

Diagnostic performance of biomarkers in colon vs. rectal cancer: A retrospective comparative study

Saad Fadhel Nassar¹, Noora Wael Rasheed², Sabah Qusay Abd-Alhussein², Rooa A Nimer²,
Mihad Shakir N. Alubaydi³, Karima Akool Al-Salihi⁴

¹DEPARTMENT OF MEDICINE, COLLEGE OF MEDICINE, AL-IRAQIA UNIVERSIT, BAGHDAD, IRAQ

²DEPARTMENT OF CHEMISTRY AND BIOCHEMISTRY, COLLEGE OF MEDICINE, AL-IRAQIA UNIVERSITY, BAGHDAD, IRAQ

³DEPARTMENT OF PHYSIOLOGY, COLLEGE OF MEDICINE AL-IRAQIA UNIVERSITY, BAGHDAD, IRAQ

⁴DEPARTMENT OF BASIC SCIENCE, COLLEGE OF DENTISTRY, AL-IRAQIA UNIVERSITY, BAGHDAD, IRAQ

ABSTRACT

Aim: Colon cancer and rectal cancer are collectively called colorectal cancer (CRC), owing to their distinct anatomical, embryological, and functional features. The study aimed to assess the diagnostic performance of various biomarkers, including liver enzymes, lipid levels, and carcinoembryonic antigen (CEA), in differentiating between colon and rectal cancers.

Materials and Methods: The study included 70 patients with confirmed histopathology of CRC (46 patients with colon cancer (CC) and 24 patients with rectal cancer (RC), and 40 healthy control individuals. Fasting blood samples were collected to measure liver enzymes, lipid levels, and CEA levels via using enzyme-linked immunosorbent assay (ELISA) method.

Results: No statistically significant age difference ($p = 0.417$) was seen in all groups. A statistically significant differences were revealed in the distribution of body mass index (BMI) ($p = 0.006$): 31.4% of colon cancer patients were overweight, compared to 14.3% of rectal cancer patients and 11.4% categorized as obese. A statistically significant difference was also observed in the distribution of sex ($p = 0.0269$): 41.4% of colon cancer patients were male, and 24.3% were female, 24.3% of rectal cancer patients were male, and 10% were female. The findings showed that the CEA, liver enzymes, and lipid levels exhibited excellent diagnostic performance for both CC and RC.

Conclusions: These results highlight the clinical significance of these biomarkers in routine evaluations which can enhance therapeutic management and early diagnosis ultimately increasing survival and cure rates.

KEY WORDS: colon cancer (CC), rectal cancer (RC), liver enzymes, lipid profiles, CEA biomarkers

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INTRODUCTION

Colorectal cancer (CRC) is the third most prevalent malignancy and the second most frequent cause of cancer-related deaths globally [1, 2]. Rectal cancer (RC) and Colon cancer (CC) are Rectal cancer and colon cancer are usually classified under colorectal cancer, based on the fact that CC and RC arise in the large intestine, which is considered a singular organ [3]. However, several biological and clinical markers show that rectal cancer differs from colon cancer. The rectum and colon differ in embryological origin, anatomy, and function. As a result, treatments for primary rectal and colon cancers vary [4, 5].

Although the incidence of CRC generally states both statistics jointly, two-thirds of CRCs are located in the

colon and one-third in the rectum [6]. Out of 129,700 newly registered CRCs, 72% were diagnosed in the colon and 28% in the rectum according to the statistics of the American Cancer Society in 2015 [7].

The carcinogenic risk to develop rectal cancer by far exceeds that of the colon mucosa since the area at risk in the colon is definitely larger than that of the rectum. The rectal mucosa has an at least four times higher risk for malignant transformation than the colon mucosa [3].

However, since 2010, CRC has represented the most common type of cancer in males and the third most common type of cancer in females [8]. Across all ages in every nation, males have a 1.5-fold greater risk of developing CRC compared with females [9].

