Original Article

Clinical Evaluation of Liver Function Tests and Carcinoembryonic Antigen Levels in Colorectal Cancer Associated with Hepatic Metastases

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ABSTRACT

Background:
Colorectal cancer (CRC) ranks as the second leading cause of cancer-related mortality globally, with hepatic metastases representing the most common and clinically significant complication. Early detection of metastasis and disease progression using biochemical markers is crucial for improving patient survival outcomes.
Objective: This study aimed to evaluate the efficacy of liver function tests (LFTs), lipid profile parameters, and carcinoembryonic antigen (CEA) levels in patients with CRC, focusing specifically on their association with hepatic metastasis.

Materials and Methods:
A case-control study design was implemented involving 58 patients with CRC, subdivided based on the presence or absence of liver metastases, and 30 healthy control individuals. Serum levels of CEA (reported as mean±SE and range), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), albumin, total protein, and cholesterol, triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) were measured. Statistical analyses included independent t-tests, Pearson's correlation coefficients, and receiver operating characteristic (ROC) curve analysis.

Results:
Significant differences ($P<0.001$) were observed in most biochemical parameters between patients with CRC and healthy controls, with elevated levels of CEA and liver enzymes notably apparent in the patient group. Parameters such as CEA, ALT, AST, ALP, and various lipid markers significantly correlated with the presence of liver metastases in patients with CRC, accompanied by notably reduced HDL levels. ROC analysis identified CEA, lipid profile (except HDL), total protein and albumin, and liver enzymes (ALT and ALP) as the most reliable diagnostic biomarkers for CRC with hepatic metastasis.

Conclusion:
The findings underscore the clinical utility of CEA, liver function tests (specifically ALT and ALP), albumin, and lipid profile parameters as valuable biomarkers for identifying CRC staging, site of involvement, and likelihood of hepatic metastasis.

Keywords: Colorectal cancer, Liver metastasis, Carcinoembryonic antigen (CEA), Liver function tests, Lipid profile, Tumor markers

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INTRODUCTION

Colorectal cancer (CRC), commonly known as colon cancer, ranks among the top three most lethal cancers worldwide, significantly contributing to global mortality. It originates in the colon or rectum, both integral parts of the large intestine, and commonly metastasizes to adjacent organs. Typically, colon cancer arises from polyps—small benign growths within the intestinal lining—that can become malignant if left untreated. Additional risk factors contributing to colon cancer include advanced age, unhealthy dietary habits, inflammatory bowel diseases (IBD), and environmental factors (1). Lifestyle factors such as tobacco smoking, heavy alcohol consumption, and diets high in fat content further increase cancer risk (2,3). Genetic predispositions, notably mutations in the APC gene and conditions such as Lynch syndrome, also significantly elevate CRC susceptibility (3). Colon cancer can develop in either the right (proximal) or left (distal) segments of the colon, each demonstrating distinct clinical characteristics. Right-sided colon cancers tend to be aggressive, often diagnosed at advanced stages due to vague symptoms such as anemia and fatigue. Conversely, left-sided colon cancers typically manifest earlier due to more apparent symptoms, including rectal bleeding and altered bowel habits. The location of the tumor substantially influences therapeutic strategies and prognosis (4,5). Various diagnostic approaches are utilized for colon cancer detection, including colonoscopy, fecal occult blood tests (FOBT), and imaging modalities. Colonoscopy remains the gold standard, allowing both diagnosis and therapeutic intervention through polyp removal. Non-invasive screening options include fecal immunochemical tests (FIT) and multi-target stool DNA tests (6). Advanced imaging techniques, such as computed tomography (CT) colonography and magnetic resonance imaging (MRI), support staging and evaluating disease spread, especially in advanced cases (7). Globally, CRC poses a substantial public health burden, with approximately 1.9 million new diagnoses and 935,000 deaths recorded in 2020. These figures are projected to double by 2040, driven largely by lifestyle changes prevalent in high-income countries, such as increased obesity and physical inactivity. Additionally, rapid urbanization and dietary shifts contribute to rising incidence rates in low- and middle-income countries (8). Currently, CRC is the third most frequently diagnosed cancer globally and ranks second in cancer-related mortality, with considerable variation in mortality rates influenced by healthcare accessibility and screening program effectiveness (9,10). A defining characteristic of CRC is its propensity for hepatic metastasis, most commonly through portal vein circulation, complicating treatment strategies significantly. Stage IV CRC, characterized by liver metastases, typically exhibits a 5-year survival rate below 10%, highlighting the aggressive nature of this disease (11,12,13,14). Treatment approaches for hepatic metastases include systemic chemotherapy, targeted therapies, and surgical interventions, depending on lesion quantity and size. Tumor markers, particularly carcinoembryonic antigen (CEA), play a crucial role in managing CRC, especially in advanced stages. CEA, a glycoprotein involved in cell adhesion, is typically elevated during fetal development and suppressed after birth. However, elevated CEA levels frequently occur in pathological conditions such as CRC, particularly during advanced disease stages. Clinically, CEA serves as a prognostic indicator post-surgical resection, effectively monitoring disease progression, recurrence, and therapeutic responses (15). Although its limited sensitivity and specificity restrict its utility in early detection, elevated postoperative CEA levels are predictive of overall survival and recurrence timing, particularly in metastatic disease (16). The integration of elevated CEA levels with advanced imaging techniques (CT or MRI) enhances detection and assessment of hepatic metastases, aiding therapeutic decision-making and prognostic evaluations (17).

