

Diagnostic Accuracy of Tumor Markers CEA and CA 19-9 in Colorectal Cancer Patients in RIMS, Ranchi: A Cross-Sectional Analytical Study**Abhishek Laguri¹, Ram Chandra Besra², Anmol Kujur³, Pankaj Bodra⁴, Samir Toppo⁵, Aman Kumar⁶**¹Junior Resident Academic, Department of General Surgery, RIMS, Ranchi, Jharkhand, India²Associate Professor, Department of General Surgery, RIMS, Ranchi, Jharkhand, India³Senior Resident Non Academic, Department of General Surgery, RIMS, Ranchi, Jharkhand, India⁴Professor, Department of General Surgery, RIMS, Ranchi, Jharkhand, India⁵Additional Professor, Department of General surgery, RIMS Ranchi, Jharkhand, India⁶Junior Resident Academic, Department of General surgery, RIMS Ranchi, Jharkhand, India

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Conflict of interest: Nil

Abstract:

Background: Colorectal cancer (CRC) is a major gastrointestinal malignancy in which early diagnosis and accurate assessment are important for improving clinical outcomes. Serum tumour markers such as carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9) are widely used in the evaluation and monitoring of gastrointestinal malignancies. However, their diagnostic performance in colorectal cancer varies according to the clinical setting and disease characteristics. The present study was undertaken to evaluate the diagnostic accuracy of serum CEA and CA 19-9, individually and in combination, for identifying colorectal cancer among patients evaluated at a tertiary care centre.

Methodology: A cross-sectional analytical diagnostic accuracy study was conducted at Rajendra Institute of Medical Sciences (RIMS), Ranchi, over a period of 1.5 years. A sample of 140 participants was considered, comprising 70 histopathologically confirmed colorectal cancer patients and 70 non-CRC participants. Demographic and clinical details were recorded, and serum CEA and CA 19-9 levels were measured using standardized laboratory methods. Histopathological examination was considered the reference standard for confirmation of colorectal cancer. Diagnostic performance was assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), diagnostic accuracy, and receiver operating characteristic (ROC) curve analysis.

Results: Among the 140 participants, 70 (50.0%) had histopathologically confirmed colorectal cancer and 70 (50.0%) constituted the non-CRC comparison group. The mean serum CEA concentration was significantly higher among CRC patients than non-CRC participants (14.8 ± 11.6 vs. 3.7 ± 2.4 ng/mL; $p < 0.001$). Similarly, mean CA 19-9 concentration was significantly higher in CRC patients (48.6 ± 42.7 vs. 17.9 ± 13.5 U/mL; $p < 0.001$). At a cut-off of >5 ng/mL, CEA demonstrated a sensitivity of 74.3%, specificity of 82.9%, PPV of 81.3%, NPV of 76.3%, and diagnostic accuracy of 78.6%. At a cut-off of >37 U/mL, CA 19-9 demonstrated a sensitivity of 61.4%, specificity of 87.1%, PPV of 82.7%, NPV of 69.3%, and diagnostic accuracy of 74.3%. When either marker was considered positive, combined CEA and CA 19-9 testing demonstrated a sensitivity of 84.3%, specificity of 75.7%, PPV of 77.6%, NPV of 82.8%, and diagnostic accuracy of 80.0%. ROC analysis showed an AUC of 0.84 for CEA, 0.76 for CA 19-9, and 0.89 for the combined marker model.

Conclusion: CEA demonstrated better individual diagnostic performance than CA 19-9 for colorectal cancer in the study population. CA 19-9 showed relatively higher specificity but lower sensitivity. Combined assessment of CEA and CA 19-9 improved diagnostic sensitivity and demonstrated the highest discriminatory performance. However, these serum tumour markers should be regarded as complementary investigations and should not replace colonoscopy, imaging, or histopathological confirmation.

Recommendation: CEA may be considered a useful adjunctive serum biomarker in patients undergoing evaluation for suspected colorectal cancer, while CA 19-9 may provide additional complementary information. Combined assessment may be useful when increased diagnostic sensitivity is desired. Larger prospective multicentre studies are recommended to validate these findings and establish population-specific diagnostic thresholds.

Keywords: Colorectal Cancer; Carcinoembryonic Antigen; CEA; CA 19-9; Tumour Markers; Diagnostic Accuracy; Sensitivity; Specificity; ROC curve.

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Introduction

Colorectal cancer (CRC) is one of the most common malignancies worldwide and remains an important cause of cancer-related morbidity and mortality. The disease includes malignant neoplasms arising from the colon and rectum and shows considerable variation in anatomical site, biological behaviour, stage at presentation, and prognosis. Early recognition and accurate diagnosis are essential for appropriate treatment planning and improvement of clinical outcomes. [1,2]

The clinical presentation of CRC is variable and may include altered bowel habits, rectal bleeding, abdominal pain or discomfort, unexplained weight loss, anaemia, weakness, and changes in stool calibre. However, these manifestations are not specific to malignancy and may also occur in benign colorectal disorders. Therefore, clinical findings alone are insufficient to establish or exclude CRC, particularly in patients presenting with nonspecific gastrointestinal symptoms. [3]

