and ischemia-modified albumin [27]. Recent research suggested that ROS could be excessively formed in chronic diseases of the gastrointestinal tract and toxic to normal cells, contributing to the increased risk of cancer [28].

In the current study we found, in comparison to the control group, individuals with stomach cancer had higher levels of oxidants (TOS) and reduced antioxidant capacity (TAS) These results are consistent with Xue-Fang Du et al where results indicate increased significant levels of TOS than that healthy control [29]. E. Fldan et al. [30] found that increased levels of oxidative stress index were detected in gastric cancer patients, and this condition may be associated with the impairment of oxidant-antioxidant balance, and also their result supported a decrease in antioxidant capacity .

Gastric cancer is connected with increased oxidative stress because tumor cells produce reactive oxygen species (ROS). Vitamin C and E are antioxidants that assist in neutralizing ROS. As a result, these vitamins may be eaten more quickly to combat oxidative stress, resulting in lower blood levels [31]. The tumor itself or surgical removal of part of the stomach can affect the absorption of vitamins from the diet, including vitamin C and vitamin E.

In our study serum levels of vitamin C and vitamin E were lower than the control and these results agree with many studies [32, 33]. Only three previous studies have examined the association between vitamin C supplement use and stomach cancer or its precursor lesions, and results have been inconsistent. A recent United States multicenter population-based case-control study included cases of both incident cardia and non-cardia stomach cancer [34]. This case-control study found vitamin C supplement use (at least weekly) was associated with decreased risk of both cardio (RR, 0.60; 95% CI, 0.41– 0.88) and non-cardia (RR, 0.71; 95% CI, 0.48–1.07) stomach cancer. Two randomized trials in high-risk populations have reported somewhat different results. In a large multifactorial trial in Linxian (China), participants were randomized to receive vitamin C (120 mg/day) in combination with molybdenum [35]. After 5 years of supplementation and follow-up, vitamin C and molybdenum treatment were not associated with a risk of incident stomach cancer (RR, 1.09; 95% CI, 0.88–1.36). In contrast, results from a trial in a very high-risk Andean area of Colombia suggested some inhibition of stomach carcinogenesis with vitamin C treatment. Precancerous stomach lesions were significantly more likely to regress in participants randomized to receive 2000 mg/day of vitamin C for 6 years than in participants receiving placebo (20% regression versus 7% [32]. Vitamin E supplement use was not associated with stomach cancer incidence in the multicenter United States case-control study Low-dose vitamin E (30 mg tocopherol/day) was not associated with

stomach cancer incidence in the Tocopherol Carotene trial among Finnish male smokers [36]. In the large multifactorial Linxian trial, a combined regimen of low-dose Vitamin E (30 mg -tocopherol/day), carotene, and selenium significantly reduced the risk of stomach cancer incidence and mortality, but this risk reduction cannot be attributed to vitamin E alone [35].

Zinc regulates key cellular functions, including response to oxidative stress, DNA replication, DNA damage repair, cell cycle progression, and apoptosis [37, 38]. It may inhibit the production of free radicals, reduce the frequency of harmful gene mutations, and ultimately provide defense against cancer initiation and progression [39]. Our study found serum levels of zinc for gastric cancer lower than the control and these results are consistent with previous studies. Some epidemiologic studies investigated the relationship between Zn intake and the risk of gastric cancer [40]. However, the results were inconsistent; for instance, some studies suggested that higher Zn intake might increase gastric cancer risk, while other studies showed higher Zn intake was linked to reducing the risk [41]. F. J.-F. and L. S.-L [42] Reported that the serum Zn level was lower in advanced gastric cancer patients [43]. In the present study, Zn's blood level was significantly reduced in the gastric cancer group compared with healthy subjects thus, it supported that the lower Zn levels were linked with an increased risk of gastric cancer [44]. A high concentration of Cu could induce growth proliferation and cancer, whereby highly reactive oxygen species are generated, which produce hydroxyl radicals that adversely modify proteins, lipids, and nucleic acids [45].

