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REVIEW ARTICLE

The Significance of Serum CEA and Haematological Materials in the Diagnosis and Prognosis of the Colorectal Carcinoma

Ali Hussein Abd-Allah[1], Haider Abd .Jabbar Alammar[1], Mazen.J.Ibrahim[2]

1 Department of Clinical Biochemistry, College of Medicine, University of Al- Qadisiyah, Iraq

2 Department of Oncology, College of Medicine, University of Baghdad, Iraq.

Corresponding author: az91664@gmail.com, Haider.alammar@qu.edu.iq

Abstract

Background: The second-leading source of neoplasm-related death and a primary factor in gastrointestinal Cancer, colorectal Cancer (CCR) affects both genders globally. Poor eating behaviors, tobacco, an intestinal inflammatory disorder, swellings, inherited characteristics, and the elderly all increase the threat of acquiring this malignancy. The illness is more hostile in patients detected at earlier ages, although 90% of patients with colorectal tumors are older than 50, with a median oldness of 64 years. American Cancer Association estimates that it caused more than 49,700 fatalities in 2015.
Objectives: The current study aims to study the correlation of CEA, with ALT, AST, ALP, TSP, TSB, Neutrophils, lymphocytes, and NLR parameters in patients with colorectal carcinoma.
Methods: The serum CEA of all subjects was measured by the ELISA technique (Enzyme enzyme-linked fluorescent Assay), ALT, AST, ALP, TSP, as well as TSB were measured by colorimetric methods, and neutrophils, lymphocytes as well and NLR were measured by an Electrical Impedance Cell Counting methods (CBC, automated machine).
Results: The {mean ± SD} of Ages and Genders among Patients with healthy groups were not significant. The neutrophil count was significantly higher in the patient subjects compared to healthy subjects. In addition, the lymphocyte count was significantly lower in the patient subjects compared to healthy subjects. Moreover, the neutrophil to lymphocyte ratio (NLR) was significantly higher in the patient subjects in comparison with the control subjects. Mean serum CEA was significantly higher in the patient subjects in comparison with the control subjects.

Conclusion: The study results of the correlation between serum CEA, hematological materials, and other parameters in colorectal carcinoma patients show a significant positive correlation of CEA, with ALT, AST, ALP, TSP, neutrophils, lymphocytes, as well as NLR and weak significance with serum TSB.

Keywords:

Colorectal carcinoma, hematological materials, CEA

Introduction:

One of the most prevalent carcinomas globally is colorectal carcinoma (CRC) (1). Adenomas are the main source of CRCs. (adenoma-carcinoma sequence). The development of an adenoma into cancer is thought to occur over at least ten years. Because of this, screening is crucial to their avoidance. CRC is rarely diagnosed in people under the age of 40. In 90% of the cases, the illness strikes people over 50 years. Colonoscopy is frequently advised as a monitoring method beginning at age 50 years (2), (3).
Currently accounting for 13% of all malignant cancers, it is the most prevalent gastrointestinal tract tumor. It is also the second most prevalent source of neoplasm-related mortality worldwide, affecting both males and females equally in developed and developing countries, and it is predicted to surpass heart disease death rates in the years to come (4)(5).
The fact that the 5-year overall existence from this malignancy stays under 50%, despite recent advances in novel therapies, emphasizes the need to advance early recognition, predictive, and prophetic biomarkers that can be utilized in repetitive clinical practice to reduce the ailment and death associated with this sickness (6).
CRC accounts for 10% of universal tumor occurrence and 9.4% of cancer mortality, just below lung malignancy, which will account for 18% of cancer-related mortalities in 2020. The number of novel CRC cases worldwide is anticipated to touch 3.2

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million in 2040 based on forecasts of aging, increasing inhabitants, and human advancement. The increased exposure to environmental risk factors brought on by the westernization of lifestyle and diet is the main cause of the rise in the prevalence of CRC (7), (8).

