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Study of Some Hematological, Biochemical, and Antioxidant markers in Colon Cancer Patients in Erbil Governorate

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ABSTRACT:

Colon cancer is a major contributor to cancer-related morbidity and mortality worldwide, with an increasing incidence in the Kurdistan Region of Iraq. The research evaluated hematological, biochemical, oxidative stress, hormonal, and tumor marker profiles in male colon cancer patients from the Erbil governorate. A total of 100 volunteers were selected for this study, comprising 70 male patients and 30 healthy male controls. Hematological data revealed significant reductions in patients' red blood cell count, hemoglobin concentration, and white blood cell count, suggesting anemia and immunosuppression. Liver function tests revealed elevated SGPT levels, indicating possible hepatic involvement, whereas renal function markers remained within normal limits. The enzyme-linked immunosorbent assay (ELISA) evaluated oxidative stress indicators, including malondialdehyde (MDA), superoxide dismutase, and glutathione peroxidase. The results demonstrated reduced activity of GPx and SOD, indicating a compromised enzymatic antioxidant defense. Furthermore, elevated levels of MDA were noted, signifying increased lipid peroxidation and antioxidant response. Hormonal analysis revealed decreased free testosterone and increased thyroid-stimulating hormone (TSH) levels in individuals; however, these changes were not statistically significant. The tumor marker carbohydrate antigen 19-9 (CA 19-9) was significantly elevated in patients, confirming its effectiveness in identifying and monitoring colon cancer. Male colon cancer patients exhibited significant hematological alterations, elevated liver enzymes (SGPT), oxidative stress dysregulation, and increased CA 19-9 levels. Hormonal changes were seen but did not reach statistical significance. These results may aid in the detection and clinical management of colorectal cancer.

Keywords: colon cancer, oxidative stress, CA 19-9, testosterone, thyroid-stimulating hormone.

1 INTRODUCTIO

Colon cancer (CC), often called colorectal cancer, is a major health issue around the world. It is the third most prevalent cancer and the second most common cause of cancer-related deaths. CC has been the third most prevalent cancer in males and the second most frequent cancer in women over the world for the past few decades [1]. It is also the third deadliest cancer in the US. While the number of fatalities from it dropped from 49,190 in 2016 to 37,930 in 2020, the number of people who get it, and is expected to rise tenfold by 2035[2]. Even while things like life expectancy, socio-economic profiles, diet, and lifestyle vary from place to place, the possibility of more illness is clear over the world [3] [4]. This disease starts in the inner lining of the colon or rectum, usually as harmless polyps that can turn into cancerous tumors over time if not treated [5].

Moreover, it's still not clear what causes colorectal neoplasms, but a lot of researches had found other risk factors. Some of these factors cannot be changed, like age and heredity, while others can be changed, like lifestyle and the surroundings [6]. Early diagnosis is crucial in detecting CC during its development, which typically spans several to numerous years [7]. Oxidative stress occurs when there are too many reactive oxygen species (ROS) and not enough antioxidant defenses [8]. A lot of fascinating researches shows that oxidative stress is strongly linked to CC and its function in its development and progression, as shown by high levels of ROS in chronic gastrointestinal tract disorders [10].

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Reactive oxygen species and the antioxidant action on the cell are two types of oxidative stress [10]. Oxidative stress needs both internal and external factors to form [10][11]. Mitochondria and peroxisomes may make up the source. Oxidative stress is one thing that can raise the risk of getting cancer [12]. Patients with ongoing inflammation have more ROS, which could attract a lot of activated cells and cause a preneoplastic event. This could also raise the level of oncogenes by changing the genetic material at the cellular level [13]. Oxidative stress might also cause the quantity of free radicals to rise. Lipid and free radical reactions create free radicals, one of which is malondialdehyde (MDA). It might change the structure of the cell membrane, which could then change DNA at the cellular level [14].