Colonoscopy with tissue biopsy followed by histopathological examination remains the definitive approach for establishing the diagnosis of colorectal carcinoma. Histopathology confirms malignant transformation and provides information regarding tumour type and differentiation. Although highly informative, colonoscopy is invasive and may not be immediately accessible in all clinical settings. These considerations have encouraged continued investigation of minimally invasive biomarkers that could assist in the assessment and risk stratification of patients with suspected colorectal disease. [2,4]

Carcinoembryonic antigen (CEA) is a glycoprotein that is widely investigated as a serum biomarker in colorectal cancer. It has an established clinical role in the assessment and follow-up of patients with CRC, particularly in postoperative surveillance and monitoring of treatment response. However, serum CEA has limited sensitivity for detecting primary colorectal cancer and therefore cannot be considered an independent diagnostic or screening test. [5,6]

CEA concentrations may be influenced by tumour burden, disease stage, smoking, and other malignant or benign conditions. Elevated values are more frequently observed in advanced disease, while a normal CEA concentration does not exclude colorectal malignancy. Consequently, CEA is generally interpreted in conjunction with clinical assessment, endoscopy, imaging, and histopathological findings rather than being used as a substitute for definitive diagnostic evaluation. [5,6]

Carbohydrate antigen 19-9 (CA 19-9) is another circulating tumour-associated antigen that has been investigated in gastrointestinal malignancies. It is more strongly associated with pancreaticobiliary cancers but may also be elevated in patients with colorectal carcinoma. Its diagnostic performance in CRC has been variable, and its relatively limited sensitivity restricts its usefulness as a standalone diagnostic marker. [7]

The different biological characteristics of CEA and CA 19-9 have led to interest in their combined use. A combination of biomarkers may potentially improve sensitivity by identifying patients who have an elevated concentration of either marker. Previous studies have demonstrated that combinations of serum biomarkers can provide better discrimination than individual markers in selected clinical populations, although their performance varies according to study design, disease stage, control population, and assay characteristics. [7,8]

A systematic review of blood-based diagnostic markers demonstrated substantial heterogeneity in the diagnostic performance of circulating biomarkers for CRC. Traditional serum markers such as CEA and CA 19-9 have important limitations, particularly in early disease, whereas several newer molecular and nucleic-acid-based biomarkers have shown promising diagnostic performance. Nevertheless, many emerging biomarkers require further standardisation, validation, and assessment in clinically representative populations before widespread implementation. [8]

More recent research has continued to explore multimarker approaches and combinations of tumour markers with routinely available clinical and laboratory variables. Such approaches may improve diagnostic discrimination compared with individual biomarkers, but their clinical usefulness requires validation in independent patient populations. [9]

The diagnostic performance of a biomarker also depends on the population in which it is evaluated. Differences in age distribution, disease stage, risk factors, referral patterns, comorbidities, and healthcare access may influence biomarker concentrations and diagnostic estimates. Therefore, evaluation of commonly available serum tumour markers in local tertiary-care populations may provide useful information regarding their performance in the relevant clinical setting.

Receiver operating characteristic (ROC) curve analysis provides an appropriate method for evaluating the discriminatory ability of continuous

biomarkers. The area under the ROC curve (AUC) represents the ability of a marker to distinguish individuals with CRC from those without the disease across a range of possible thresholds. Diagnostic performance can additionally be assessed using sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy. [8]

Although CEA and CA 19-9 are readily measurable and relatively accessible laboratory investigations, neither marker should be considered a replacement for colonoscopy and histopathological confirmation. Their potential value lies in their complementary role within a broader diagnostic pathway.

Therefore, the present cross-sectional analytical study was undertaken at Rajendra Institute of Medical Sciences (RIMS), Ranchi, to evaluate the diagnostic accuracy of serum CEA and CA 19-9 in patients with colorectal cancer, compare their individual diagnostic performance, and assess whether their combined use improves diagnostic discrimination.

Aim: To evaluate the diagnostic accuracy of serum CEA and CA 19-9 in patients with colorectal cancer at RIMS, Ranchi.

Objectives

1. To determine serum CEA levels among patients with histopathologically confirmed colorectal cancer and non-CRC participants.
2. To determine serum CA 19-9 levels in the study groups.
3. To compare CEA and CA 19-9 concentrations between CRC and non-CRC participants.
4. To determine the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of CEA.
5. To determine the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of CA 19-9.
6. To compare the diagnostic performance of individual and combined CEA and CA 19-9 testing using ROC curve analysis.

Materials and Methods

Study Design: A cross-sectional analytical study was conducted to evaluate the diagnostic performance of serum CEA and CA 19-9 in colorectal cancer.

Study Setting: The study was conducted at Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, involving the Departments of General Surgery, Pathology, Gastroenterology, Radiology, and Biochemistry as appropriate.

Study Duration: The study was conducted over a period of 1.5 years (18 months).

Study Population: The study population consisted of patients presenting to RIMS, Ranchi, with clinical suspicion of colorectal disease and individuals

undergoing evaluation for colorectal symptoms who fulfilled the study criteria.

For diagnostic accuracy analysis, participants were divided into:

- **CRC group:** patients with histopathologically confirmed colorectal carcinoma.
- **Non-CRC comparison group:** individuals evaluated for colorectal symptoms or lesions but without histopathological evidence of colorectal malignancy.