Objective: The primary objective of this study was to assess the clinical efficacy of liver function tests (LFTs), lipid profiles, and CEA levels in patients with CRC, specifically examining their correlation with hepatic metastases.

MATERIALS AND METHODS

Clinical Design

This case-control study included 88 participants: 58 patients with histologically confirmed CRC at various disease stages, and 30 apparently healthy individuals serving as controls. Patients with CRC were further stratified into two subgroups according to the presence or absence of hepatic metastases:

- **CRM:** CRC with liver metastases
- **CRNM:** CRC without liver metastases

The age of participants ranged from 33 to 73 years, with both sexes represented. All CRC diagnoses were confirmed using American Joint Committee on Cancer (AJCC) staging criteria (8th edition), and hepatic metastases were verified via CT scan interpreted by an oncology specialist.

Inclusion criteria:

- Histologically confirmed CRC (stages I–III) based on AJCC staging.
- No evidence of extra-hepatic metastases.

Exclusion criteria:

- Malignancies in organs other than the colon and rectum.

• Metastases to non-hepatic sites.
• History of inflammatory bowel disease, chronic liver disorders, or autoimmune diseases.
• Pregnancy or lactation.

Patient Classification

Disease staging followed the Tumor, Node, Metastasis (TNM) classification system, which evaluates:
• **T:** Extent of primary tumor invasion.
• **N:** Regional lymph node involvement.
• **M:** Presence of distant metastases.

Biochemical Measurements

• **Tumor Marker** –CEA: Quantified using the Elabscience Human CEA ELISA kit (Catalog No. E-EL-H6047, USA) on a HumaReader HS analyzer.

• LFTs:

• Alanine Aminotransferase (ALT) and Aspartate Aminotransferase (AST): Determined via IFCC-endorsed kinetic enzymatic methods to assess hepatocellular integrity.
• Alkaline Phosphatase (ALP): Measured by a colorimetric method.
• Albumin and Total Serum Protein (TSP): Measured using the bromocresol green (BCG) method and biuret reaction, respectively.

• **Lipid Profile:** Total cholesterol, triglycerides (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and very low-density lipoprotein (VLDL) were assessed using enzymatic colorimetric methods to investigate lipid metabolism changes in CRC and metastatic disease.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics software (version 20). Continuous variables were expressed as mean±standard error (SE). Group comparisons were conducted using independent t-tests. Associations between biochemical parameters and clinical variables were assessed using Pearson's correlation coefficient. Diagnostic performance was evaluated via receiver operating characteristic (ROC) curve analysis. Frequencies and percentages (%) were calculated for categorical variables. A P value < 0.05 was considered statistically significant.

RESULTS

There was no statistically significant difference in mean age between the CRC group and the healthy control group (P>0.05), indicating comparable age distribution between the two populations. However, highly significant differences (P<0.01) were observed in most biochemical and anthropometric parameters, with patients with CRC generally exhibiting elevated values compared with controls, except for body mass index (BMI), which was significantly lower in the patient group.

As shown in Table 1, patients with CRC had a significantly lower BMI (26.98±0.42 kg/m²) compared with controls (28.65±0.35 kg/m²; P=0.003). In contrast, CEA levels were markedly higher in patients with CRC (3.74±0.167 ng/mL) than in controls (0.87±0.067 ng/mL; P=0.001). Significant elevations were also observed in liver enzymes (ALT, AST, ALP), serum albumin, total protein, total cholesterol, TG, VLDL, and LDL, whereas HDL was significantly reduced in patients with CRC (P<0.01 for all comparisons).

