

# Clinical significance and role of CEA level in diagnosis of colorectal cancer

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**ABSTRACT**— Colorectal cancer is a widespread illness that begins with unusual growth of the inner colon or rectum and progresses to the entire thickness of the epithelial lining before spreading to nearby lymph nodes and tissues and eventually distant metastases. It's one of the most challenging cancers to treat, with severe symptoms that worsen, become more obvious and specific as the disease progresses, with a high mortality rate and minimal survival if detected late or untreated. The serum carcinoembryonic antigen isn't created in large amounts after birth, but it's raised in colorectal cancer. The participants of the study were 180 cases, comprising patients and healthy people, separated into two categories: The first had 90 patients, 47 men, and 43 women. The second group had 90 healthy individuals including 60 men and 30 women. All individuals were subjected to blood sampling for measuring their serum CEA using the Sandwich principle (Cobas E411). The mean serum CEA concentration was significantly higher ( $P = 0.013$ ) in CRC than healthy controls. Determine the effectiveness and validity of blood CEA levels in diagnosing colorectal cancer.

**KEYWORDS:** Carcinoembryonic antigen, Colorectal cancer

## 1. INTRODUCTION

Colorectal cancer (CRC) is the most frequent kind of cancer. This is the third most frequent cancer in males and the second most prevalent cancer in female in the world. Males have a much greater incidence than females [1]. WHO predicts that by 2030, there will be 27 million new cases of colorectal cancer. CRC is a tumor of malignant epithelial origin in the large intestine. Over 90% of CRCs are adenocarcinomas, which develop from glandular structures in epithelial tissue; this might trigger alterations in the intestinal microenvironment that contribute to colorectal carcinogenesis [2], [3]. Most individuals with CRC die from organ metastasis. The prognosis varies widely across individuals and is highly dependent on metastatic patterns [4].

CRC is caused by a complicated interaction of inherited susceptibility and environmental factors [5]. A blood-based tumor marker such as glycoprotein carcinoembryonic antigen (CEA), this may have an impact on the prognosis, therapy, and follow-up of patients with CRC [6]. In gastrointestinal cancer, determining particular tumor marker levels in the blood is critical for screening, diagnosis, treatment management, and monitoring advanced illness [7], [8]. CEA has prognostic significance, with greater CEA levels related to a worse preoperative fate [9].

CEA is also useful in surgical follow-up and the early diagnosis of recurrent disease [10]. Because of its limited sensitivity in early cancer stages, CEA cannot be utilized for screening. It may also be increased in benign conditions [11]. Preoperative CEA elevation predicted increasing overall survival in CRC, with a 62 % mortality risk compared to normal CEA levels [12]. CEA levels should fall exponentially after the

therapeutic operation and hence the removal of the cause of CEA. CEA levels that did not return to normal after the operation were indicative of chronic or recurring illness [13]. The study's goal is to determine the clinical importance of carcinoembryonic antigen levels in the diagnosis of colorectal cancer patients.

## 2. Materials and Methods

The participants in this study were 180 cases, comprising patients and healthy people, separated into two groups: The first group included 90 patients comprising 47 (52.22%) males, and 43 (47.77%) female. The second group had 90 healthy individuals, 60 of whom were men (66.66%) and 30 of whom were women (33.33%). A venous blood sample was taken from each of the subjects, where It was permitted to clot before being centrifuged for 10 minutes at 3000 revolutions per minute. All tube samples were kept at (-20°C) deep-freezing until they are analyzed. Serum CEA levels were measured by Cobas E411 (Roche Diagnostics, Germany).

The data of the study were analyzed using IBM Statistical Package for Social Sciences (SPSS) Statistics software, version 27. All numerical variables were expressed as mean  $\pm$  Standard deviation, and all statistical comparisons were performed using the independent t-test while Chi- square test (X<sup>2</sup>) used to compare frequency with  $P \leq 0.05$  was considered statistically significant.