Many studies have found superoxide dismutase (SOD) in cells. SOD comes in three forms: cuprum SOD or SOD1, which is found in the cytosol, the inner mitochondrial membrane, and the nucleus. The most important kind of SOD at the cellular level is SOD2, which is also known as manganese SOD [15]. Glutathione peroxidase (GPx) accelerates the process of turning H2O2 into water and lipid peroxides into their alcohols [16]. This requires glutathione reductase activity. Glutathione is a natural part of cellular metabolism; it is a tripeptide made up of γ-γ-glutamine-cysteine-glycine [17], this study aimed to investigate hematological parameters, renal function parameters, liver function parameters, malondialdehyde, superoxide dismutase, Glutathione peroxidase, and CA 19-9 tumor marker in Colon Cancer Patients in Erbil Governorate" Understanding and treatment of the disease. Biochemical alterations are studied to identify metabolic markers that can be used to track the course of a disease and the effectiveness of treatment.

2 MATERIALS AND METHODS

2.1 STUDY DESIGN

This study was conducted at the Department of Oncology and Clinical Laboratory at Nanakali Hospital in Erbil, Kurdistan, Iraq, from 15/8/2024 to 15/12/2024. It was designed to evaluate the hematological and biochemical alterations in colon cancer patients and investigate their potential role as diagnostic or prognostic indicators.

2.2 STUDY PARTICIPANTS

This study included 100 men, 70 of whom had colon cancer and 30 who were healthy controls matched for age and sex. Patients had to be between 19 and 75 years old and have histopathological proof of colon cancer at any stage (I-IV) to be included. All the healthy controls were volunteers with no history of cancer, chronic inflammatory disease, or other serious health problems, confirmed through a detailed medical history, physical examination, and routine laboratory tests—including complete blood count, C-reactive protein, and erythrocyte sedimentation rate—to rule out acute or chronic inflammation.

2.3 SAMPLE COLLECTION

Venous blood samples were collected from all subjects under aseptic conditions. Approximately [5–10 mL] of blood was drawn from each participant. Then, each blood sample was poured into two tubes: a gel tube for biochemical and hormonal tests and an EDTA-containing tube for later use in complete blood count (CBC). The tubes were labeled and kept at 4°C until further use (usually 2-3 hours). Serum was separated by centrifugation (LC-04 CENTERFUGE, Country) at 3000 rpm for 5 to 10 minutes at room temperature and stored at –80°C until further analysis. Samples were collected between 8:00 AM and 12:00 PM after an overnight fast of at least 8 hours to minimize diurnal and dietary variations in biochemical parameters.

2.4 BIOCHEMICAL AND HORMONAL ANALYSIS

The analysis of biochemical and hormonal parameters, including Carbohydrate Antigen 19-9 (CA 19-9), SGOT, SGPT, serum creatinine, blood urea nitrogen (BUN), and hormones (TSH and free testosterone), was performed using the COBAS INTEGRA® 400 plus system (Roche Diagnostics Ltd., Rotkreuz, Switzerland), with Roche diagnostic kits (Germany). Additionally, the Roche Cobas e 411 and HITACHI systems were used. Antioxidants were assessed using commercially available ELISA kits (Sunlong Biotech Co., Ltd., China) according to the manufacturer's protocol. Serum biomarker concentrations were determined with a microplate ELISA reader (BioTek ELx800, BioTek Instruments, Winooski, VT, USA), obtained locally through Aflo Ltd. All assays were performed following the kit manufacturer's instructions. Optical density (OD) was measured at 450 nm, with a reference wavelength of 620 nm to correct for background absorbance.

2.5 HEMATOLOGICAL ANALYSIS

Following blood collection, hematological analysis was performed immediately to ensure the accuracy and reliability of the measured parameters. When the blood sample is collected, hematological analysis is done right away using the Convergys® X3 NG automated 3-part differential hematology analyzer (Convergent Technologies GmbH & Co. KG, Germany). A fully automated Swelab Alfa Plus 3-part hematology analyzer was used to analyze complete blood counts, including total white blood cell count (WBC), lymphocyte count and percentage, granulocyte count and percentage, total red blood cell count (RBC), hemoglobin (Hb), hematocrit (HCT), and RBC indices like mean corpuscular volume

(MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW%), platelet count, and mean platelet volume (MPV).