Table 1. Mean comparison of measured parameters between the study groups

Parameters	Studied groups	N	Mean± SE	t-test	Significance
AGE	Control	30	59.21±1.76	0.928	0.356
	CR disease	58	57.17±1.31		
BMI	Control	30	28.65±0.35	2.593	0.003*
	CR disease	58	26.98±0.42		
CEA	Control	30	0.87±0.067	-12.108-	0.001*
	CR disease	58	3.74±0.167		
ALT	Control	30	28.75±0.76	-11.403-	0.001*
	CR disease	58	46.67±1.056		
AST	Control	30	30.24±0.34	-10.323-	0.001*
	CR disease	58	46.64±1.13		
ALP	Control	30	121.52±0.71	-8.502-	0.001*
	CR disease	58	166.16±3.75		
Albumin	Control	30	3.56±0.007	-10.173-	0.001*
	CR disease	58	4.20±0.045		
Total Protein	Control	30	4.31±0.025	-8.541-	0.001*
	CR disease	58	5.91±0.134		
Cholesterol	Control	30	202.47±0.73	-8.209-	0.001*
	CR disease	58	241.39±3.38		
TG	Control	30	185.06±1.16	-7.620-	0.001*
	CR disease	58	215.63±2.82		
HDL	Control	30	45.055±1.31	11.554	0.001*
	CR disease	58	28.91±0.74		
VLDL	Control	30	37.012±0.23	-7.620-	0.001*
	CR disease	58	43.13±0.56		
LDL	Control	30	120.41±1.81	-9.782-	0.001*
	CR disease	58	169.35±3.47		

*The mean difference is significant at P< 0.01 level.

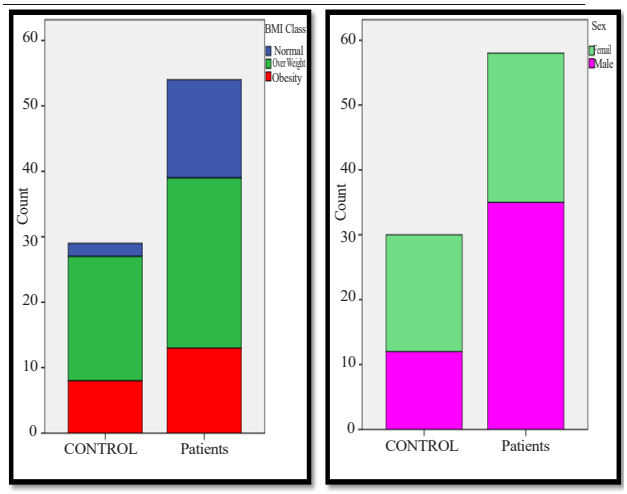

Figure1&2. Comparison between the study groups according to (a) BMI, (b) Sex

Figure 2 illustrates BMI and sex distribution across the study groups, showing a predominance of overweight individuals and a higher proportion of males among patients with CRC. When patients with CRC were sub-classified according to the presence or absence of hepatic metastases (Table 2), the majority in both subgroups had colon cancer, predominantly grade 2.

Overweight status was the most frequent BMI category, with male predominance being more pronounced in the metastatic group.

Table 2. Comparison between patients sub-classified according to metastasis of the disease

	Sub-classes	CRC-without metastasis	CRC-with metastasis
		Frequency (Percentage)	Frequency (Percentage)
BMI	Normal	10 (30.0)%	7 (20%)
	Over weight	15 (45.5%)	13 (52%)
	Obese	6 (18.2%)	7 (28%)
Sex	Female	15 (45.5%)	8 (32%)
	Male	18 (54.5%)	17 (68%)
Site of Cancer	Colon:	21 (63.6%)	18 (72%)
	Right colon	13 (39.4%)	9 (36%)
	Left colon	8 (24.2%)	9 (36%)
	Rectum	12 (36.4%)	7 (28%)
Grade	1	2 (6.1%)	0 (0%)
	2	30 (90.9%)	21 (84%)
	3	1 (3%)	4 (16%)

Receiver operating characteristic (ROC) analysis (Table 3 and Figure 3) demonstrated that CEA, liver enzymes, lipid profile components, and protein markers exhibited high diagnostic accuracy in differentiating patients with CRC from healthy controls.

Notably, CEA achieved 100% sensitivity and specificity at a cutoff value of 1.50 ng/mL (AUC=1.000).