Accurate and prompt cancer diagnosis is vital for enhancing prognosis and survival rates. Biomarkers are crucial in diagnosis, helping clinicians distinguish malignant from benign conditions effectively [10, 11]. Carcinoembryonic antigen (CEA) is utilized as a tumor marker for CRC (12, 13); however, its diagnostic precision necessitates continuous assessment in conjunction with other biochemical markers, such as lipid levels and liver enzymes [14].

AIM

The purpose of this study is to assess the diagnostic value of liver enzyme lipid measurements and CEA in differentiating between healthy people and those with colon and rectal cancer. The objective is to improve the understanding of how biomarkers can be used for the early detection of cancer.

MATERIALS AND METHODS

STUDY DESIGN

The study is a retrospective comparative study designed to assess biomarker levels in 70 patients with confirmed histopathology of primary CRC, with or without metastatic disease; 46 have colon cancer, and 24 have rectal cancer, compared with 40 healthy control individuals. The study was conducted in the Oncology Teaching Hospital, Baghdad. Informed consent was obtained from all participants. The sample collection period is from December 2024 to May 2025.

DATA COLLECTION

Demographic information was collected, and body mass index (BMI) was calculated from direct measures of body weight (kg) divided by height (m²) for all participants. Primary CRC diagnosis and clinical staging were confirmed by gastrointestinal surgeons and radiologists through a combination of clinical evaluation, imaging studies including colonoscopy, biopsy, imaging studies such as magnetic resonance imaging (MRI) and computer tomography scanning (CT), and the histopathological analysis. The anatomical location of the primary lesion was determined for colon cancer and rectum cancer.

PATIENT CLASSIFICATION

- Forty-six Colon cancer patients, 29 males and 17 females, ages 29 to 75 years.
- Rectal cancer group: 24 patients, aged 26-72, including 17 males and 7 females.

- Overall, 35 patients had metastatic disease, with metastases in the liver (25), lungs (7), or both (3).
- Forty healthy control participants, including 16 males and 24 females, aged 24-77.

INCLUSION CRITERIA

- Histologically confirmed primary colon and rectal cancers at different stages.
- No prior history of malignancy in controls.

EXCLUSION CRITERIA

- Any condition impairing liver function or lipid metabolism, Liver disease, or hematological disorders.

BLOOD SAMPLES

5 mL of fasting blood was obtained for evaluation of:

- Liver Function Tests:
 - Use kinetic enzyme techniques approved by the IFCC for ALT and AST. A colorimetric assay was used to quantify ALP. Albumin and TSP were determined by bromocresol green and biuret methods, respectively [15, 16].
 - Lipid Profile: Total cholesterol, triglycerides, HDL, LDL, and VLDL were measured through enzymatic colorimetric methods.
 - CEA: Elabscience Human CEA ELISA kit on a HumanReader HS analyzer was used to measure CEA levels.

STATISTICAL ANALYSIS

SPSS v27 was used for data analysis. Clinical and demographic data were analyzed using descriptive statistics. Sex and the presence of metastases were assessed using chi-square tests. Biomarker values were compared using one-way ANOVA. Sensitivity, specificity, and cutoff points were calculated using ROC curve analysis. Subsequently, the area under the curve (AUC) of each biomarker was calculated to assess diagnostic accuracy. A p-value less than 0.05 was considered statistically significant when examining correlations between biomarker levels.