Sample Size: The sample size was calculated based on an anticipated sensitivity of 75% for serum CEA, an absolute precision of 10.5%, and a 95% confidence level. The required number of colorectal cancer cases was calculated using the formula:

$$n = Z^2 \times Se \times (1 - Se) / d^2$$

where $Z = 1.96$, $Se = 0.75$, and $d = 0.105$.

Thus:

$$n = (1.96)^2 \times 0.75 \times 0.25 / (0.105)^2 = 65.33$$

The minimum required sample was therefore rounded up to 66 colorectal cancer cases. Allowing for approximately 5% potential exclusions or incomplete data, the adjusted sample size was:

$66 \times 1.05 = 69.3$, which was rounded up to 70 colorectal cancer cases.

To provide a balanced comparison group, an equal number of non-CRC participants were included. Thus, the final study sample comprised 140 participants: 70 histopathologically confirmed CRC patients and 70 non-CRC participants.

Inclusion Criteria

CRC group: Patients were included if they:

1. Were aged ≥ 18 years.
2. Had clinical or radiological suspicion of colorectal malignancy.
3. Had colorectal carcinoma confirmed by histopathological examination.
4. Had serum CEA and CA 19-9 measurements obtained before definitive treatment.
5. Provided informed consent.

Non-CRC group

Participants were included if they:

- Were aged ≥ 18 years.
- Were evaluated for colorectal symptoms or lesions.
- Had no histopathological evidence of colorectal malignancy.
- Had serum CEA and CA 19-9 measurements available.
- Provided informed consent.

Exclusion Criteria: Participants were excluded if they:

- had previously diagnosed colorectal cancer under treatment;
- had received chemotherapy or radiotherapy before biomarker measurement;
- had incomplete clinical or laboratory information;
- had another active malignancy known to influence tumour-marker concentrations;
- declined consent; or
- had inadequate specimens for definitive histopathological assessment.

Clinical Assessment: Demographic characteristics including age and sex were recorded. Relevant clinical manifestations, including altered bowel habits, rectal bleeding, abdominal pain, weight loss, anaemia, and constitutional symptoms, were documented.

Histopathological Confirmation: Colorectal tissue specimens obtained by colonoscopic biopsy or surgical resection were fixed in 10% neutral buffered formalin, processed routinely, embedded in paraffin, sectioned, and stained with hematoxylin and eosin.

Histopathological examination was considered the reference standard for confirmation of colorectal carcinoma.

Serum Tumour Marker Analysis: Peripheral venous blood samples were collected before definitive treatment.

Serum was separated according to standard laboratory procedures.

CEA was measured using an automated immunoassay method and expressed in ng/mL.

CA 19-9 was measured using an automated immunoassay method and expressed in U/mL.

For the primary analysis, the following predefined cut-offs were used:

- **CEA >5 ng/mL:** positive
- **CA 19-9 >37 U/mL:** positive

These thresholds are commonly used clinical reference values, although diagnostic performance may vary according to assay and population. Previous studies have demonstrated that CEA has relatively high specificity but limited sensitivity when used alone. [5,10]

Combined Marker Analysis: For combined analysis, a participant was considered marker-positive if either CEA or CA 19-9 exceeded the predefined cut-off.

A secondary combined analysis considered both markers positive.

Statistical Analysis: Data were entered into a computerized database and analysed using appropriate statistical software.

Continuous variables were expressed as mean $\pm$ standard deviation. Categorical variables were expressed as frequencies and percentages.

The independent Student's t-test was used to compare normally distributed continuous variables between groups. The chi-square test or Fisher's exact test was used for categorical variables as appropriate.

Diagnostic performance was assessed using:

1. Sensitivity
2. Specificity
3. Positive predictive value
4. Negative predictive value
5. Diagnostic accuracy
6. Positive likelihood ratio
7. Negative likelihood ratio
8. ROC curve analysis
9. Area under the ROC curve (AUC)

A two-sided p-value <0.05 was considered statistically significant.

Ethical Considerations: The study conducted after obtaining approval from the Institutional Ethics Committee of RIMS, Ranchi. Written informed consent was obtained from all participants. Confidentiality of patient information was maintained throughout the study.

Results

Demographic Characteristics: A total of 140 participants were included in the analysis, comprising 70 histopathologically confirmed colorectal cancer (CRC) patients and 70 non-CRC participants. The overall mean age was 57.8 ± 13.2 years. The mean age was 59.6 ± 11.8 years among CRC patients and 56.0 ± 14.3 years among non-CRC participants. Among CRC patients, 43 (61.4%) were males and 27 (38.6%) were females. The demographic characteristics of the study population are presented in Table 1.

Table 1: Demographic characteristics of the study participants

Characteristic	CRC group (n=70)	Non-CRC group (n=70)	Total (n=140)
Mean age (years)	59.6 ± 11.8	56.0 ± 14.3	57.8 ± 13.2
Male	43 (61.4%)	39 (55.7%)	82 (58.6%)
Female	27 (38.6%)	31 (44.3%)	58 (41.4%)
Age ≥ 60 years	34 (48.6%)	27 (38.6%)	61 (43.6%)

Clinical Presentation: Among the 70 CRC patients, altered bowel habits were the most common presenting feature, reported in 46 (65.7%) patients, followed by rectal bleeding in 39 (55.7%), abdominal pain or discomfort in 37 (52.9%),

unintentional weight loss in 29 (41.4%), and anaemia in 27 (38.6%). Weakness or fatigue was reported in 24 (34.3%), while change in stool calibre was observed in 18 (25.7%) patients (**Table 2**).