Table 3. ROC analysis for the measured parameters between the study groups

ROC Test Parameters	AUC	Asymptotic Significance[b]	Cutoff point	Sensitivity %	Specificity %
ALT	0.992	0.001	33.005	96.6	100
AST	0.988	0.001	32.48	98.3	100
ALP	0.956	0.001	128.37	93.1	100
Albumin	0.997	0.001	3.65	96.6	100
Total Protein	0.949	0.001	4.585	87.9	100
Cholesterol	0.971	0.001	209.76	93.1	100
TG	0.948	0.001	192.245	93.1	933
VLDL	0.948	0.001	38.45	93.1	93.3
LDL	0.982	0.001	134.61	94.8	100
CEA	1.000	0.001	1.50	100	100

b. Null hypothesis: true area = 0.5; AUC: area under the curve

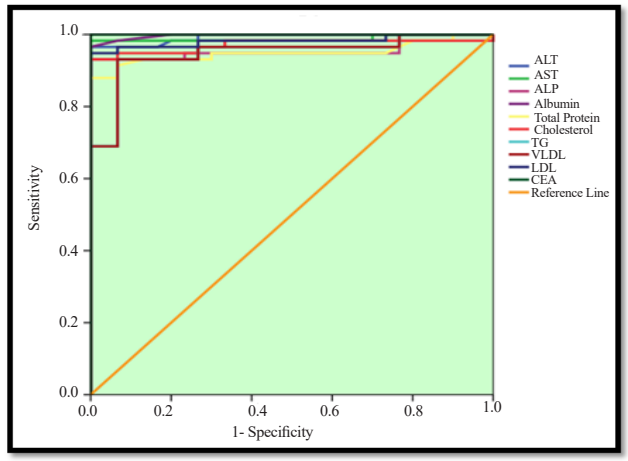

Figure 3. ROC curve between the study groups

Correlation analysis (Table 4) revealed significant positive correlations between CEA and ALT, AST, ALP, albumin, total protein, cholesterol, and LDL, along with a significant negative correlation with HDL, indicating that CEA levels reflect multiple biochemical alterations in CRC.

Table 4. Correlations among parameters in the disease group

Parameters	Pearson Correlation (r-value)	Significance (P value)
CEA*ALT	0.401**	0.002
CEA*AST	0.295*	0.025
CEA*ALP	0.364**	0.005
CEA*Albumin	0.399**	0.002
CEA*Total Protein	0.374**	0.004
CEA*Cholesterol	0.341**	0.009
CEA*HDL	-0.277-*	0.035
CEA*LDL	0.357**	0.006

* The Correlation is significant at P< 0.05 level.

**The Correlation is highly significant at P< 0.01 level.

Number of patients is 58

Comparison between patients with metastatic and non-metastatic CRC (Table 5) showed significantly higher CEA, ALT, AST, ALP, albumin, total protein, cholesterol, TG, VLDL, and LDL levels in the metastatic group, whereas HDL levels were significantly lower (P<0.05 for all). Age and BMI showed no significant differences between the two subgroups.

Table 5. Mean comparison in patients classified according to metastasis of the CRC

Study groups	Disease group 1 (without metastasis) NO. 33	Disease group 2 (liver metastasis) NO. 25	t-test	Significance
Parameters	Mean±SE	Mean±SE		
BMI	26.61±0.56	27.10±0.77	-1.034-	0.306
AGE	57.21±1.84	57.12±1.88	0.036	0.972
CEA	3.17±0.167	4.50±0.25	-4.605-**	0.001
ALT	42.58±1.23	52.06±1.17	-5.449-**	0.001
AST	44.29±1.48	49.72±1.55	-2.494-*	0.016
ALP	151.15±3.96	185.97±4.58	-5.753-**	0.001
Albumin	4.013±0.045	4.45±0.054	-6.201-**	0.001
Total Protein	5.37±0.143	6.61±0.16	-5.743-**	0.001
Cholesterol	224.87±2.55	263.19±4.078	-8.326-**	0.001
TG	205.73±2.68	228.69±4.29	-4.740-**	0.001
HDL	31.67±0.80	25.27±0.97	5.118**	0.001
VLDL	41.15±0.54	45.74±0.86	-4.740-**	0.001
LDL	152.06±2.44	192.18±4.197	-8.726-**	0.001

*The Correlation is significant at P<0.05 level.

**The Correlation is highly significant at P<0.01 level.

NO.: number of patients in each group

Within the CRC cohort, ROC analysis (Table 6 and Figure 4) confirmed that ALT, ALP, albumin, total protein, cholesterol, LDL, and CEA had strong discriminatory power in identifying hepatic metastases, with LDL achieving the highest AUC (0.948).