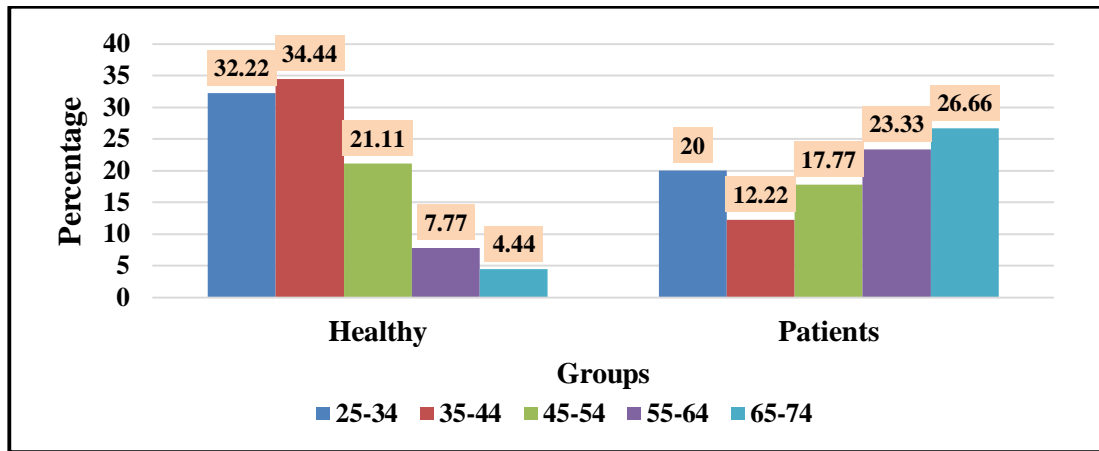
## 3. Results

Table (1) shows the statistical distribution (frequency and percentage) of study groups (patients and control) by their sex and age. The participants in this study were 180 cases comprising patients and healthy people, separated into two groups: The first group included 90 patients 47 (52.22%) were male patients, and 43 (47.77%) were female patients. The second group comprised 90 healthy individuals, 60 (66.66%) were men and 30 (33.33%) were women. The descriptive statistics and differences of study groups by sex were significant differences between patients and control groups ( $P$ -value = 0.048). The same table revealed that the highest percentage of the age subgroup is (65-74 years), which that constituted 24 (26.66 %) patients.

**Table 1.** Demographic Characteristics of study groups (patients and control)

Character	Category	Groups		Calculated P value
		Healthy No.=90	Patients No.=90	
<b>Gender</b> No. (%)	Male	60(66.66)	47(52.22)	0.048
	Female	30(33.33)	43(47.77)	
<b>Age</b> (Year) No. (%)	25-34	29(32.22)	18(20)	<0.001
	35-44	31(34.44)	11(12.22)	
	45-54	19(21.11)	16(17.77)	
	55-64	7(7.77)	21(23.33)	
	65-74	4(4.44)	24(26.66)	

High Significant at  $P \leq 0.01$ , Significant difference at  $P < 0.05$



**Figure 1:** Bar chart for statistical distribution (percentage) of age subgroups for CRC patients and control

Age is the most important factor in determining the risk of CRC development. The patient's age ranged from 25-74 years. The distribution of patients among age groups was as follows: (25-34 years) included 18 (20%) patients, (35-44 years) included 11 (12.22%) patients, (45-54 years) included 16 (17.77%) patients, (55-64 years) included 21 (23.33%) patients, and (65-74 years) included 24 (26.66%) patients. Table (1) demonstrate that a highly significant ( $p < 0.001$ ) difference in the age of the patients' group as compared to the control group, as illustrates in Figure (1).