RESULTS

An overview of clinical and demographic traits among the study groups is given in Table 1. The study included Forty-six subjects with colon cancer, twenty-four patients with rectal cancer, and Forty healthy people as a control group. All groups had comparable mean

Table 1. Demographic and clinical features among colorectal cancer patients and healthy controls

Parameters	Participants			P value
	Colon (46)	Rectum (24)	Healthy (40)	
Age (years) (26-75 years)	55.8 ± 11.2	55.3 ± 12.4	58.8 ± 13.3	0.416
BMI- Kg/m2	26.4209 ± 3.9	27.7549 ± 3.6	28.7472 ± 2.2	0.006
Normal	16 (22.9%)	6 (8.6%)	2 (5%)	
Overweight	22 (31.4%)	10 (14.3%)	25 (26.5%)	
Obese	8 (11.4%)	8 (11.4%)	13 (32.5%)	
Sex	46 (65.7%)	24 (34.3%)	(%)	0.0269
Male	29 (41.4%)	17(24.3%)	16 (40%)	
Female	17 (24.3%)	7 (10%)	24 (60%)	
Metastasis	(%)	(%)		0.613
Non-Metastasis	24 (34.3%)	11(15.7%)		
	22 (31.4%)	13 (18.6%)		

Source: Own materials

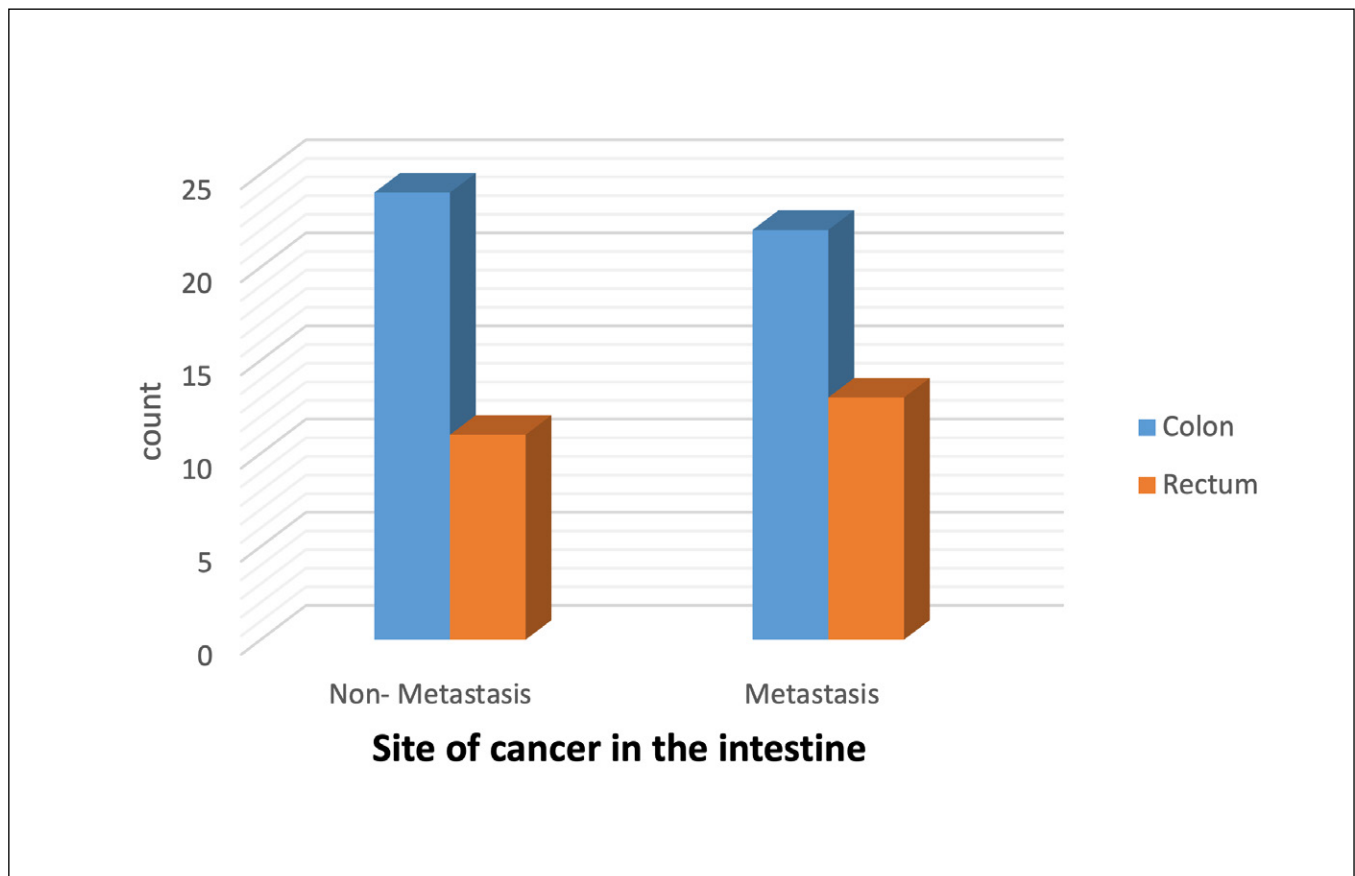


Fig. 1. Metastasis rates among colon and rectal cancer patients

Source: Own materials

ages and statistical analysis revealed no statistically significant age difference ($p = 0.417$). Nonetheless, statistically significant differences were revealed in the distribution of body mass index (BMI) ($p = 0.006$): 31.4% of colon cancer patients were overweight, compared to 14.3% of rectal cancer patients and 11.4% categorized as obese. Additionally, a statistically significant difference was observed in the distribution of sex

($p = 0.0269$): 41.4% of colon cancer patients were male, and 24.3% were female, 24.3% of rectal cancer patients were male, and 10% were female. Metastases prevalence rates were not significantly different between the cancer groups ($p < 0.613$): 34.3% for colon cancer and 15.7% for rectal cancer, as shown in Figure 1.