2.6 STATISTICAL ANALYSIS

GraphPad Prism (GraphPad Software version 10, San Diego, CA, USA) was used to analyze the data, and the results were presented as mean ± standard error (SE). The Shapiro-Wilk normality test was used to determine whether the distribution was normal. Every variable under analysis has a normal distribution ($p > 0.05$). A student t-test, unpaired, was used for statistical analysis to compare the groups of CC patients and control healthy groups. The threshold for statistical significance was set at $p<0.05$.

3 RESULTS

The results of the antioxidant levels are shown in Table 1. For each antioxidant, significant differences in oxidative stress markers were observed between colon cancer patients and healthy controls. Glutathione peroxidase (GPx) activity was significantly lower in patients (27.41 ± 1.597 pmol/ml) than in controls (29.97 ± 1.449 pmol/ml; $p = 0.0055$). Similarly, SOD levels also shown a significant decrease in patients (6.21 ± 0.297) in comparison to controls (8.02 ± 0.408, p-value = 0.0003). Malondialdehyde (MDA) levels, a marker of lipid peroxidation, were markedly elevated in patients (312.2 ± 12.14) relative to controls (259.2 ± 16.05ng/ml, $p = 0.0353$), reflecting increased oxidative damage.

Table 1. Mean ± SE Antioxidant levels for CC patients and Control groups

Parameters/ Mean ± SE	Controls	CC Patients
GPX (pmol/ml)	29.97 ± 1.449	27.41 ± 1.597**
SOD (ng/ml)	8.02 ± 0.408	6.21 ± 0.297***
MDA (ng/ml)	259.2 ± 16.05	312.2 ± 12.14*

ns: non-significant difference control vs CC group *: denotes significant difference control vs CC group p<0.05 **: denotes significant difference control vs CC group p<0.01 *: denotes significant difference control vs CC group p<0.001**

Furthermore, renal and hepatic functions were evaluated, as illustrated in Figure 1. Renal function was assessed using serum creatinine and blood urea nitrogen levels. Serum creatinine levels were comparable in the control group (0.857 ± 0.026 mg/dL) and the patient group (0.856 ± 0.041 mg/dL), with no statistically significant difference detected ($p = 0.9791$). Blood urea levels were marginally increased in patients (31.56 ± 1.638 mg/dL) relative to controls (28.14 ± 1.696 mg/dL). Nonetheless, this disparity did not attain statistical significance ($p = 0.1993$). Liver function was assessed using the measurement of serum SGOT and SGPT levels. SGOT levels in the sick group (30.91 ± 3.540 U/L) were elevated compared to the control group (23.97 ± 2.177 U/L); yet, this increase was not statistically significant ($p = 0.1423$). In contrast, SGPT levels were markedly elevated in the patient group (28.12 ± 2.168 U/L) compared to the control group (20.72 ± 1.954 U/L), yielding a p-value of 0.0361.

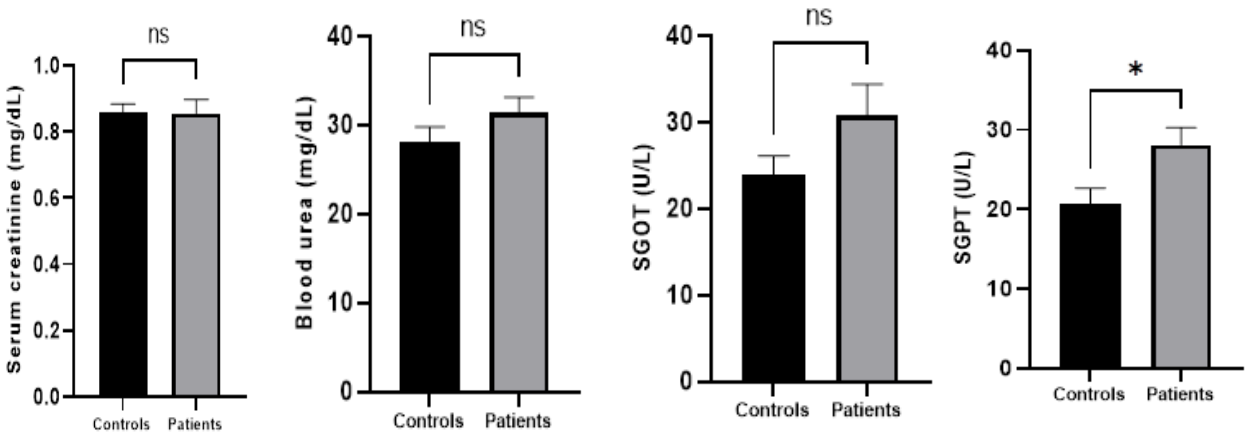

FIGURE 1. Mean ± SEM values for Serum levels of renal and liver function biomarkers in CC and control groups.