**Table 2.** Serum biomarker CEA between CRC Patient and control group

Parameters	Groups		P value
	Healthy	Patients	
	Mean±SD	Mean±SD	
CEA	1.66±0.04	28.44±10.51	0.013

Table 2 exhibited the differences in the measurement of CEA levels between CRC patients and control group. The mean CEA concentration in CRC patient group (28.44±10.51) was significantly increase ( $P=0.013$ ) than the healthy control group (1.66±0.04).

**Table 3.** Serum biomarker CEA levels according to the gender among CRC patients

Parameters	Category		P value
	Male	Female	
	Mean±SD	Mean±SD	
CEA	34.26±17.15	22.08±11.65	0.566

Non-significant at P value  $> 0.05$

Table 3 shows that the mean serum concentration in male CRC patients (34.26±17.15) was not significantly ( $p\text{-value}=0.566$ ) different than that in female CRC patients (22.08±11.65).

**Table 4.** levels of serum biomarker CEA according to the age among CRC patients.

Parameters	Category (Year)					P value
	25-34	35-44	45-54	55-64	65-74	
	Mean±SD	Mean±SD	Mean±SD	Mean±SD	Mean±SD	
<b>CEA</b>	11.27±4.39	9.34±2.72	8.09±2.95	46.01±26.11	48.27±31.78	<b>0.532</b>

Non-significant at P value >0.05

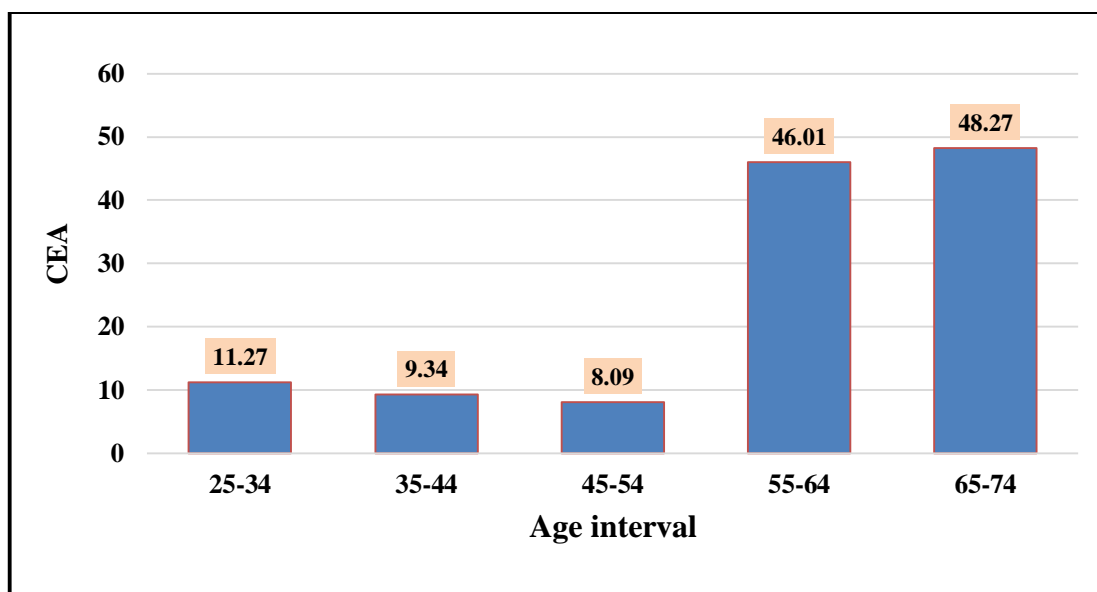


Figure 2. Bar chart for statistical distribution (Mean) of CEA according the age among CRC patients

Table 4 shows that there were non-significant differences in the serum biomarker CEA levels according to the age among CRC patients (P-value < 0.05). Figure 2 shows statistical distribution (Mean) of CEA according to the age among CRC patients.