Colorectal cancer is another most prevalent female tumor and the third most prevalent cancer in males. In 2020, an additional 1.9 million cases were reported (9). The colorectal tumor is the second most pervasive cancer-related cause of mortality, accounting for an estimated 935,00 cancer fatalities each year (10). It is one of the malignancies whose prevalence is rising and accounts for 11% of all cancer cases worldwide (11).

CRC is the third main tumor-related cause of mortality globally, with a projected 419,536 deaths for women and 515,637 deaths for men in 2020. CRC impacts more than 5.25 million people worldwide (5-year survival), just somewhat fewer than breast tumors, which account for 7.79 million tumor cases. 0.94 million people died from CRC in 2020 (12).

In the United States, mutually the incidence and fatality ratio has been gradually falling (13). About 151,030 novel cases of large bowel malignancy are reported each year, 106,180 of which are colon malignancy cases, and the rest are rectal malignancy cases (14).

It ranks third among male malignancies and second among female malignancies in frequency. By 2035, there will be 2.5 million new cases of colorectal cancer worldwide, with women experiencing a 25% lower incidence and mortality rate than men (15).

According to the Iraqi National Cancer Registry (INCR), the general (men and women) CRC index percentage (CIP) grew from 2.28 to 6.18 per 100 000 people in 2000 and 2019, correspondingly, with a yearly percentage change (APC) of 5.11%. (16).

Carcinoembryonic antigen (CEA) has been identified as a tumor parameter and a glycoprotein that may be found in the blood and tumor cells of adenocarcinomas since 1965. CEA is an intracellular adhesion protein generated in fetal gut tissue and epithelial tumor cells that aids in angiogenesis. It has a half-life of one to three days; Colorectal tumors, breast tumors, gastric tumors, lung tumors, ovarian tumors, and pancreatic tumors have increased CEA heights in the blood. However, many non-malignant diseases, such as tobacco use, drinking, chronic inflammatory bowel disease, pancreatitis, and hepatic disease, can elevate CEA (17). CEA is a group of toughly bound glycoproteins expressed in intestinal tissue from the human germinal stage to the fetus. CEA is mostly generated by adult colon mucosal cells, with a tiny quantity paid by different cells. There is a tiny quantity of extent in the blood. It has a two-day half-life in the blood. CEA is a diagnostic marker in clinical practice as an embryonic tumor antigen since it is highly expressed in colorectal tumors (18), (19).

The NLR, which measures the proportional difference among baseline neutrophil and lymphocyte numbers, has been identified as a possible marker of bad prognosis in various malignancies, including colon and rectal tumors. These biomarkers of systematic inflammatory reaction have been vastly investigated as helpful indicators for the prediction of patients with cancer (20). Many malignancies are brought by prolonged contagion; this accounts for about 15% of all malignancies globally. Continuous reactions to long conditions and environmental toxins lead to a chronic inflammatory reaction. Thus, inflammatory responses play a crucial role in carcinogenesis. Numbers of inflammatory cells, like neutrophils, lymphocytes, platelets, and monocytes, in addition to innate immune system coding molecules, are implicated in tumor progression (21). Peripheral blood elements might celebrate patients' inflammatory and immune responses to virulent cancers and are climacteric for determining cancer patients' therapy response and clinical results. Inflammation-related markers that estimate the systemic inflammatory reaction have generated predictive value autonomous of the TNM staging system. Between these markers is the peripheral blood NLR (22). The function of inflammation in the tumor is now fully understood and depicted at various stages of neoplasm growth (initiation, stimulation, attack, and metastasis). Functional provocative cells are foundations of reactive oxygen species and reactive nitrogen species that can enhance DNA destruction and genome variability, thus stimulating tumor initiation (23).In recent years, inflammatory blood parameters have appeared as diagnostic and predictive indicators, mainly the neutrophil-to-lymphocyte ratio (NLR) and the ratio among the absolute neutrophil and lymphocyte amounts (24).

2. The Aims of the Study

The present study aims to achieve the following:

1. Assessing hepatic function among individuals diagnosed with colorectal cancer and establishing its correlation with the disease's pathological condition.
2. Evaluating the hematological parameters and tumor marker CEA levels in individuals who were diagnosed with colorectal carcinoma and establishing a correlation between them, if any.