Findings showed that the mean CEA level in CC patients was 3.8 ± 1.5 ng/mL; in contrast, RC patients

Table 2. Assessment of carcinoembryonic antigen (cea) levels in colorectal cancer patients and healthy controls

Parameters	Colon (46)	Rectum (24)	Healthy (40)	Significance
CEA ng/ml	3.7900 ± 1.5396	4.1118 ± 1.2905	.9094 ± .3741	0.001

Source: Own materials

Table 3. Evaluation of LFT parameters in colon and rectal cancer patients compared to healthy controls

Parameters	Participants			P value
	Colon (46)	Rectum (24)	Healthy (40)	
ALT- U/L	46.9780 ± 8.45	48.1092 ± 7.19	28.4368 ± 4.44	0.001
AST- U/L	47.6196 ± 8.98	46.5700 ± 8.59	30.1995 ± 2.08	0.006
ALP- U/L	169.8413 ± 30.08	169.4513 ± 29.45	121.5021 ± 3.96	0.001
Albumin- g/dL	4.2363 ± .35	4.2519 ± .35	3.5653 ± .04	0.001
Globulin- g/dL	1.7891 ± .72	1.7808 ± .69	.7402 ± .13	0.001
Total Protein- g/dL	6.0254 ± 1.07	6.0329 ± 1.04	4.3055 ± .14	0.001

Source: Own materials

Table 4. Evaluation of lipid profile in colon and rectal cancer patients compared to healthy controls

Parameters	Participants			P value
	Colon (46)	Rectum (24)	Healthy (40)	
Cholesterol- mg/dL	244.8811 ± 25.5	245.4729 ± 27.5	202.2463 ± 3.9	0.001
TG- mg/dL	218.4824 ± 20.5	216.9967 ± 23.1	184.7225 ± 5.8	0.001
HDL- mg/dL	28.4972 ± 5.5	28.2292 ± 5.3	45.5265 ± 7.2	0.001
VLDL- mg/dL	43.6965 ± 4.1	43.3993 ± 4.6	36.9445 ± 1.7	0.001
LDL- mg/dL	172.6874 ± 26.1	173.8444 ± 27.9	119.7752 ± 9.9	0.001

Source: Own materials

Table 5. Relationship between sex and colon versus rectal cancer, on metastatic and non-metastatic cases