#### 4. Discussion

The descriptive statistics and differences in study groups by sex were significant differences between patients and control groups (P-value = 0.048). CRCs are less common in women, and colonoscopy studies show that females have fewer colorectal adenomas [14], [15]. The occurrence of bleeding in colon lesions differs across sex (16); few colorectal adenomas and carcinomas were correlated with low amounts of hemoglobin in feces. It's still a well-known fact that women have very little hemoglobin in their feces compared to men [17], [18].

These findings are consistent with [24] who found no significant (p = 0.8) link between CEA levels and gender. On the other hand, the results disagree with [19] who reported that the male patients exceeded female patients by a statistically significant (p≤0.01) ratio.

According to the present findings, the age category with the greatest proportion is 65–74 years. The current investigation supported the findings of [20] who found a link between CRC risk and advanced age. On the other hand, the results disagreed with [21] who claimed that the age-specific incidence of CRC rose

dramatically among those aged 35 to 64 years compared with those aged  $\geq 65$  years. Similarly, [22] have observed that most CRC patients were males, aged 40–60 years, with 30% being under 40 years old. Patients with CRC under the age of 50 exhibited higher survival rates than their older counterparts at all stages of diagnosis. On the other hand, individuals  $< 65$  years had the lowest survival rates due to age-related disadvantages such as comorbidity [23].

The present findings coincide with [24] who found no significant change in CEA levels throughout old age ( $p = 0.6$ ). In large Korean research, serum CEA was revealed to be a major risk factor for the development of advanced colorectal neoplasms in both young (50 years) and old ( $> 50$  years) patients [25]. A case series study of 956 colorectal cancer patients between the ages of 25 and 50 showed that they were significantly ( $p \leq 0.01$ ) more likely to suffer than those between the ages of  $> 50$  years or  $< 25$  years [26].

The results showed a significantly increased ( $P=0.013$ ) in CRC people in comparison to healthy people, with a sensitivity of (60%) and specificity of (83%). The results of this study agreed with previous studies [27], [28] that showed CEA sensitivity ranging from 56.4-64.9 percent. However, [29] concluded that the combined assessment of four tumor markers, TK1, CEA, CA 19-9, and CA 72-4, performed even better, which may be useful for early colorectal cancer detection. On the other hand, [26]. It has been found that serum from people with CRC had higher levels of CEA than serum from healthy people, as it demonstrated (83.6%) for patients with equal or more than 5 ng/mL, and may be utilized as a tumor marker for the diagnosis of colorectal cancer.

CEA is an oncofetal glycoprotein that is generally produced by mucosal cells. It is overexpressed in several cancers. It is most typically linked with prognostic relevance in patients with colorectal cancer, particularly with hepatic metastases [4]. However, other malignancies may also raise it, such as the breast, liver, stomach, and pancreas. Changes in CEA depend on the stage, grade, location, and dissemination of colorectal cancer to the liver [27]. The clinical importance of this finding is that CEA might be used as a prognostic indicator for advanced or metastatic CRC and does not seem to be a good marker for early stage disease [24]. These findings are corroborated by [25] who observed that higher CEA levels were related to advanced CRC stages and poor clinical outcomes.

## 5. Conclusions

The available data demonstrates that CEA has a role in the prognosis, management planning, and monitoring of patients with CRC. Considered as some of biomarkers such as CEA predicts a CRC cancer aggressive as an aid tool for to predict the stages of the development of the disease, sustain life, and live longer with the disease through.

## 6. REFERENCES

- [1] Li S, Chen Y, Xie L, et al. Sex hormones and genetic variants in hormone metabolic pathways associated with the risk of colorectal cancer. *Environ Int.* 2020;137(February):105543. doi:10.1016/j.envint.2020.105543
- [2] Cruz BCS, Sarandy MM, Messias AC, Gonçalves R V., Ferreira CLLF, Peluzio MCG. Preclinical and clinical relevance of probiotics and synbiotics in colorectal carcinogenesis: A systematic review. *Nutr Rev.* 2020;78(8):667-687. doi:10.1093/nutrit/nuz087
- [3] Ryan ÉJ. Improving the histopathological diagnosis and management of colorectal cancer with mismatch repair deficiency. 2019;1.