3. Materials and Methods

3.1. The Subjects

The study was conducted on individuals who were clinically, and laboratory diagnosed with colorectal cancer and who attended the Oncology Teaching Hospital/ Medical City and Gastroenterology and Hepatology Teaching Hospital /Medical City in Baghdad – Iraq. The samples and all information were taken from the patients, as well as healthy people who were selected for the study. Laboratory tests were carried out in the laboratories of the Clinical Biochemistry Branch / College of Medicine / University of Al-Qadisiyah. Some laboratory tests were also conducted in the Clinical Chemistry Unit / Laboratory Division of the Oncology Teaching Hospital. One hundred and twenty-nine individuals participated in the study between September 2022 and May 2023 and were divided into two groups the patient subjects included sixty people were patients with colorectal carcinoma selected from the Oncology Teaching Hospital and Gastroenterology and Hepatology Teaching Hospital after confirming their clinical and laboratory diagnoses. The control subjects included sixty-nine healthy people who did not have any disease. These groups were established after asking people and conducting all required laboratory analyses.

3.2. Blood Sample Collection

Six milliliters of blood were drawn from each participant's vein and placed in two test tubes 2ml with an EDTA tube for neutrophils and lymphocytes and NLR, and 4ml with a gel tube for biochemical analysis. The whole blood was processed and

subjected to the necessary studies directly. At the same time, blood samples were centrifuged in gel tubes for ten minutes at a force of 3000 x g to obtain a sample (serum), which was then kept in three separate Eppendorf tubes at -44 C in the deep freeze until the analysis time.

3.3. The Inclusion Criteria

All the patients with and without metastatic colorectal carcinoma without tumorectomy were included in the study.

3.4. The Exclusion Criteria

The study excluded the patients who had cancer (breast, ovarian, pancreatic, lung, kidney, and prostatic cancers), Inflammatory bowel disease, Cardiovascular diseases, and Renal diseases.

3.5. The Statistical Analysis

The statistical analysis was performed using version 25 of the Statistical Package for the Social Sciences (SPSS) from IBM on a Windows® platform. Continuous variables were represented by mean and standard deviation. The comparison between the patients group and the healthy group was conducted using analysis of variance student T-test, and a P-value of ≤ 0.05 indicated a statistical significance. The strength and direction of the correlation were measured by the Pearson correlation coefficient (r) value, with significant association indicating the direction of the correlation. The Pearson correlation coefficient (r) measures the strength and direction of the association between two variables. A weak correlation was indicated by an r-value less than 0.5, a moderate correlation was indicated by an r-value between 0.4 and 0.7, and a strong correlation was indicated by an r-value greater than 0.7.

4. Results

4.1. The Frequency Distribution of the Individuals with Colorectal Cancer as Claimed by the Grade and Stage of Tumor

The frequency distribution of the participants with colorectal cancer, as claimed by the grade of disease, is shown in Figure 1. The patients were categorized into eight conditions of well-differentiated grade I Cancer (13.3 %), 43 conditions of moderately differentiated grade II tumors (71.7 %), and nine conditions of poorly differentiated grade III cancer (15.0 %).

The frequency distribution of colorectal cancer individuals according to the disease stage is shown in Figure 2. The patients were categorized into 13 conditions of stage II disease (21.7 %), 17 states of stage III disease (28.3 %), and 30 conditions of stage IV disease (50.0 %).

The frequency distribution of individuals with colorectal cancer as claimed to metastasize is shown in Figure 3. 50 % of cases (30 in number) had metastasis. The site of metastasis is shown in Table 1.

The most common site was the liver accounting for 46.7 % of cases, followed by the lung (16.7 %), then by bone (13.3 %), then by peritoneum, uterus, and ovary (6.7 % for each), and finally by spleen (3.3 %).

4.2. The Demographic Correlation of the Individuals with Colorectal Cancer and Control Subjects

Table 1 indicates that there was no significant alteration in mean age between the patients and control groups, 52.97 ±11.92 years versus 51.81 ±12.61 years, respectively (p = 0.561). In addition, there was no significant alteration in the proportions of males and females between both subjects (p = 0.660).

