

Assessment of Carcino-embryonic Antigen and Carbohydrate Antigen 19-9 Serum Levels in Pre-operative Sudanese Colorectal Carcinoma

Waleed A. Salim^{1*}, Omer Fadl Idris², A. H. Khatab³, Abubaker M. Hamad⁴,
Abdelgadir Elmugadam⁵

College of medical laboratory science / Al-Neelain University, Sudan)(Corresponding author)

²(Faculty of Science and Technology / Al-Neelain University, Sudan)

³(Faculty of medicine / University of Khartoum, Sudan)

⁴(College of medical laboratory science / University of Gezira, Sudan)

⁵(College of medical laboratory science / Sudan University of science and technology, Sudan)

Corresponding Author: Waleed A. Salim

Abstract: Colorectal cancer (CRC) is one of the most common cancer related causes of morbidity and mortality in developed countries. The use of tumor markers is a good way to improve the prognosis and treatment. This study aimed to evaluate the prognostic value of the two markers in fifty patients with CRC (as a test group) compared to twenty five apparently healthy persons (as a control group).

The test group included in this study was from National Cancer Institute (NCI-Sudan), the test and the control groups were matched in term of age. Tumor markers Carcinoembryonic antigen (CEA) and CA 19-9 were determined by Electrochemiluminescence Immunoassay (ECLIA) using commercial kits from Roche Company (Germany) and Cobas e 411 Immunoassay Analyzer.

Patients with colorectal cancer showed highly significant increases in CEA and CA19-9 compared to the control group ($p < 0.01$), and more advanced tumor stage showed a highly significant increase in the levels of CEA and CA 19-9, and also a significant increase in patients above 60 years of age ($p < 0.05$) but no relationship between the levels of CEA and CA 19-9 levels with sex.

Our results suggest that; serum concentrations of CEA and CA 19-9 can be helpful in the diagnosis and staging of colorectal carcinoma (CRC). On the other hand we suggest these marker levels could be of great screening value to detect CRC in its early stage.

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I. Introduction

One of the most important health problems in the world is colorectal cancer (CRC), with 1.2 million new cases and about 600,000 deaths each year¹.

Tumor markers play an important role in cancer diagnosis, prognosis, treatment, and monitoring, serum tumor marker detection has been widely used in clinical practice. To get valuable serum tumor markers, many efforts have been made to assist in the diagnosis and management of CRC².

Carcinoembryonic antigen (CEA) is cell surface antigen expressed in large quantities in about 95 % of colorectal carcinoma that has been known to favor progress neoplasm in colorectal carcinoma (CRC)³. Current clinical use of CEA has been confined mainly to surveillance after colon and rectal cancer resection to permit early identification of recurrence⁴.

CA 19-9 is a helpful tumor-associated antigen for the serological diagnosis and that can be hired to monitor patients with advanced colorectal carcinoma (CRC). The staining pattern of CA 19-9 in tumor tissues aid in prognosis prediction in addition to classic prognostic factors available to the surgical pathologist⁵. To assess the prognostic value of CEA and CA 19-9 we studied a test group (50 patients with colorectal carcinoma) compared to the control group (25 individuals apparently healthy).

II. Materials And Methods

A cross-sectional hospital based study was performed between June 2016 and February 2017. A total of fifty patients (28 males and 22 females) with colorectal cancer as a test group and 25 healthy subjects as a control group were included in this study. Interview and sample collection were done to all patients with CRC before starting chemotherapy and radiotherapy (i.e. serum samples were collected before beginning treatment) included the taking of a full history (age, sex, site of the tumor, onset of disease and stage of tumor).

A questionnaire was specifically designed to obtain information which helps in either including (Sudanese patients with Colorectal Carcinoma) or excluding (Healthy Sudanese people) certain individuals in or from study respectively. The patients were divided into two groups, patients were being in stage I or II of the disease (Group A), and patients in stage III or IV of the disease (Group B).

The ethical clearance was approved by the Research Ethical Committee of the Ministry of Health (Sudan). Data and samples were collected after informing and agreement of colorectal cancer patients about the purpose and importance of the study.