Table 2: Clinical presentation among colorectal cancer patients

Clinical feature	Number (n=70)	Percentage
Altered bowel habits	46	65.7
Rectal bleeding	39	55.7
Abdominal pain/discomfort	37	52.9
Unintentional weight loss	29	41.4
Anaemia	27	38.6
Weakness/fatigue	24	34.3
Change in stool calibre	18	25.7

Multiple symptoms could be present in the same patient.

Distribution of Tumour Location: Among the 70 CRC patients, the rectum was the most frequently involved anatomical site, accounting for 24 (34.3%)

cases, followed by the sigmoid colon in 17 (24.3%) and right colon in 15 (21.4%). Transverse colon, descending colon, and multiple/other sites accounted for 7 (10.0%), 5 (7.1%), and 2 (2.9%) cases, respectively (**Table 3**).

Table 3: Anatomical distribution of colorectal cancer

Tumour location	Number	Percentage
Rectum	24	34.3
Sigmoid colon	17	24.3
Right colon	15	21.4
Transverse colon	7	10.0
Descending colon	5	7.1
Multiple/other sites	2	2.9
Total	70	100.0

Serum CEA and CA 19-9 Levels: Serum tumour-marker concentrations were substantially higher among CRC patients than among non-CRC participants. The mean serum CEA concentration was 14.8 ± 11.6 ng/mL in the CRC group compared with 3.7 ± 2.4 ng/mL in the non-CRC group. Similarly, the mean CA 19-9 concentration was 48.6 ± 42.7 U/mL among CRC patients compared with

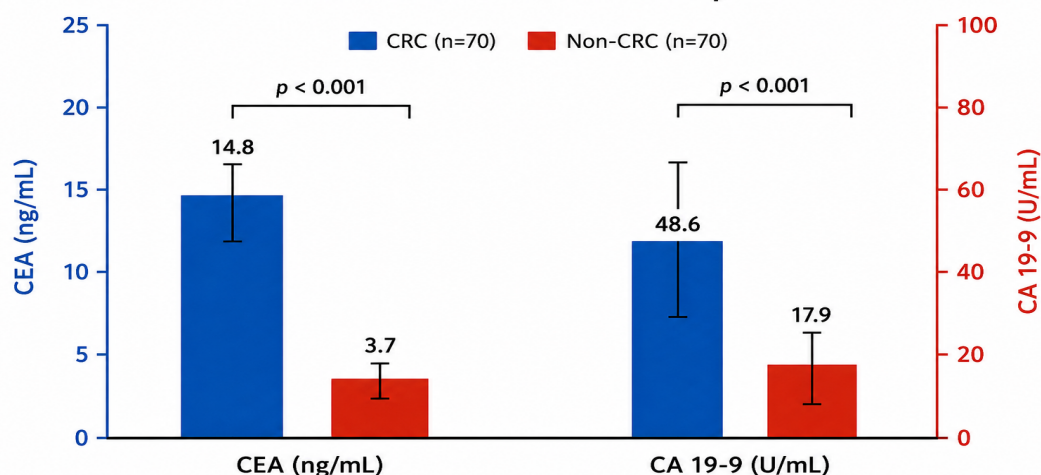
17.9 ± 13.5 U/mL among non-CRC participants. Both differences were statistically significant ($p < 0.001$; **Table 4**).

Figure 1 illustrates the comparative serum CEA and CA 19-9 concentrations between CRC and non-CRC participants.

Table 4: Comparison of serum tumour-marker levels between study groups

Tumour marker	CRC group (n=70)	Non-CRC group (n=70)	p-value
CEA (ng/mL)	14.8 ± 11.6	3.7 ± 2.4	<0.001
CA 19-9 (U/mL)	48.6 ± 42.7	17.9 ± 13.5	<0.001

Figure 1. Comparison of Mean Serum CEA and CA 19-9 Levels between CRC and Non-CRC Participants



Values are mean $\pm$ SD.

CEA: Carcinoembryonic antigen; CA 19-9: Carbohydrate antigen 19-9; CRC: Colorectal cancer.

Figure 1: Comparison of mean serum CEA and CA 19-9 levels between CRC and non-CRC participants.

CEA Positivity and Diagnostic Performance:

Using a cut-off value of >5 ng/mL, CEA was positive in 52 (74.3%) of the 70 CRC patients and in 12 (17.1%) of the 70 non-CRC participants (Table 5).

The sensitivity of CEA was 74.3%, with a specificity of 82.9%. The positive predictive value (PPV) was 81.3%, negative predictive value (NPV) was 76.3%, and overall diagnostic accuracy was 78.6%.