Table 6. ROC analysis between patient subgroups according to liver metastasis of the CRC disease

ROC Test Parameters	AUC	Asymptotic Significance[b]	Cutoff point	Sensitivity %	Specificity %
ALT	0.848	0.001	45.005	96	69.7
ALP	0.852	0.001	170.635	76	81.8
Albumin	0.876	0.001	4.225	80	78.8
Total Protein	0.861	0.001	6.015	80	81.8
Cholesterol	0.937	0.001	249.065	84	93.9
TG	0.808	0.001	216.15	72	75.8
VLDL	0.808	0.001	43.23	72	75.8
LDL	0.948	0.001	165.88	92	87.9
CEA	0.847	0.001	3.855	80	78.8

b. Null hypothesis: actual area = 0.5

AUC: Area Under the Curve

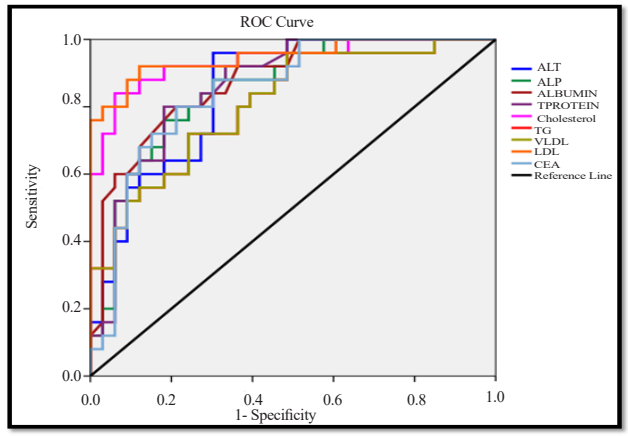

Figure 4. ROC curve between patients sub-grouped according to metastasis

Further stratification according to TNM stage T3 (Table 7) demonstrated that metastatic patients had significantly higher CEA, ALT, ALP, albumin, total protein, cholesterol, TG, VLDL, and LDL compared with non-metastatic patients (P<0.01), while AST and age did not differ significantly.

Table 7. Mean comparison of parameters between the two diseased groups in patients with the T 3 sub-group.

Parameters	Studied gps	N	Mean	Std. Error Mean	95% Confidence Interval of the Difference		Significance
					Lower	Upper	
CEA	CRNM	20	3.43	0.22	-2.15-	-0.55-	0.002**
	CRM	17	4.78	0.34			
ALT	CRNM	20	43.92	1.46	-12.22-	-3.60-	0.001**
	CRM	17	51.82	1.53			
AST	CRNM	20	45.88	1.76	-9.42-	1.29	0.131
	CRM	17	49.94	1.96			
ALP	CRNM	20	154.60	4.86	-46.86-	-15.42-	0.001**
	CRM	17	185.74	6.16			
Albumin	CRNM	20	4.056	0.051	-.56-	-0.205-	0.001**
	CRM	17	4.44	0.075			
Total protein	CRNM	20	5.51	0.17	-1.65-	-0.540-	0.001**
	CRM	17	6.60	0.22			
Cholesterol	CRNM	20	223.88	3.15	-50.22-	-25.005-	0.001**
	CRM	17	261.50	5.63			
TG	CRNM	20	206.57	3.55	-34.32-	-7.34-	0.003**
	CRM	17	227.40	5.88			
HDL	CRNM	20	31.20	1.13	2.049	9.016	0.003**
	CRM	17	25.67	1.31			
VLDL	CRNM	20	41.31	.71	-6.86-	-1.47-	0.003**
	CRM	17	45.48	1.17			
LDL	CRNM	20	151.36	2.97	-51.57-	-26.39-	0.001**
	CRM	17	190.34	5.76			
BMI	CRNM	20	26.35	0.62	-4.14-	0.058	0.05*
	CRM	14	28.39	0.86			
AGE	CRNM	17	56.47	2.40	-8.029-	5.67	0.729
	CRM	17	57.65	2.35			

P is significant* at value ≤ 0.05, and highly** significant at level < 0.01

Finally, analysis across T classifications (T2, T3, and T4) (Table 8) showed significantly higher CEA levels in T3 patients (P=0.037), with no statistically significant variations in other biochemical parameters among the T subgroups. Lipid profile parameters tended to be higher in advanced stages, although these differences did not reach statistical significance.