Gender	Site of cancer in the intestine	Total	Pearson Chi-Square/ Asymp. Significance
Female	Metastasis	15	.615
	Non-Metastasis	9	
Pearson Chi-Square/ Asymp. Significance		0.132	
Male	Metastasis	20	.615
	Non-Metastasis	26	
Pearson Chi-Square/ Asymp. Significance		0.809	

Metastasis (*): non- metastasis, Metastasis (**): Metastasis out side intestine

Source: Own materials

had a slightly higher mean CEA level of 4.11 ± 1.3 ng/mL. In contrast, the mean CEA level in healthy control subjects was just 0.91 ± 0.4 ng/mL. With a p-value of 0.001, statistical analysis shows a significant difference in CEA levels across the groups, with a p-value of 0.001 (Table 2).

The findings revealed a significant difference in LFT across the groups. The cancer patients showed statistically significant raises in ALT, AST, and ALP levels, with

p-values <0.01 (Table 3).

Furthermore, Lipid profiles differed significantly; as shown in Table 4, patients with colon and rectal cancer had greater levels of total cholesterol, triglycerides, LDL, and VLDL, while HDL was noticeably lower than in healthy controls.

The association between tumor metastasis and patient sex is examined in Table 5. Six females had rectal cancer with metastases and nine had colon cancer.

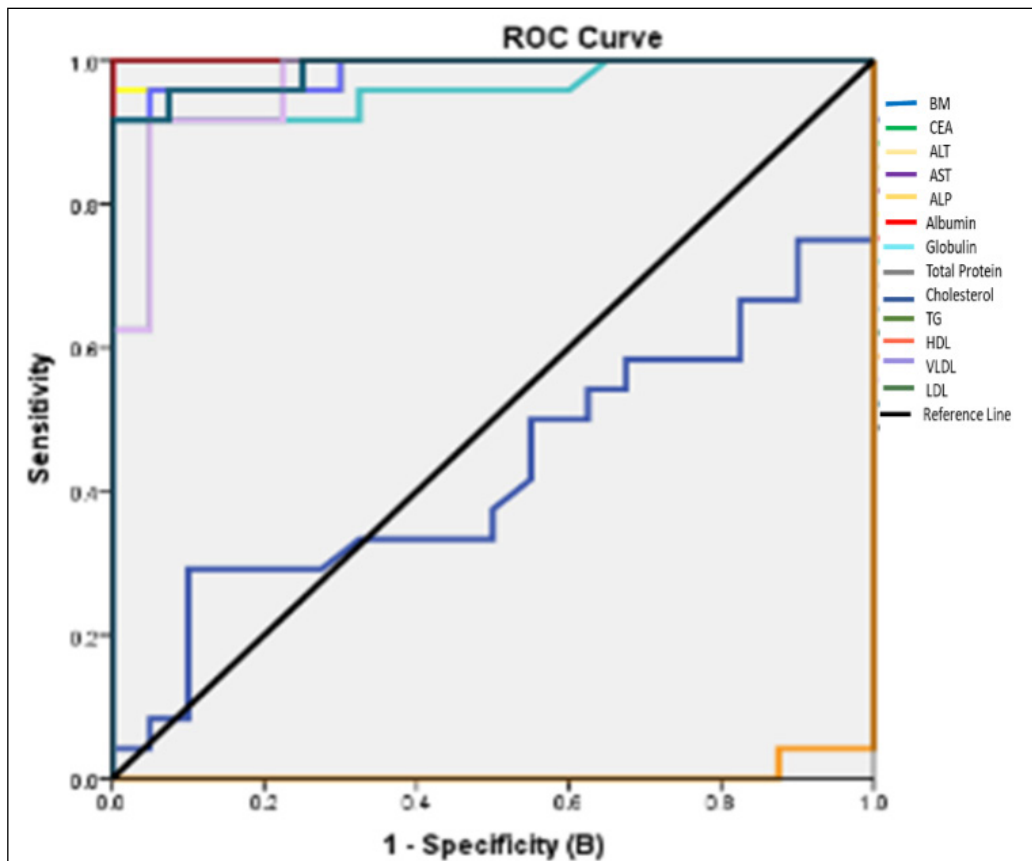


Fig. 2. ROC curves, evaluation parameters in the colon cancer (A) and rectal cancer; (B) in comparison to the healthy control group
Source: Own materials