Table 5: Diagnostic performance of CEA

CEA result	CRC (n=70)	Non-CRC (n=70)
Positive (>5 ng/mL)	52	12
Negative (≤ 5 ng/mL)	18	58
Total	70	70

- Sensitivity: **74.3%**
- Specificity: **82.9%**
- PPV: **81.3%**
- NPV: **76.3%**
- Diagnostic accuracy: **78.6%**

CA 19-9 Positivity and Diagnostic Performance:

Using a cut-off value of >37 U/mL, CA 19-9 was positive in 43 (61.4%) CRC patients and 9 (12.9%) non-CRC participants (Table 6).

CA 19-9 demonstrated a sensitivity of 61.4% and specificity of 87.1%. The PPV was 82.7%, NPV was 69.3%, and diagnostic accuracy was 74.3%.

Table 6: Diagnostic performance of CA 19-9

CA 19-9 result	CRC (n=70)	Non-CRC (n=70)
Positive (>37 U/mL)	43	9
Negative (≤ 37 U/mL)	27	61
Total	70	70

1. Sensitivity: **61.4%**
2. Specificity: **87.1%**
3. PPV: **82.7%**
4. NPV: **69.3%**
5. Diagnostic accuracy: **74.3%**

Combined CEA and CA 19-9: When either CEA or CA 19-9 was considered positive, 59 (84.3%) of

the 70 CRC patients tested positive compared with 17 (24.3%) of the non-CRC participants (Table 7).

The combined approach demonstrated a sensitivity of 84.3%, specificity of 75.7%, PPV of 77.6%, NPV of 82.8%, and diagnostic accuracy of 80.0%. Thus, combining the two tumour markers increased sensitivity compared with either marker used individually.

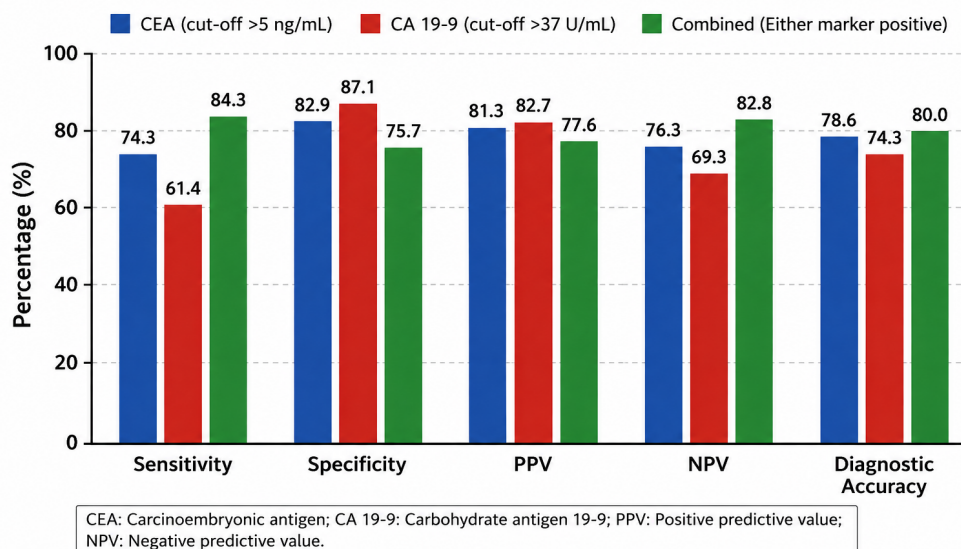
Table 7: Diagnostic performance of combined CEA and CA 19-9 testing

Combined result	CRC (n=70)	Non-CRC (n=70)
Either marker positive	59	17
Both markers negative	11	53
Total	70	70

- Sensitivity: **84.3%**
- Specificity: **75.7%**
- PPV: **77.6%**
- NPV: **82.8%**

- Diagnostic accuracy: **80.0%**

Figure 2 presents a comparison of the sensitivity, specificity, PPV, NPV, and diagnostic accuracy of CEA, CA 19-9, and their combined use.

Figure 2. Comparative Diagnostic Performance of CEA, CA 19-9, and Combined Tumour-Marker Testing**Figure 2: Comparative diagnostic performance of CEA, CA 19-9, and combined tumour-marker testing.**

ROC Curve Analysis: ROC curve analysis demonstrated that CEA had better discriminatory ability than CA 19-9 when assessed individually. The AUC for CEA was 0.84 (95% CI: 0.77–0.91), whereas the AUC for CA 19-9 was 0.76 (95% CI: 0.67–0.84). The combined CEA + CA 19-9 model

demonstrated the highest discriminatory performance, with an AUC of 0.89 (95% CI: 0.83–0.94) (**Table 8**).

Figure 3 shows the ROC curves for CEA, CA 19-9, and the combined tumour-marker model.