- [4] Michl, M., F. Taverna, J. Kumbrink, T. S. Schiergens, V. Heinemann, J. Engel, T. Kirchner, and Jens Neumann. 2021. "Biomarker Alterations Associated with Distinct Patterns of Metastatic Spread in Colorectal Cancer." *Virchows Archiv* 478(4):695–705. doi: 10.1007/s00428-020-02983-6.
- [5] Mohammed RK, Fezea SM. Determination of Some Trace Element Levels in Iraqi Male patients with Colorectal Cancer. *Ibn AL- Haitham J Pure Appl Sci.* 2017;29(2):254-261. <http://jihcoed.com/ihj/index.php/j/article/view/114>
- [6] Singh S, Kumar R, Kumar U, Kumari R. Clinical Significance and Role of TK1, CEA, CA 19-9 and CA 72-4 levels in Diagnosis of Colorectal Cancers. *Asian Pacific J Cancer Prev.* 2020;21(11):3133-3136. doi:10.31557/APJCP.2020.21.11.3133
- [7] Zhang S, Lin M, Zhang H. Diagnostic value of carcinoembryonic antigen and carcinoma antigen 19-9 for colorectal carcinoma. 2015;8(8):9404-9409.
- [8] Dolscheid-Pommerich RC, Manekeller S, Walgenbach-Brünagel G, et al. Clinical performance of CEA, CA19-9, CA15-3, CA125 and AFP in gastrointestinal cancer using LOCITM-based assays. *Anticancer Res.* 2017;37(1):353-359. doi:10.21873/anticancer.11329
- [9] Thirunavukarasu, Pragatheeshwar, Shyamsunder Sukumar, Magesh Sathaiah, Meredith Mahan, Kothai Divya Pragatheeshwar, James F. Pingpank, Herbert Zeh Iii, Christopher J. Bartels, Kenneth K. W. Lee, and David L. Bartlett. 2011. "C-Stage in Colon Cancer : Implications of Carcinoembryonic Antigen Biomarker in Staging , Prognosis , and Management." 689–97. doi: 10.1093/jnci/djr078.
- [10] Sturgeon CM, Duffy MJ, Stenman U, et al. Biochemistry Laboratory Medicine Practice Guidelines for Use of Tumor Markers in Testicular , Prostate , Colorectal , Breast , and Ovarian Cancers METHODS : RESULTS : 2008;79. doi:10.1373/clinchem. 2008.105601
- [11] Thomas DS, Fourkala E, Apostolidou S, et al. Evaluation of serum CEA , CYFRA21-1 and CA125 for the early detection of colorectal cancer using longitudinal preclinical samples. *Br J Cancer.* 2015;:268-274. doi:10.1038/bjc.2015.202
- [12] Becerra AZ, Probst CP, Tejani MA, et al. Evaluating the Prognostic Role of Elevated Preoperative Carcinoembryonic Antigen Levels in Colon Cancer Patients : Results from the National Cancer Database. Published online 2016. doi:10.1245/s10434-015-5014-1
- [13] Hall C, Clarke L, Pal A, et al. A review of the role of carcinoembryonic antigen in clinical practice. *Ann Coloproctol.* 2019;35(6):294-305. doi:10.3393/ac.2019.11.13
- [14] Secretan BL, Ph D, Vilahur N, Ph D, Bianchini F, Ph D. *Spe ci a l R e p o r t The IARC Perspective on Colorectal Cancer Screening.* Published online 2018.
- [15] White A, Ironmonger L, Steele RJC, Ormiston-smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence , screening uptake , routes to diagnosis , cancer stage and survival in the UK. Published online 2018:1-11.
- [16] Selby, Kevin, Emma H. Levine, Cecilia Doan, Anton Gies, Hermann Brenner, Charles Quesenberry,

Jeffrey K. Lee, and Douglas A. Corley. 2019. "Effect of Sex, Age, and Positivity Threshold on Fecal Immunochemical Test Accuracy: A Systematic Review and Meta-Analysis." *Gastroenterology* (October):1–12. doi: 10.1053/j.gastro.2019.08.023.