There is no significant relationship between sex and tumor site or metastasis, according to the Pearson's chi-squared test result of roughly 0.132. Thirteen colon and seven rectal metastases were found in 20 male individuals; the chi-squared value was 0.809, indicating no significant correlation.

Table 6 assesses the diagnostic accuracy of several biochemical markers - CEA, ALT, AST, Albumin, cholesterol, triglycerides, VLDL, and LDL - in differentiating colorectal cancer patients from healthy controls. CEA performed exceptionally well, with significant asymptotic p -values ($p = 0.001$). The ideal cut-offs for rectal and colon cancer were 1.4840 and 1.6955, respectively, with 100% sensitivity and specificity. High diagnostic value was also demonstrated by liver marker. ALT, AST, and albumin had a significant performance for rectal and colon cancer with high sensitivity and specificity. Lipid profile, including total cholesterol, triglycerides, VLDL, and LDL, demonstrated remarkable diagnostic capacities, with high specificity and sensitivities (Fig. 2).

DISCUSSION

Our results show that there was a significant difference in the BMI distribution between the study groups ($p =$

0.006). Colon cancer associated with increasing BMI and Overweight. A higher body BMI has a stronger association with colon cancer compared to rectal cancer, primarily because the metabolic impact of visceral fat has a more significant effect on the proximal colon due to elevated insulin levels, persistent inflammation, and altered adipokines. On the other hand, rectal cancer generally shows weaker or inconsistent connections with these risk factors. This is probably due to the fact that alterations in insulin resistance, metabolic pathway, and cumulative exposure to an obesogenic environment might encourage the precancerous pathophysiological processes [17]. However, another study showed that overweight and obese individuals had 18% and 32% increased risk of colon cancer compared and rectal cancer, respectively [18].

Furthermore, our study revealed significant variations in sex among the study groups ($p = 0.0269$). Literature reported that men tend to have a greater overall incidence of both colon and rectal cancer than women, with higher risk for rectal cancer. However, although rectal cancer is more frequently reported in men, women are more prone to developing colon cancer. Additionally, males were often exhibiting higher prevalence and mortality rates than females (19). Men are

Table 6. ROC: assessment of parameters in colon and rectal cancer groups compared to the healthy control group

Parameters		Area under the curve (AUC)	Asymptotic sig.	CUT-OFF point	Sensitivity	Specificity
CEA	Colon	1.000	0.001	1.6955	1.000	1.000
	rectum	1.000	0.001	1.4840	1.000	1.000
ALT	Colon	.990	0.001	33.0050	0.957	1.000
	rectum	1.000	0.001	33.7850	1.000	1.000
AST	Colon	.984	0.001	32.4800	.978	1.000
	rectum	1.000	0.001	33.0550	1.000	1.000
ALP	Colon	.949	0.001	128.3700	.935	1.000
	rectum	.991	0.001	129.8650	.958	1.000
Albumin	Colon	.997	.003	3.6500	.957	1.000
	rectum	1.000	0.001	3.6700	1.000	1.000
Globulin	Colon	.908	.038	.9500	.870	1.000
	rectum	.960	0.001	1.0100	.917	1.000
Total Protein	Colon	.943	.030	4.7200	.870	1.000
	rectum	.988	0.001	4.5850	.958	1.000
Cholesterol	Colon	.973	.022	209.7600	.957	1.000
	rectum	.985	0.001	211.7100	.917	1.000
TG	Colon	.959	.024	192.2450	.957	0.950
	rectum	.967	0.001	193.1450	.917	0.950
VLDL	Colon	.959	.024	38.4490	.957	0.950
	rectum	.967	0.001	38.6290	.917	0.950
LDL	Colon	.985	.015	134.6060	.978	1.000
	rectum	.986	0.001	135.5720	.917	1.000

Source: Own materials

more prone to colon and rectal cancers due to their higher rates of smoking, alcohol consumption, and accumulation of visceral fat. Additionally, molecular factors, gut microbes, or changes in sex hormones could be the cause of these variations.