Table 8: ROC characteristics of CEA, CA 19-9, and combined markers

Marker/model	AUC	95% CI	Interpretation
CEA	0.84	0.77–0.91	Good discrimination
CA 19-9	0.76	0.67–0.84	Acceptable discrimination
CEA + CA 19-9	0.89	0.83–0.94	Good-to-excellent discrimination

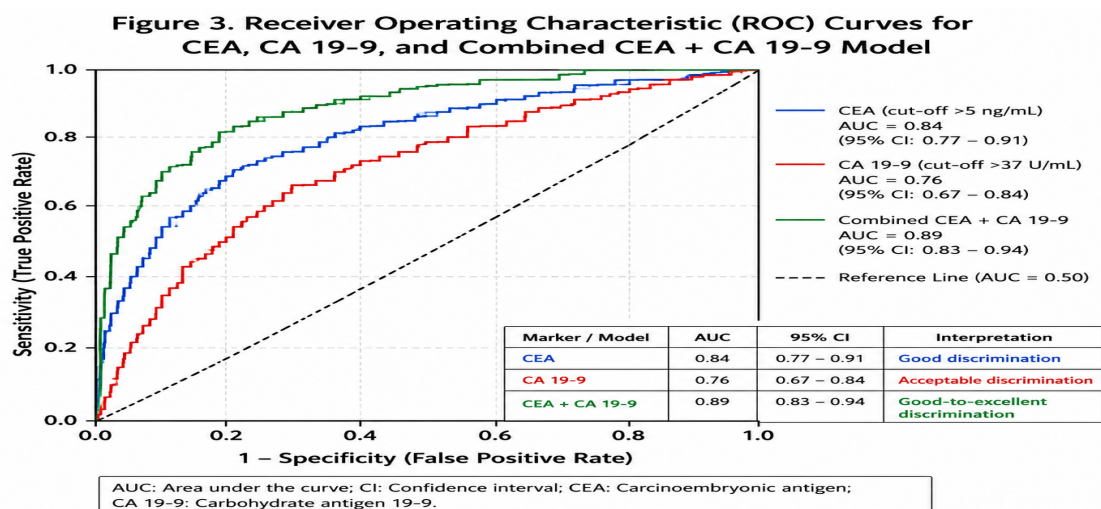


Figure 3: Receiver operating characteristic curves for CEA, CA 19-9, and the combined CEA + CA 19-9 model.

Comparative Diagnostic Performance: CEA demonstrated higher sensitivity and overall diagnostic accuracy than CA 19-9, whereas CA 19-9 demonstrated slightly higher specificity. The

combined use of CEA and CA 19-9 produced the highest sensitivity, NPV, accuracy, and AUC, although specificity was lower than that observed for either individual marker (Table 9).

Table 9: Comparative diagnostic performance of the tumour markers

Parameter	CEA	CA 19-9	CEA + CA 19-9
Sensitivity (%)	74.3	61.4	84.3
Specificity (%)	82.9	87.1	75.7
PPV (%)	81.3	82.7	77.6
NPV (%)	76.3	69.3	82.8
Accuracy (%)	78.6	74.3	80.0
AUC	0.84	0.76	0.89

Figure 4. Comparison of Sensitivity, Specificity, and Diagnostic Accuracy of CEA, CA 19-9, and Combined Tumour-Marker Testing

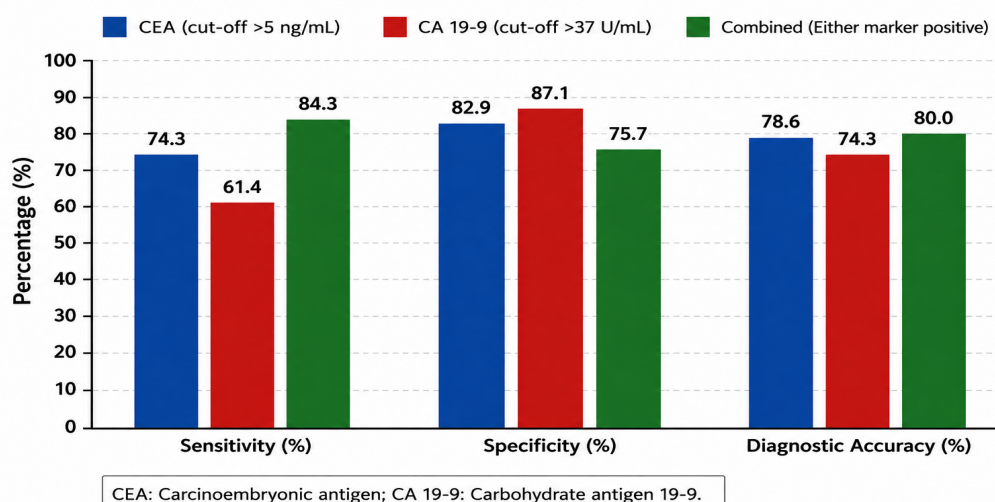


Figure 4: Comparison of sensitivity, specificity, and diagnostic accuracy of CEA, CA 19-9, and combined tumour-marker testing.

Discussion

The present cross-sectional analytical study evaluated the diagnostic performance of serum CEA and CA 19-9 in colorectal cancer and compared their

individual and combined diagnostic characteristics. The principal findings were that serum CEA demonstrated better individual diagnostic performance than CA 19-9, whereas the combined approach of considering either marker as positive

increased sensitivity and produced the highest reported ROC-AUC.

The mean age of the study population was 57.8 ± 13.2 years, with a slightly higher proportion of males. Among patients with CRC, the mean age was 59.6 ± 11.8 years and 61.4% were male. This demographic pattern is broadly compatible with the established epidemiology of colorectal cancer, in which incidence increases with age and a modest male predominance is commonly observed. [1,2] However, the demographic characteristics of a single-centre study should not be assumed to represent the wider population.