Table 8. Mean comparison of parameters in CRC's patients sub-grouped according to T- Classification

Parameters	T sub-groups	N	Mean	Std. Error	95% Confidence Interval for Mean		Significance
					Lower bound	Upper bound	
AGE	2	4	47.3333	3.71	31.36	63.30	0.136
	3	37	57.0588	1.65949	53.68	60.44	
	4	17	59.2500	2.20322	54.55	63.95	
BMI	2	4	26.2548	1.05769	21.70	30.81	0.784
	3	37	27.1935	.52962	26.12	28.27	
	4	17	26.6550	.84444	24.84	28.47	
CEA	2	4	2.9553	.65119	.88	5.027	0.037*
	3	37	4.0515	.22303	3.60	4.50	
	4	17	3.2421	.18739	2.84	3.64	
ALT	2	4	41.6075	2.71540	32.96	50.25	0.345*
	3	37	47.5484	1.23301	45.047	50.05	
	4	17	45.9467	2.29943	41.07	50.82	
AST	2	4	41.9725	3.37649	31.23	52.72	0.338
	3	37	47.7446	1.33525	45.037	50.45	
	4	17	45.3235	2.35910	40.32	50.32	
ALP	2	4	145.3650	9.43622	115.33	175.40	0.293
	3	37	168.9070	4.60093	159.57	178.24	
	4	17	165.0818	7.45939	149.27	180.90	
Albumin	2	4	3.9587	.11054	3.61	4.31	0.305
	3	37	4.2330	.05384	4.123	4.34	
	4	17	4.1841	.09158	3.99	4.38	
Total protein	2	4	5.1750	.30653	4.20	6.15	0.292
	3	37	6.0095	.16179	5.68	6.34	
	4	17	5.8512	.27464	5.27	6.43	
Cholesterol	2	4	228.9025	9.47250	198.76	259.05	0.544
	3	37	241.1611	4.36764	232.30	250.02	
	4	17	244.8294	6.19503	231.70	257.96	
TG	2	4	203.1450	7.07800	180.62	225.67	0.48
	3	37	216.1381	3.69584	208.64	223.63	
	4	17	217.4547	4.96552	206.93	227.98	
HDL	2	4	32.8600	.77682	30.39	35.33	0.357
	3	37	28.6611	.96027	26.71	30.61	
	4	17	28.5276	1.38710	25.59	31.47	
VLDL	2	4	40.6290	1.41560	36.12	45.13	0.48
	3	37	43.2276	.73917	41.73	44.73	
	4	17	43.4909	.99310	41.38	45.60	
LDL	2	4	155.4135	8.25743	129.13	181.70	0.503
	3	37	169.2724	4.44706	160.25	178.30	
	4	17	172.8108	6.52880	158.97	186.65	

P is significant* at value≤0.05

DISCUSSION

This study investigated the association between CEA, biochemical markers, and liver function parameters in patients with CRC, with and without hepatic metastases, compared with healthy controls. Significant intergroup differences were observed in most parameters, highlighting the potential diagnostic and prognostic value of these biomarkers.

In Table 1, patients with CRC exhibited a significantly lower BMI (26.98±0.42 kg/m²) than healthy controls (28.65±0.35 kg/m², P=0.003). This finding is consistent with the observations of Zhou and colleagues (19), who reported that weight loss is common in advanced cancer stages, often due to cancer-related cachexia or the side effects of chemotherapy.

CEA levels were markedly elevated in patients with CRC (3.74 ± 0.167 ng/mL) compared with controls (0.87±0.067 ng/mL, P=0.001). Similar findings were reported by Muñoz Montaño and others (20), who demonstrated that persistently high postoperative CEA levels are associated with poor prognosis and increased recurrence risk. Liver enzymes (ALT, AST, and ALP) were also significantly elevated among patients with CRC, suggesting hepatic involvement or early metastatic activity. This observation aligns with Cervantes and colleagues (21), who documented elevated liver enzyme levels in metastatic CRC due to hepatocyte injury. The CEA range in this study (0.65–5.20 ng/mL) further supports its diagnostic relevance.

Interestingly, patients with CRC also exhibited significantly higher albumin and total protein levels, potentially reflecting metabolic or inflammatory responses to tumor progression. Additionally, marked dyslipidemia was observed, with increased cholesterol, TG, LDL, and decreased HDL, consistent with the findings of Wu and others (22), who highlighted lipid metabolism disturbances as contributors to CRC pathogenesis.

Correlation analysis (Table 4) revealed moderate positive correlations between CEA and ALT (r=0.401, P=0.002), AST (r=0.295, P=0.025), ALP (r=0.364, P=0.005), cholesterol (r=0.341, P=0.009), and LDL (r=0.357, P=0.006), as well as a negative correlation with HDL (r = −0.277, P=0.035). These associations mirror the findings of Zeineddine and colleagues (23), who reported that biochemical perturbations in patients with CRC and liver metastases are closely linked to elevated CEA.