However, our findings showed significant variations in CEA levels among the cancer groups with high sensitivity and specificity (100%). Distinct biological behavior, cancer stages, and tumor aggressiveness may be associated with varying CEA levels. Furthermore, our results corroborate previous findings indicating varied CEA levels in CRC [20]. Although CEA is not a disease-specific marker, our results may be useful in predicting of establishing and staging of lesion particularly in rectal cancer patients. However, further studies were needed to support this suggestion.

Additionally, our findings showed that ALT, AST, and albumin levels varied significantly among cancer groups, with p-values <0.01. Elevations of these enzymes may indicate liver involvement. Furthermore, the study observed that notable diagnostic potential has established by ALT, AST, and albumin for colon and rectal cancers with high sensitivity and specificity. Hepatic enzymes can offer important insights into the

progression of cancer and are known to be involved in the disease. The specificity and accuracy of ALT and CEA levels in predicting liver metastases in CRC patients have been shown in recent studies which may improve the early detection and treatment of such problems [21]. Furthermore, studies have indicated that liver enzymes are crucial biomarkers in the treatment of colorectal cancer, serving as key indicators of cancer metastasis to the liver. Regarding long-term risks, research suggests that elevated blood levels of liver enzymes are more strongly associated with the development of colon cancer than with rectal cancer [22].

Otherwise, other studies have found that hepatic enzymes are not a substitute for imaging studies in detecting liver metastases, as their levels can be normal even with a small metastatic burden [23].

Furthermore, diagnostic evaluation found that elevated levels of total cholesterol, triglycerides LDL and VLDL have been associated with colon and rectal cancer. However, based on recent meta-analyses and studies, dyslipidemia associations with CRC show distinct differences between colon and rectum cancer, with higher triglyceride levels being more associated with colon cancer and higher total cholesterol with rectal cancer [24]. These

variations could result from dietary variations altered metabolic environments or the impact of gut microbes.

CONCLUSIONS

By illustrating the variations in the tumor-marker profiles of RC and CC this study highlights the distinctions

between rectal and colon cancers. As evidenced by the elevated CEA levels and altered liver and lipid profiles the hosts reaction to these tumors may vary throughout the body. Comprehending these variations is crucial for develop individualized treatment plans and diagnostic techniques that can ultimately improve prognosis and survival rates.

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CORRESPONDING AUTHOR

Karima Akool AISalihi

Department Of Basic Science

College of Dentistry

Al- Iraqia University

Baghdad, Iraq

e-mail: kama18_akool@aliraqia.edu.iq

ORCID AND CONTRIBUTIONSHIP

Saad Fadhel Nassar: 0009-0007-8755-7993 [A](#) [B](#) [F](#)

Noora Wael Rasheed: 0000-0001-9079-7049 [B](#) [C](#) [D](#)

Sabah Qusay Abd-Alhussein: 0009-0002-0821-5666 [B](#) [D](#) [E](#)

Rooa A Nimer: 0009-0006-1086-5843 [B](#) [C](#) [E](#)

Mihad Shakir N. alubaydi: 0009-0001-0575-4165 [B](#) [C](#) [E](#)

Karima Akool Al-Salihi: 0000-0002-5698-2678 [F](#)

[A](#) – Work concept and design, [B](#) – Data collection and analysis, [C](#) – Responsibility for statistical analysis, [D](#) – Writing the article, [E](#) – Critical review, [F](#) – Final approval of the article

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