4.3. The Results of the Biochemical Parameters

Table 2 indicates that the mean serum AST was significantly higher in the patient subjects compared to the healthy subjects, 36.40 ±18.58 IU/L versus 22.02 ±12.21 IU/L, respectively (p <0.001). In addition, mean serum ALT was significantly higher in the patient's subject compared to a healthy subject, 34.27 ±9.89 IU/L versus 21.73 ±7.40 IU/L, respectively (p <0.001). Furthermore, mean serum ALP was significantly higher in the patient's subject compared to a control subject, 114.32 ±40.10 IU/L versus 95.08 ±27.26IU/L, respectively (p =0.002).

Mean serum TSP was significantly lower in the patient's subject compared to a healthy subject, 60.23 ±18.33 g/dl versus 67.12 ±8.31 g/dl, respectively (p =0.006). However, mean serum TSB was significantly higher in the patient's subject than in the healthy subject, 0.65 ±0.60 mg/dl versus 0.43 ±0.38 mg/dl, respectively (p =0.017).

4.4.Results of hematological parameters

Table 3 indicates that the Neutrophil count was significantly higher in the patient's subject compared to a healthy subject, 7.23 ±3.98 X109/L versus 4.41 ±1.71 X109/L, respectively (p <0.001). In addition, lymphocyte count was significantly lower in the patient subjects compared to the healthy subjects, 1.76 ±1.37 X109/L versus 2.74 ±1.00 X109/L, respectively (p <0.001). Moreover, the neutrophil to lymphocyte ratio (NLR) was significantly higher in the patient subjects in comparison with the control subjects, 13.91 ±6.59 versus 1.85 ±1.02, respectively (p <0.001).

4.5. The Results of the Tumor Marker CEA

Table 4 indicates that the mean serum CEA was significantly higher in the patient subjects in comparison with the control subjects, 133.28 ±94.33 ng/ml versus 1.77 ±1.07 ng/ml, respectively (p <0.001).

4.6. The Correlation Study

Table 6 indicates that the grade of disease was negatively linked to lymphocyte numbers and positively related to NLR and AST. The stage of disease was negatively associated with lymphocyte number and completely related to neutrophil numbers, NLR, AST, ALP, and CEA. Metastasis was negatively related to lymphocyte numbers and positively correlated to neutrophil count, NLR, AST, ALT, ALP, and CEA.

5. Discussion

The positive correlation of the grade and disease stage with increasing NLR follows the findings of several previous authors (22), (25). High concentrations of blood neutrophils were seen in individuals with advanced tumors and were related to worse survival (26), (27). There was a great indication of a negative predictive value of neutrophil to lymphocyte ratio in colorectal tumors. Many studies revealed that higher NLR was related to worse survival (28), (29), (30), (31), and the latest meta-analysis found that higher NLR was related to both poorer disease-free survival and general survival (28).

In this study, there was no significance in the age and gender between the individuals with colorectal tumors and the healthy subjects, respectively (p = 0.561), (p = 0.660). The mean age of the individuals with colorectal tumors in the present study is comparable to that obtained by previous studies (32), (33). The colorectal tumor is the third ultimate prevalent neoplasm globally and the second most prevalent cause of tumor-related death (34). Over the past few decades, the United States and

other high-income nations have seen an alarming rise in states of early-onset colon-rectal tumors, defined as a diagnosis in individuals younger than 50 (35). Early-onset colon-rectal tumors now account for about 10% of all new diagnoses of this neoplasm, and an accompanying rise in colon-rectal tumor–related death during the past decade had also been detected among younger individuals (36), (37).

This study showed significantly higher liver function test levels in colorectal tumor individuals with hepatic metastases compared to the control subjects. Previous studies showed elevated liver function tests in colorectal tumor individuals with hepatic metastases (38). The present study showed a significant elevation in serum ALT, AST, and ALP in colorectal tumor individuals with hepatic metastases compared to the control subjects, which was established by previous studies (39), (40). In addition, previous studies showed increased ALP levels in colorectal cancer individuals with bone metastases (41). In addition, the current study showed low serum TSP levels in colorectal cancer individuals compared to the control group, and this result was supported by previous studies that indicated low levels of TSP in individuals with colorectal carcinoma compared to the control subjects (42).