When comparing metastatic and non-metastatic CRC groups (Table 5), patients with hepatic metastases demonstrated significantly higher CEA, liver enzyme, and lipid profile values. These results are consistent with the European Society for Medical Oncology (ESMO) guidelines, which emphasize the importance of liver assessment in metastatic disease management (21). Similarly, Santagata and others (24) confirmed substantial metabolic disruptions in patients with CRC with liver metastases.

Receiver operating characteristic (ROC) analysis demonstrated excellent diagnostic performance for several markers, particularly CEA (AUC=1.000), ALT (AUC=0.992), and LDL (AUC=0.982) in distinguishing patients with CRC from healthy controls. In differentiating metastatic from non-metastatic CRC, LDL achieved the highest accuracy (AUC=0.948), followed by cholesterol (AUC=0.937) and CEA (AUC=0.847). These findings align with both ASCO and ESMO recommendations regarding the use of biochemical and tumor markers in CRC management (21).

Within the T3 subgroup (Table 7), metastatic patients exhibited significantly elevated CEA, ALT, ALP, albumin, total protein, cholesterol, triglycerides, VLDL, and LDL, with a concomitant reduction in HDL (P<0.01 for most parameters). These biochemical changes strongly suggest metabolic reprogramming associated with metastatic progression, as noted in recent literature (23,24).

Finally, analysis across T-classifications (Table 8) revealed significantly higher CEA levels in T3 patients compared with other stages (P=0.037). While other parameters did not differ significantly, the upward trend in lipid and liver enzyme levels in advanced stages supports previous findings that these biochemical alterations may serve as adjunct biomarkers for tumor progression and metastasis risk (20, 22).

In summary, this study reinforces the clinical relevance of monitoring CEA, liver enzymes, and lipid parameters in patients with CRC, particularly for early detection of hepatic metastases and prognostic evaluation. These biomarkers may complement existing diagnostic tools, contributing to more precise disease staging and tailored therapeutic strategies.

CONCLUSION

The present study demonstrates that CEA and selected liver function tests—particularly ALT, AST, ALP—alongside lipid profile variables, hold substantial diagnostic and prognostic value in CRC management. These biomarkers not only assist in differentiating disease stages but also provide important insights into the likelihood of hepatic metastasis. Their integration into clinical evaluation protocols may facilitate earlier detection, more accurate prognostication, and improved monitoring of therapeutic response.

Limitations of the Research

Several limitations should be acknowledged. First, the

relatively small and uneven sample sizes, particularly within the T2 subgroup, limit the statistical power and generalizability of the findings. Second, the cross-sectional design restricts the ability to establish causal relationships between the biochemical parameters and tumor progression. Third, the single-center setting may reduce the external validity of the results across diverse populations. Furthermore, potential confounding variables—such as age, BMI, dietary habits, medication use, lifestyle factors, and comorbid conditions—were not fully controlled, which could have influenced the biochemical profiles observed.

Strengths of the Research

Despite these limitations, the study offers several notable strengths. It provides a comprehensive biochemical characterization of patients with CRC across different stages, contributing to a deeper understanding of the metabolic and biochemical alterations associated with disease progression. The significant differences observed in CEA levels across patient groups offer valuable clinical insight for patient monitoring and individualized treatment planning. Moreover, the inclusion of multiple biochemical markers strengthens the robustness of the findings and supports their potential application in guiding early intervention strategies and tailored therapeutic approaches.

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ETHICS STATEMENT

This study was conducted in compliance with ethical research standards and received formal approval from the Ethics Committee of the College of Medicine at Al-Iraqia University. All procedures were carried out in accordance with the 2013 Declaration of Helsinki, ensuring the protection of participants' rights, safety, and well-being. Prior to their inclusion in the study, written informed consent was obtained from all participants, confirming their voluntary participation and understanding of the study's purpose and procedures.

CONFLICT OF INTEREST:

The authors have no conflicts of interest to declare related to this work.