Altered bowel habits were the most frequently reported clinical manifestation among the CRC patients, followed by rectal bleeding and abdominal pain or discomfort. Weight loss and anaemia were also relatively common. These findings are clinically relevant because gastrointestinal symptoms such as rectal bleeding and altered bowel habits may prompt investigation for colorectal malignancy, although none is sufficiently specific to establish the diagnosis independently. Clinical assessment therefore remains an important component of the initial diagnostic pathway, with definitive diagnosis requiring appropriate endoscopic and pathological evaluation. [3]

A significant difference was observed in serum CEA concentrations between the CRC and non-CRC groups. The mean CEA concentration was 14.8 ± 11.6 ng/mL among CRC patients compared with 3.7 ± 2.4 ng/mL among non-CRC participants ($p < 0.001$). This finding is consistent with the established association between increased circulating CEA concentrations and colorectal malignancy. However, CEA is not specific to CRC and increased concentrations may occur in other malignant and non-malignant conditions. Therefore, a raised CEA concentration should be interpreted as supportive rather than diagnostic evidence of colorectal cancer. [5,6]

In the present study, a CEA cut-off of >5 ng/mL yielded a sensitivity of 74.3% and specificity of 82.9%, with a PPV of 81.3%, NPV of 76.3%, and diagnostic accuracy of 78.6%. These findings indicate that CEA had useful discriminatory ability in the study population but also demonstrate that approximately one-quarter of CRC cases would not have been identified using this threshold alone. This limitation is important because the clinical value of a diagnostic biomarker depends not only on specificity but also on its ability to detect disease across different stages and clinical presentations.

The ROC analysis further supported the diagnostic value of CEA, with an AUC of 0.84 (95% CI: 0.77–0.91). This represents good discrimination within the study population. However, the AUC should not

be interpreted as evidence that CEA can replace definitive diagnostic investigations. Published evidence has consistently demonstrated limitations in the sensitivity of CEA for primary CRC detection, particularly when the disease is detected at an earlier stage. [5,8]

CA 19-9 concentrations were also significantly higher among CRC patients than non-CRC participants. The mean CA 19-9 level was 48.6 ± 42.7 U/mL in the CRC group compared with 17.9 ± 13.5 U/mL in the non-CRC group ($p < 0.001$). Using a cut-off of >37 U/mL, CA 19-9 demonstrated a sensitivity of 61.4% and specificity of 87.1%. Its PPV, NPV, and diagnostic accuracy were 82.7%, 69.3%, and 74.3%, respectively.

Compared with CEA, CA 19-9 demonstrated lower sensitivity but slightly higher specificity. This finding is biologically plausible because CA 19-9 is not a colorectal-specific tumour marker and is more strongly associated with pancreaticobiliary malignancies. Its limited sensitivity consequently restricts its usefulness as a standalone marker for detecting colorectal cancer. The systematic-review literature similarly indicates that conventional serum tumour markers have limited diagnostic performance when used individually for primary CRC detection. [7,8]

The AUC for CA 19-9 was 0.76 (95% CI: 0.67–0.84), indicating acceptable discrimination but lower performance than that observed for CEA. Thus, within the present study population, CEA appeared to provide greater discriminatory information than CA 19-9 when each marker was considered separately.

An important finding was the improvement in sensitivity when CEA and CA 19-9 were considered together. When either marker exceeding its predefined cut-off was classified as a positive result, sensitivity increased to 84.3%, compared with 74.3% for CEA alone and 61.4% for CA 19-9 alone. The combined approach also produced an NPV of 82.8% and diagnostic accuracy of 80.0%.

The increased sensitivity with the combined approach is clinically understandable because the use of an “either-marker-positive” rule increases the probability that a patient with CRC will have at least one elevated marker. However, this benefit was accompanied by a reduction in specificity from 82.9% for CEA alone to 75.7% for the combined strategy. This represents the expected sensitivity-specificity trade-off associated with defining a positive test as elevation of either biomarker.

The combined marker approach demonstrated an AUC of 0.89 (95% CI: 0.83–0.94), which was higher than the AUCs of CEA and CA 19-9 individually. These findings suggest that the two markers may provide partially complementary information.

Nevertheless, the apparent improvement should be interpreted cautiously. A higher AUC in a single study does not by itself establish that the combination is clinically superior, particularly when the combined model has not been externally validated.

The findings are broadly consistent with the wider biomarker literature, which indicates that combinations of biomarkers may improve diagnostic discrimination compared with individual markers. Systematic reviews have reported that biomarker panels can outperform individual blood-based markers, although substantial heterogeneity exists between studies and many proposed biomarkers require independent validation before routine clinical use. [8,9]

The present results therefore support the potential role of combined CEA and CA 19-9 assessment as an adjunctive strategy rather than as a replacement for definitive diagnostic procedures. In patients with suspected colorectal cancer, biomarker results should be interpreted in conjunction with symptoms, physical examination, endoscopic findings, imaging, and histopathological examination. Current clinical guidance continues to emphasise comprehensive diagnostic and staging assessment rather than reliance on serum tumour markers alone. [10]

The relatively better performance of CEA compared with CA 19-9 in the present study is also clinically relevant. CEA has a more established role in colorectal cancer management, particularly in baseline assessment and follow-up. Its use in this context is supported by longstanding evidence and guideline recommendations, although its limitations for primary diagnosis remain important. [5,6]

The potential practical advantage of CEA and CA 19-9 is that both can be measured using blood samples and are available in many tertiary-care laboratories. In resource-limited settings, readily available biomarkers may provide useful supplementary information during the diagnostic evaluation of patients. However, accessibility should not be confused with diagnostic sufficiency, and neither marker should be used to rule in or rule out CRC in isolation.