In addition to the aforementioned measures, hematological parameters were also evaluated. The findings are presented in Table 2. In comparison to healthy controls, CC patients presented in Table 2 demonstrated significantly diminished red blood cell (RBC) counts (4.31 ± 0.09 vs. 5.28 ± 0.08 $\times 10^{12}$/L, $p < 0.0001$), hemoglobin concentrations (12.31 ± 0.30

vs. 15.46 ± 0.36 g/dL, p < 0.0001), hematocrit levels (36.58 ± 0.88 vs. 44.18 ± 0.86%, p < 0.0001), and white blood cell (WBC) counts (5.85 ± 0.33 vs. 7.28 ± 0.43 ×10⁹/L, p = 0.0018),. Red blood cell indices demonstrated significant reductions in mean corpuscular volume (MCV: 82.62 ± 1.36 vs. 85.47 ± 0.91 fL, p = 0.0432) and mean corpuscular hemoglobin (MCH: 28.54 ± 0.51 vs. 30.42 ± 0.23 pg, p = 0.0318), while red cell distribution width (RDW) was markedly elevated (14.74 ± 0.31 vs. 12.55 ± 0.17%, p = 0.0001), indicative of microcytic, hypochromic anemia. Mean platelet volume (MPV) was decreased in patients (8.64 ± 0.19 vs. 9.32 ± 0.13 fL, p = 0.0017), indicating modified platelet production or activation. The MID cell fraction was markedly elevated in patients (p = 0.0264). No notable variations were seen in platelet count, MCHC, lymphocyte %, or granulocyte percentage (p > 0.05).

Table 2. Alterations in Complete Blood Count Parameters in CC Patients Compared to Controls.

Parameters/ Mean ± SE	Controls	CC Patients
RBC ($10^{\wedge 12}$/L)	5.28 ± 0.08	4.31 ± 0.09****
WBC ($10^{\wedge 9}$/L)	7.28 ± 0.43	5.85 ± 0.33**
Hb (g/dL)	15.46 ± 0.36	12.31 ± 0.30****
HCT (%)	44.18 ± 0.86	36.58 ± 0.88****
Platelets ($10^{\wedge 9}$/L)	204.2 ± 9.69	224.4 ± 21.08^{ns}
MCV (fL)	85.47 ± 0.91	82.62 ± 1.36*
MCH (pg)	30.42 ± 0.23	28.54 ± 0.51*
MCHC (g/dL)	34.87 ± 0.21	33.79 ± 0.32^{ns}
LYM (%)	32.42 ± 1.35	28.02 ± 1.61^{ns}
MID (%)	5.53 ± 0.23	7.57 ± 0.54*
GRA (%)	63.21 ± 1.53	64.76 ± 1.81^{ns}
MPV (fL)	9.32 ± 0.13	8.64 ± 0.19**
RDW (%)	12.55 ± 0.17	14.74 ± 0.31***

ns: non-significant difference control vs CC group *: denotes significant difference control vs CC group p<0.05 **: denotes significant difference control vs CC group p<0.01 *: denotes significant difference control vs CC group p<0.001 **** denotes significant difference control vs CC group p<0.000.**

The current study also evaluated free testosterone serum levels, thyroid-stimulating hormone (TSH), and carbohydrate antigen 19-9 (CA 19-9) in the control and patient groups to assess potential hormonal and tumor marker differences. As shown in Table 3, free testosterone levels were significantly lower in the patient group (3.311 ± 0.339 ng/dL) compared to the control group (4.348 ± 0.242 ng/dL), with a p-value of 0.0095, showing a statistically significant difference. Although TSH levels appeared higher in patients (2.396 ± 0.603 mU/L) than in controls (1.925 ± 0.161 mU/L), the difference was not statistically significant (p = 0.2362). In contrast, CA 19-9 levels were highly significantly (P = 0.0001) elevated in the patient group (54.07 ± 6.177 U/mL) compared to the control group (10.62 ± 1.489 U/mL).