About 15% of the CRC states would have advanced metastases at identification, and 50% of the individuals with locally progressive illness would induce metachronous metastases, driving them to death in less than two years of follow-up, despite good operating and adjuvant therapy (42). Different pathologic, clinical, and biological factors determine the outcome of CRC. Between them, the cancerous stage (TNM organization) was the most specific factor in determining the prognosis of CRC individuals. Initial stages (Stage 1) are related to a good prognosis, with a 5-year persistence rate near 90% (43). Many factors determine that the patients with identical cancerous stages present different results. Between them, the presurgical feeding condition has been concurrent with the long-term oncologic prognosis of recurrence of death (44).

Metastasis refers to invading tumor cells from the origin site to additional body parts in the present study. The most common location was the liver, accounting for 46.7 % of cases, followed by the lung (16.7 %), then by bone (13.3 %), then by peritoneum, uterus and ovary (6.7 % for each), and finally by spleen (3.3 %). The proportions of disease metastasis in the present study are comparable to that seen in other studies (45).

In this study, there was elevated neutrophil count, and low lymphocyte count in individuals with colorectal carcinoma when compared with the control subjects, additionally there was significantly higher NLR in colorectal tumor individuals when compared to the healthy subjects, and previous studies confirmed these results (46), (47), (48).

Many studies indicated that inflammatory reaction plays a critical role in the growth of the tumor microenvironment, a few variations of provocative cells could be an index for progress, and changes of cellular immune elements in peripheral venous blood could reveal tumor irritation condition for indicating persistent prediction (49), (50). Systemic inflammatory reaction plays a critical role as a leading reason for neoplastic practicability, and it was vigorously involved in the formation and proliferation of different tumors (51). It is known that peripheral blood components, including leukocytes, neutrophils, lymphocytes, and thrombocytes, can indicate systemic inflammation. NLR and the PLR have been established as the prognosis index for various malignancies like biliary tract and gastric cancer (52). Systemic inflammation has been associated with the bad progress of colorectal tumors (53).

In this study, serum CEA was considerably increased in colorectal tumor individuals compared to the control subjects. CEA is a readily presented cancer parameter that aids in managing colon-rectal tumors. Higher preoperative CEA levels independently predict whole and disease-free persistence rates (54)(55)(56). CEA has been utilized postsurgical to index tumor surveillance. Additionally, individuals with early-stage colon cancer that is node-negative but who also have increased presurgical CEA levels would have comparable progress to that of patients with node-positive illness, possibly as a result of cancer upstaging, and could thus be nominees for adjuvant treatment (57). CEA is a glycoprotein engaged in adherence normally generated by the gut throughout foetal growth (58). It is a cell surface glycoprotein that aids as functional colon tumor ligands which are climacteric to the metastatic distribution of colonic tumors (59), (60). Presently, serum CEA levels have been commended by the "National Institute of Clinical Excellence European Group on Tumor Markers" and the "American Society of Clinical Oncology" for surveillance following therapeutic amputation of colorectal tumors (61).

In the present study, the grade of disease was positively correlated to lymphocyte count, NLR, and AST. In contrast, the stage of illness was positively related to CEA, NLR, AST, ALP, neutrophils, and lymphocytes. The positive correlation of the location of disease with liver enzymes can be attributed to liver metastasis causing damage to liver cells and liberation of their enzymes into circulation.

6. Conclusion

The study found a statistically considerable variation in the average neutrophil computation, lymphocyte computation, and NLR between patients diagnosed with colorectal carcinoma and healthy control individuals. In addition. The study observed notable alterations in the serum level of liver function tests among patients with colorectal carcinoma. The mean AST, ALT, ALP, and TSB levels were significantly elevated, while the serum level of TSP exhibited a significant decrease in the patient subjects compared to the control subjects. This observation indicated that serum CEA and hematological materials measurement could be reliable predictors of colorectal carcinoma.