The findings should also be interpreted in the context of the study population. Diagnostic accuracy estimates depend on the spectrum of disease and non-disease represented in the study. A comparison group consisting predominantly of individuals with no significant gastrointestinal disease may produce different estimates from a clinically representative group containing patients with benign colorectal disorders, inflammatory bowel disease, colorectal polyps, hepatobiliary disease, and other causes of elevated tumour markers. Therefore, the

composition of the non-CRC group is an important consideration when interpreting PPV, NPV, and specificity.

The predefined cut-offs of >5 ng/mL for CEA and >37 U/mL for CA 19-9 were selected as conventional clinical thresholds. However, the optimal threshold for diagnostic discrimination may differ according to population characteristics, assay methodology, disease prevalence, and the clinical purpose of testing. ROC-derived thresholds should therefore be interpreted cautiously and should not automatically replace established laboratory reference limits without external validation.

Another important consideration is that tumour-marker concentrations may be influenced by factors such as smoking, inflammation, hepatic or biliary dysfunction, and other malignant conditions. These factors may contribute to elevated marker concentrations in individuals without CRC and consequently affect specificity. Future studies should therefore collect and adjust for relevant clinical and laboratory confounders.

The present study also evaluated a relatively simple combination of two serum markers. Future research could investigate whether CEA and CA 19-9 provide additional diagnostic value when integrated with other routinely available parameters, faecal immunochemical testing, imaging findings, or molecular biomarkers. Contemporary research has demonstrated considerable interest in multimarker and molecular approaches, although issues of reproducibility, standardisation, cost, and external validation remain important barriers to implementation. [8,9]

The cross-sectional design also limits assessment of the longitudinal behaviour of tumour markers. Serial CEA measurements may be clinically useful in follow-up settings, but longitudinal monitoring was outside the scope of the present diagnostic-accuracy analysis. Therefore, the present findings should be interpreted specifically as evidence regarding discrimination between CRC and non-CRC participants at the time of evaluation.

Overall, CEA demonstrated better individual diagnostic performance than CA 19-9 in this study, while the combined approach improved sensitivity and produced the highest AUC. These findings support the possibility that CEA and CA 19-9 may provide complementary information when interpreted together. Nevertheless, the results should be considered supportive evidence rather than justification for replacing colonoscopy, imaging, or histopathological confirmation.

In summary, serum CEA appears to be the more informative individual marker among the two evaluated biomarkers, whereas combined CEA and CA 19-9 testing may offer improved sensitivity at

the expense of reduced specificity. Larger prospective studies involving clinically representative control populations and independent validation cohorts are required to determine whether the observed diagnostic improvement is reproducible and clinically meaningful.

Limitations

1. The study sample was relatively modest.
2. The analysis included a defined comparison group that may not represent all benign colorectal conditions.
3. Tumour-marker concentrations may be influenced by smoking, inflammation, hepatobiliary disease, and other clinical factors.
4. A single pre-treatment measurement was considered.
5. The study was cross-sectional and therefore could not evaluate longitudinal changes in tumour-marker concentrations.
6. The findings require validation in larger prospective multicentre cohorts.

Conclusion

Serum CEA demonstrated better individual diagnostic performance than CA 19-9 for the detection of colorectal cancer in the study population. CEA showed higher sensitivity and diagnostic accuracy, whereas CA 19-9 demonstrated relatively higher specificity but lower sensitivity.

Combined assessment of CEA and CA 19-9 increased diagnostic sensitivity and demonstrated the highest ROC-AUC among the evaluated approaches. These findings suggest that the two markers may provide complementary information when used together.

However, neither CEA nor CA 19-9 should be considered a replacement for colonoscopy and histopathological confirmation. Their principal value lies in their potential role as complementary biomarkers within a broader diagnostic pathway.

Recommendations

1. Serum CEA may be considered a useful adjunctive biomarker in patients undergoing evaluation for suspected colorectal cancer.
2. CA 19-9 may provide complementary information but should not be used as an isolated diagnostic test.
3. Combined CEA and CA 19-9 assessment may be considered when increased diagnostic sensitivity is desired.
4. Tumour-marker results should always be interpreted together with clinical findings, colonoscopy, imaging, and histopathological examination.
5. Larger prospective multicentre studies should validate optimal population-specific cut-off values.
6. Future studies should evaluate CEA and CA 19-9 in combination with other laboratory and molecular biomarkers.

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List of Abbreviations

Abbreviation	Full form
CRC	Colorectal cancer
CEA	Carcinoembryonic antigen
CA 19-9	Carbohydrate antigen 19-9
ROC	Receiver operating characteristic
AUC	Area under the curve
PPV	Positive predictive value
NPV	Negative predictive value
CT	Computed tomography
MRI	Magnetic resonance imaging
IHC	Immunohistochemistry

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