Table 3. Mean ± SEM of Serum Free Testosterone, TSH, and CA 19-9 in Control and Patient Groups

Parameters/ Mean ± SE	Controls	CC Patients
Free testosterone (ng/dL)	4.348 ± 0.242	3.311 ± 0.339**
TSH (mU/L)	1.925 ± 0.161	2.396 ± 0.603^{ns}
CA 19-9 (U/mL)	10.62 ± 1.489	54.07 ± 6.177****

ns: non-significant difference control vs CC group *: denotes significant difference control vs CC group p<0.05 **: denotes significant difference control vs CC group p<0.01 *: denotes significant difference control vs CC group p<0.001 **** denotes significant difference control vs CC group p<0.0001**

4 DISCUSSION

Colon cancer is the third most common type of cancer [18][19]. the second leading cause of cancer related deaths in the world with an estimated number of 1.8 million new cases and about 881,000 deaths worldwide in 2018[20][21] Reactive oxygen species are produced by the metabolic redox reactions that happen in normal cell metabolism. Oxidative stress can happen when there are too many ROS or not enough of them are removed. This can lead to serious metabolic problems and cell damage [22]. An imbalance in redox states causes oxidative stress, which is a key part of the pathogenesis of many diseases, such as cancer and neurodegenerative disorders [23]. This imbalance causes damage to cells, messes with signaling pathways, and changes metabolic homeostasis, which speeds up the onset of disease [24]. Cancer stem cells are a special type of tumor cell that can regenerate itself and is responsible for starting, growing, and spreading tumors [25]. These cells have learned how to protect themselves from the harmful effects of free radicals by turning on redox-sensitive transcription factors and making more antioxidant enzymes and anti-apoptotic proteins [26]. Numerous

publications have highlighted the significance of oxidative stress as a critical etiological factor in colorectal carcinogenesis and the function of antioxidants in mitigating oxidative stress and preventing colorectal cancer. Nevertheless, limited research has associated oxidative stress levels with prevalent clinical indicators of tumor advancement [27].

The current study aimed to assess oxidative stress indicators and antioxidant enzymes specifically glutathione peroxidase (GPX), superoxide dismutase (SOD), and malondialdehyde (MDA) in the serum of colon cancer patients and healthy controls. The results showed that colon cancer patients had far lower levels of GPX and SOD than healthy people, which means that their enzymatic antioxidant defense system was not working properly. Also, MDA, a well-known indication of oxidative damage and lipid peroxidation, was also much higher in patients. GPX level was decreased in current study the fact of reduced peroxide detoxifying capacity is supported by the reported decrease in glutathione peroxidase (GPx) activity among patients as compared to controls [17][28]. This result is in line with researches that found lower levels of GPx, indicating that decreased GPx activity would lead to the buildup of lipid peroxide and hydrogen peroxide, which would increase oxidative damage and carcinogenesis [29][30]. In the current study SOD was reduced in patient groups according to healthy controls these results are different from earlier studies that showed higher levels of SOD in the blood and more active antioxidant enzymes in people with colorectal cancer. For instance, [31] SOD levels were much higher in the blood of CRC patients. This suggests that oxidative stress caused antioxidant enzyme overexpression [31]. Also, colon cancer patients had far higher amounts of MDA than controls. This is in line with recent results that showed that cancer cells have more lipid peroxidation. For example, [32] demonstrated that elevated MDA levels are a hallmark of Oxidative stress in cancer patients is linked to membrane damage, DNA adduct formation, and tumor progression. Increased MDA has been frequently reported in colorectal cancer tissues and plasma, reflecting enhanced oxidative degradation of lipids [33].