7. Acknowledgment

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4.Rotational abnormalities such as horseshoe or pelvic kidney and duplex collecting systems may also cause UPJ obstruction. [12] While all of above consider primary UPJO, the secondary include:In children, vesicoureteral reflux can lead to upper tract dilation with subsequent elongation, tortuosity, and kinking of the ureter. [13]

The acquired causes include: stone, fibroepithelial polyps, urothelial malignancy. [13]

In the infant population, hydronephrosis is usually diagnosed

prenatally with the use of maternal ultrasonography. [14]

Figure 1: Pie chart showing the frequency distribution of individuals with colorectal cancer as claimed to a grade of a tumor

8. Figures

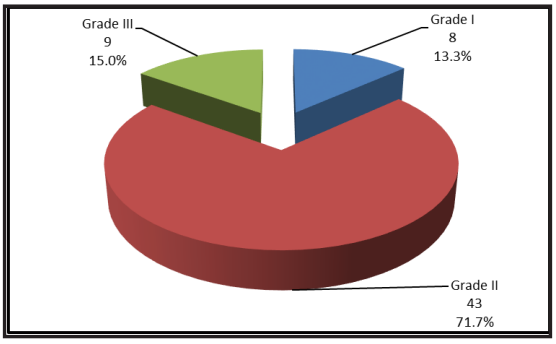

Figure 1: Pie chart showing the frequency distribution of individuals with colorectal cancer as claimed to a grade of a tumor

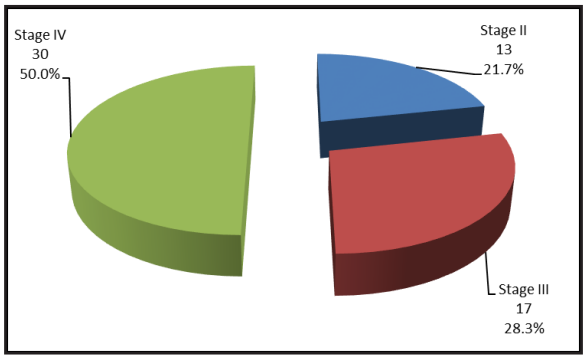

Figure 2: Pie chart showing the frequency distribution of individuals with colorectal cancer as claimed to the stage of tumor

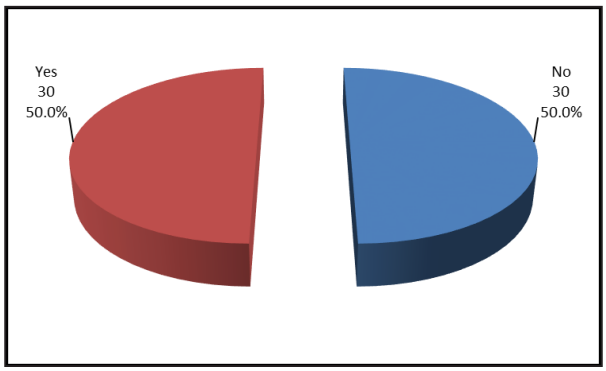

Figure 3: Pie chart showing the frequency distribution of people with colorectal cancer as claimed to metastasis

9. Tables

Table 1: Frequency of sites of metastasis

Site	Number of cases	%
Liver	14	46.7
Lung	5	16.7
Bone	4	13.3
Peritoneum	2	6.7
Uterine	2	6.7
Ovary	2	6.7
Spleen	1	3.3

Table 2: Demographic correlation of individuals with colorectal Cancer and control subject

Characteristic	Colorectal Cancer n = 60	Control group n = 69	p
Age (years)			
Mean ±SD	52.97 ±11.92	51.81 ±12.61	0.561 I NS
Range	20 -77	21 -65	
Gender			
Male, n (%)	36 (60.0 %)	44 (63.8 %)	0.660 C NS
Female, n (%)	24 (40.0 %)	25 (36.2 %)	

n: number of cases; SD: standard deviation; I: independent samples t-test; C: chi-square test; NS: not significant; ***: significant at $p \leq 0.001$