Abnormally high serum Cu levels are found in patients with many types of progressive tumors, making Cu an obligatory co-factor in the angiogenesis process [41]. Many studies have shown higher Cu levels in both serum and tumor tissues in gastric cancer patients compared to their healthy counterparts [24]. Its deficiency may increase cellular susceptibility to oxidative damage [46]. Reddy and coworkers [47] have reported significant decreases in Cu concentrations in gastric tumor tissues than normal samples. M. Hashemian [48] found elevated Cu levels in the serum of malign stomach patients than in normal donors. A significant decrease in the Cu concentration was found in gastric cancer tissue than normal tissue these findings align with our study [28].

Iron plays an important role during inflammation and the immune response to infection [49]. Abnormal accumulation of Fe and subsequent excess ROS causes oxidative stress, which incurs damage to DNA, proteins, lipids, or other biomolecules and even results in cell death. There is definitive evidence that Fe overload induces oxidative stress and DNA strand breaks, inactivates enzymes, depolymerizes polysaccharides, and initiates lipid peroxidation damage, which can enhance carcinogenic risk and ultimately accelerate tumor initiation [49]. Fe deficiency also increases oxidative stress and DNA damage, which might increase carcinogenesis risk, especially in the gastrointestinal tract. Some epidemiological studies have indicated an increased risk of gastrointestinal tumors among individuals with low Fe intake. In vivo, data from rodent cancer models indicates the early progression of gastrointestinal tumors during iron deficiency [50]. However, marked Fe deficiency was observed in the tissue of the carcinoma stomach than in the normal stomach tissue [51]. Reddy and coworkers have reported a significantly lower Fe in gastric cancer tissue than in normal tissue [47]. Case-control studies have demonstrated an inverse relationship between dietary Fe intake and gastric adenocarcinoma these results are consistent with our research. 09+ [49].

The findings underscore the significance of oxidative stress in gastric carcinogenesis and highlight potential avenues for therapeutic intervention and diagnostic refinement. By elucidating the relationships between these parameters, our research contributes to a deeper understanding of the molecular mechanisms underlying gastric cancer pathogenesis.

In conclusion, the present study highlights the important role of oxidative stress in the pathogenesis of gastric carcinogenesis. Our findings reveal a severe imbalance in the oxidant-antioxidant system, characterized by an increase in oxidant status (TOS) and a concomitant decrease in total antioxidant status (TAS) and vitamin C and E levels significantly reduced A in gastric cancer patients compared to healthy controls was observed, highlighting the possibility of deterioration due to oxidative stress or impaired absorption. Furthermore, studies have emphasized the importance of trace elements, especially zinc, copper, and iron, for gastric cancer. The observed deficiencies of these micronutrients suggest their involvement in the disease, possibly through their role in antioxidant defense systems or other cellular processes. The close relationship between TOS, TAS, vitamins, and trace elements highlights the complex interplay of these factors in gastric cancer. The excellent discriminatory power of these parameters, as evidenced by ROC curve analysis, highlights their potential as diagnostic biomarkers. In conclusion, this study provides compelling evidence for the relationship between oxidative stress, antioxidant depletion, and micronutrient imbalance in gastric cancer These findings contribute to a deeper understanding of the pathophysiology of the disease and may lead to new therapeutic strategies targeting oxidative stress and micronutrient supply. Future studies are needed to elucidate the mechanisms involved and to explore the clinical utility of these biomarkers in the early and prognostic diagnosis of gastric cancer.

Author Contribution Statement

Montadher Ali contributed to the study design and idea. Montadher, Yasser Jaaium, Rusul saad, and saad Abd carried out the experimental work, data collection, and data analysis. Montadher and Rusul contributed to the results discussion, writing, drafting, and editing of the paper. All of the authors checked and approved the overall manuscript, and approved the final version of the manuscript.

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Ethical Approval

All procedures performed in studies involving human participants followed the ethical standards of the research committee of "Mustansiriyah University" and with the 1964 "Helsinki Declaration" and its later amendments or comparable ethical standards.

Informed Consent

All of the study's subjects provided informed consent.

Conflict of Interest

The authors declare that they have no conflict of interest.

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