[17] Grobbee J, Wieten E, Hansen BE, et al. Fecal immunochemical test-based colorectal cancer screening : The gender dilemma. Published online 2017. doi:10.1177/2050640616659998

[18] Hultcrantz R. Aspects of colorectal cancer screening , methods , age and gender. Published online 2020. doi:10.1111/joim.13171

[19] Al-Saigh T, Al-Bayati S, Abdulmawjood S, Ahmed F. Descriptive Study of Colorectal Cancer in Iraq, 1999-2016. *Ann Coll Med Mosul*. 2019;41(1):81-85. doi:10.33899/mmed.2019.161330

[20] Wong MCS, Ding H, Wang J, Chan PSF, Huang J. Prevalence and risk factors of colorectal cancer in Asia. 2019;17(3):317-329.

[21] Gondran G., A. L. Fauchais M. Lambert K. Ly D. Launay V. Queyrel H. Benazahari E. Liozon V. Loustaud-Ratti E. Hachulla M. O. Jauberteau P. Y. Hatron and E. Vidal. 2018. "Primary Sjögren's Syndrome in Men." *Scandinavian Journal of Rheumatology* 37(4):300–305. doi: 10.1080/03009740802001426.

[22] Singh S, Kumar R, Kumar U, Kumari R. Clinical Significance and Role of TK1, CEA, CA 19-9 and CA 72-4 levels in Diagnosis of Colorectal Cancers. *Asian Pacific J Cancer Prev*. 2020;21(11):3133-3136. doi:10.31557/APJCP.2020.21.11.3133

[23] Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin*. 2020;70(3):145-164. doi:10.3322/caac.21601

[24] Naicker YD, Moolla Z, Madiba T. The role of carcinoembryonic antigen as an assessment tool for predicting disease severity among patients with colorectal cancer in resource-poor setting of Kwazulu-Natal, South Africa. *The Pan African Medical Journal*. 2021;39.

[25] Kim JY, Jung YS, Park JH, Kim HJ, Cho YK, Sohn CI, Jeon WK, Kim BI, Choi KY, Park DI. Different risk factors for advanced colorectal neoplasm in young adults. *World journal of gastroenterology*. 2016 Apr 7;22(13):3611.

[26] Al-Saigh TH, Al-Bayati SA, Abdulmawjood SA, Ahmed FA. Descriptive Study of Colorectal Cancer in Iraq, 1999-2016. *Annals of the College of Medicine, Mosul*. 2019 Jun 30;41(1):81-5.

[27] Singh S, Kumar R, Kumar U, Kumari R. Clinical Significance and Role of TK1, CEA, CA 19-9 and CA 72-4 levels in Diagnosis of Colorectal Cancers. *Asian Pacific J Cancer Prev*. 2020;21(11):3133-3136. doi:10.31557/APJCP.2020.21.11.3133

[28] Ning S, Wei W, Li J, Hou B, Zhong J, Xie Y, Liu H, Mo X, Chen J, Zhang L. Clinical significance and diagnostic capacity of serum TK1, CEA, CA 19-9 and CA 72-4 levels in gastric and colorectal cancer patients. *Journal of Cancer*. 2018;9(3):494.

[29] Dang L, Ma H, Hei A, Xu S, Zhou J, He E, Skog S. A meta-analysis of serological thymidine kinase 1 as a marker for colorectal benign and malignant tumor risk assessment. *Molecular and Clinical Oncology*. 2020 May 1;12(5):440-50.



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