Table 3: Comparison of liver parameters between individuals with colorectal tumor and control subject

Characteristic	Colorectal Cancer n = 60	Control group n = 69	p
AST (IU/L)			
Mean ±SD	34.27 ±9.89	21.73 ±7.40	<0.001 I ***
Range	18.6 -58.3	10.3 -43	
ALT (IU/L)			
Mean ±SD	36.40 ±18.58	22.02 ±12.21	<0.001 I ***
Range	16.7 -83.7	4.7 -61.4	
ALP (IU/L)			

Mean ±SD	114.32 ±40.10	95.08 ±27.26	0.002 I **
Range	41.6 -210.3	42.2 -169.3	
TSP (g/dl)			
Mean ±SD	60.23 ±18.33	67.12 ±8.31	0.006 I **
Range	23.9 -93	41.7 -87.8	
TSB (mg/dl)			
Mean ±SD	0.65 ±0.60	0.43 ±0.38	0.017 I *
Range	0.3 -2.5	0.1 -2.6	

n: number of cases; **SD**: standard deviation; **AST**: aspartate transaminase; **ALT**: alanine transaminase; **ALP**: alkaline phosphatase; **TSP**: total serum protein; **TSB**: total serum bilirubin; **I**: independent samples t-test; *: significant at $p \leq 0.05$; **: significant at $p \leq 0.01$; ***: significant at $p \leq 0.001$

Table 4: Comparison of haematological parameters between individuals with colorectal Cancer and control subject

Characteristic	Colorectal Cancer n = 60	Control group n = 69	p
Neutrophils X10^9/L			
Mean ±SD	7.23 ±3.98	4.41 ±1.71	<0.001 I ***
Range	2 -15.5	2 -7.2	
Lymphocyte X109/L			
Mean ±SD	1.76 ±1.37	2.74 ±1.00	<0.001 I ***
Range	0.1 -4.5	1.5 -4.5	
NLR			
Mean ±SD	13.91 ±6.59	1.85 ±1.02	<0.001 I ***
Range	0.49 -59	0.44 -4.5	

NLR: neutrophil to lymphocyte ratio; SD: standard deviation; n: number of cases; I: independent samples t-test; ***: significant at p ≤ 0.001

Table 5: Comparison of CEA between individuals with colorectal tumours and healthy group

Characteristic	Colorectal Cancer n = 60	Control group n = 69	p
CEA (ng/ml)			
Mean ±SD	133.28 ±94.33	1.77 ±1.07	<0.001 I ***
Range	14.7 -300.2	0.18 -4.2	

CEA: carcinoembryonic antigen; SD: standard deviation; n: number of cases; I: independent t-test; ***: significant at p ≤ 0.001

Table 6: Correlations of grade, stage, and metastasis to other characteristics of patients

Characteristic	Grade		Stage		Metastasis	
	r	p	r	p	r	p
Gender	0.234	0.071	0.199	0.127	0.000	1.000
Age	0.201	0.124	0.241	0.063	0.192	0.142
Neutrophils	0.235	0.071	0.739	<0.001***	0.446	<0.001***
Lymphocyte	-0.463	<0.001***	-0.732	<0.001***	-0.445	<0.001***
NLR	0.388	0.002 **	0.765	<0.001***	0.467	<0.001***
AST	0.320	0.013*	0.329	0.010**	0.410	0.001 ***
ALT	0.207	0.112	0.222	0.088	0.359	0.005**
ALP	0.150	0.251	0.301	0.019*	0.432	0.001***
TSP	-0.050	0.703	-0.125	0.342	-0.204	0.118
TSB	0.211	0.106	0.026	0.845	0.220	0.091
CEA	0.320	0.013	0.755	<0.001***	0.433	0.001***

NLR: neutrophil to lymphocyte ratio; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TSP: total serum protein; TSB: total serum bilirubin; CEA: carcinoembryonic antigen; *: significant at p ≤ 0.05; **: significant at p ≤ 0.01; ***: significant at p ≤ 0.001

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