REFRENCES:

1. World Health Organization. Colorectal cancer fact sheet. 2020. Available at: https://www.who.int/news-room/fact-sheets/detail/colorectal-cancer
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2021;71(3):209-249.
3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin*. 2018;68(1):7-30.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2018;68(6):394-424.
5. Knudsen AB, Rutter CM, Peterse EF, Lietz AP, Seguin CL, Meester RGS, et al. Colorectal cancer screening: an updated modeling study for the US Preventive Services Task Force. *JAMA*. 2021;325(19):1998-2011.
6. Lin JS, Piper MA, Perdue LA, Rutter CM, Webber EM, O'Connor E, et al. Screening for colorectal cancer: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2576-2594.
7. Atkin W, Dadswell E, Wooldrage K, Kralj-Hans I, von Wagner C, Edwards R, et al. Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomized trial. *Lancet*. 2013;381(9873):1194-1202.
8. Jasperson KW, Tuohy TM, Neklason DW, Burt RW. Hereditary and familial colon cancer. *Gastroenterology*. 2010;138(6):2044-2058.
9. Missiaglia E, Jacobs B, D'Ario G, Di Narzo AF, Soneson C, Budinska E, et al. Distal and proximal colon cancers differ in terms of molecular, pathological, and clinical features. *Ann Oncol*. 2014;25(10):1995-2001.
10. Locker GY, Hamilton S, Harris J, Jessup JM, Kemeny N, Macdonald JS, et al. ASCO 2006 update of recommendations for the use of tumor markers in gastrointestinal cancer. *J Clin Oncol*. 2006;24(33):5313-5327.
11. Duffy MJ, Lamerz R, Haglund C, Nicolini A, Kalousova M, Holubec L, et al. Tumor markers in colorectal cancer, gastric cancer and gastrointestinal stromal cancers: European Group on Tumour Markers 2014 guidelines update. *Int J Cancer*. 2014;134(11):2513-2522.
12. Goldstein MJ, Mitchell EP. Carcinoembryonic antigen in the staging and follow-up of patients with colorectal cancer. *Cancer Invest.* 2005;23(4):338-351.
13. Muñoz-Montaño WR , López-Basave HN , Castillo-Morales A , Castillo-Morales C , Sánchez-Trejo K , Catalán R ,et al. Persistent high levels of carcinoembryonic antigen after tumor resection in colon cancer. *BMC Cancer*. 2023;23:678.
14. Li Y, Wang J, Ma X, Tan L, Yan Y, Xie Q, et al. Prognostic value of pre- and postoperative carcinoembryonic antigen in colorectal cancer: a meta-analysis. *J Natl Cancer Inst*. 2024;djad030.
15. Cervantes A , Adam R , Roselló S , Arnold D , Normanno N , Taïeb J, et al. ESMO Clinical Practice Guideline for metastatic colorectal cancer: diagnosis and treatment. *Ann*

Oncol. 2023;34(1):11-20.
16. Zeineddine FA, Zeineddine MA, Yousef A, Gu Y , Chowdhury S , Dasari A , et al. Survival improvement in metastatic colorectal cancer over 20 years. *NPJ Precis Oncol*. 2023;7:16.
17. Santagata S, Rea G, Castaldo D, Napolitano M , Capiluongo A , D'Alterio C, et al. Hepatocellular carcinoma vs. colorectal cancer liver metastasis: tumor microenvironment comparison. *Hepatol Int*. 2024;18:568-581.
18. Wu Z, Chen K, Li J, Dai X. Global trends in colorectal cancer burden: a 30-year analysis. *J Public Health*. 2024;32:609-618.
19. Adam R, Bhangui P, Poston G, Mirza D, Nuzzo G, Barroso E, et al. Is perioperative chemotherapy useful for solitary, metachronous, colorectal liver metastases? *Ann Surg*. 2010;252(5):774-787.
20. Van Cutsem E, Cervantes A, Adam R, Sobrero A, Van Krieken JH, Aderka D, et al. ESMO consensus guidelines for the management of patients with metastatic colorectal cancer. *Ann Oncol*. 2016;27(8):1386-1422.
21. Arnold D, Lueza B, Douillard JY, Peeters M, Lenz HJ, Venook A, et al. Prognostic and predictive value of primary tumour side in patients with RAS wild-type metastatic colorectal cancer treated with chemotherapy and EGFR-directed antibodies in six randomized trials. *Ann Oncol*. 2017;28(8):1713-1729.
22. American college surgeon/ american joint committee on cancer/Cancer Staging Systems. 2025.
23. Abdul Kareem NG, Mahmood WT, Ahmed SH, Alkkaban M. Biochemical correlations among liver and kidney functions with anthropometric measurements in limited numbers of individuals. *J Biosci Appl Res*. 2021;21(Supp-01):2029.
24. Muneam SA, Muneam N, Muayed A. Biofactors' impact on diabetes prognosis. *J Biosci Appl Re*s. 2024;10(4):816-825.