To get a whole picture of how colon cancer affects the body, this study also looked at liver function, kidney function, and blood parameters. Tests of liver function, such SGOT and SGPT, give us information about the health of the liver and whether it might be affected by metastasis or treatment-related toxicity. We checked the liver's health by looking at the serum levels of SGOT and SGPT. The findings showed that the CC group's SGPT levels were greater than the controls', but the difference wasn't statistically significant. This suggests a probable but inconclusive tendency towards hepatocellular activity. On the other hand, the CC group had far higher levels of SGOT than the control group. These results are very similar to those of a study that came before [34].

In the current study, the renal function markers like serum creatinine and urea were evaluated to keep an eye on how well the kidneys were working and to look for any evidence of nephrotoxicity or systemic malfunction. In the present study, renal function parameters, including serum creatinine and urea, did not show significant changes in colon cancer patients compared to the control group. This finding is not entirely consistent with previous studies. The correlation between CC and impaired renal function on presentation was statistically significant [35].

In this study, hematological parameters CBC were evaluated. Recently, Hematological indicators have garnered clinical interest due to their demonstrated utility in the diagnosis and prognosis of specific malignancies [36][37]. However, the result showed significantly lower RBC, MPV, and HCT in RBC, MPV, and HCT of the patient group in comparison to the control group, which may lead to anemia [38]. At the same time, RDW was elevated in the patient in comparison to the control group. The test results found that RDW was significantly sensitive to CC patients, which leads to anemia. The current result aligned with previous studies [38][39]. the current study also showed WBC is reduced in people with colon cancer, a low white blood cell count is most often caused by chemotherapy-induced myelosuppression, which stops the bone marrow from making neutrophils for a short time [40]. However, it can also happen when metastatic tumor cells invade the marrow and crowd out normal blood cell production, when the disease is advanced, or the person is malnourished, or when pelvic radiation damages the marrow reserves [41][42]. No significant differences were observed in platelet count, MCHC, lymphocyte percentage, or granulocyte percentage. Further studies are required to validate these findings and achieve more comprehensive results.

Elevated CA 19-9 levels of CC patients, according to healthy groups observed in the current study are consistent with its known role as a tumor-associated marker, especially in gastrointestinal malignancies, its elevation may reflect tumor progression or metastasis, and its parallel with earlier studies, which found that the mean serum levels of CA19-9 were significantly higher colon cancers than in healthy control subjects [43][44]. In the current study it was observed that free testosterone levels were significantly lower in the patient group compared to the control group indicating a statistically significant difference, higher levels of testosterone associated with a decrease in risk for developing colon cancer, The findings of the current study support earlier research, showing that lower testosterone levels in men are linked to a higher risk of developing colorectal cancer [45].

Thyroid-stimulating hormone is the main growth agent for thyroid cells and the main regulator of thyroid functions. TH affects the expression of several sets of genes, which controls a number of cellular processes in vertebrates, such as cellular proliferation, differentiation, and death [46][47]. Because TH is so important for keeping the balance between

cell growth and differentiation [48]. Not unexpectedly, TH activity has a big effect on how stem/progenitor cells self-renew and differentiate. TH and the Tα1 receptor control the neural stem cell niche. These two factors impact whether neural stem cells decide to self-renew or differentiate, which leads to the formation of diverse progenitor cells such neurons, oligodendrocytes, and astrocytes [49]. In the present investigation, TSH levels were elevated in patients compared to controls; nevertheless, the difference lacked statistical significance, indicating no substantial change in thyroid function between the two groups.

CONCLUSION

The present study indicates that colon cancer patients in Erbil Governorate exhibited marked hematological, biochemical, and oxidative stress alterations, including anemia, elevated liver enzymes, reduced antioxidant enzymes (GPx, SOD), and increased lipid peroxidation (MDA). CA 19-9 levels were significantly elevated, underscoring its diagnostic and prognostic potential. These changes highlight the role of oxidative stress imbalance and tumor markers as key indicators in the clinical management of colon cancer. Nevertheless, extensive study involving larger cohorts and molecular analysis is required to validate their complete potential.

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CONFLICTS OF INTEREST

The author declares no conflict of interest.

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