The tumor marker Carcinoembryonic antigen (CEA) and CA 19-9 were determined using a two-site immunoenzymometric assay, which is performed entirely in the AIA-PACK. CEA and CA 19-9 present in the test sample were bound with monoclonal antibody immobilized on a magnetic solid phase and enzyme-labeled monoclonal antibody in the AIA-PACK. The magnetic beads were washed to remove unbound enzyme-labeled monoclonal antibody and incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled monoclonal antibody that binds to the beads were directly proportional to the CEA and CA 19-9 concentration in the test sample. A standard curve was constructed, and unknown sample concentrations were calculated by using the curve. The upper limit of the normal range is less than 2.0 ng/ml for CEA and 30 U/ml for CA 19-9. Each tumor was histopathologically classified according to the American Committee on Cancer Classification and Staging System. Results were tabulated, analyzed and compared using an independent sample T test (p. value of < 0.05 is considered to be significant).

III. Result

Fifty patients were 28 males and 22 females, 19 patients (38%) being in age before 60 and 31 patients (62%) in age after 60. Patients group was consist of two groups as 22 patients (44%) had tumor originating in the colon and 28 patients (56%) had tumor originating in the rectum were studied.

The clinical criteria of all patients with CRC compared to the control group is shown in table 1. We found significant increases in serum concentrations of CEA and CA 19-9 in all cancer patients from groups A and B compared to the control group (p < 0.01). Also CEA and CA 19-9 levels were significantly higher in the more advanced tumor stages group B compared to those in group A (table 2, 3; figures 1, 2).

Table 1: Comparison of the means of serum CEA and CA 19-9 of the test group (50 patients with CRC) and the control group

Parameter	Test group Mean ± SD	Control group Mean ± SD	p-value
CEA (ng/dl)	64.4±41.5	3.2±0.7	< 0.01
CA 19-9 (U/ml)	62.7±34.2	4.7±1.6	< 0.01

- The table shows the means ± SD and probability (P).
- t- Test was used for comparison.
- P < 0.05 is considered significant.

Table 2: Mean and SD for CEA, and CA 19-9 among Group A, Group B and control group

Parameter	Group A (Mean ± SD) 29 patients	Group B (Mean ± SD) 21 patients	Control (Mean ± SD) 25 patients
CEA (ng/dl)	40.6±16.1	97.4.1±43.7	3.2±0.7
CA 19-9 (U/ml)	44.8.2±12.3	87.5±39.3	4.7±1.6

Table 3: Mean and SD for CEA, and CA 19-9 among Group B and control group

Parameter	Group B (Mean ± SD) 21 patients	Control (Mean ± SD) 25 patients	p-value
CEA (ng/dl)	97.4.1±43.7	3.2±0.7	<0.01
CA 19-9 (U/ml)	87.5±39.3	4.7±1.6	<0.01

- The table shows the means ± SD and probability (P).
- t- Test was used for comparison.
- P < 0.05 is considered significant.

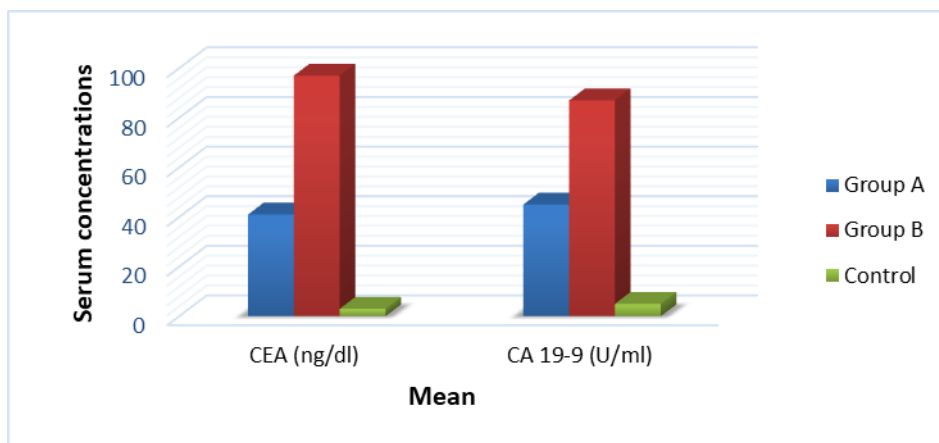


Figure 1: Relation of serum CEA & CA 19-9 in all patients with colorectal carcinoma; group A, group B and control group.

Table 4: shows the relation between serum levels of CEA and CA 19-9 with age and sex. There were a significant differences in CEA and CA 19-9 concentrations in patients over the age of 60 years compared to those below 60 years of age ($p < 0.05$) but there were no differences in CEA and CA 19-9 concentrations related to sex.

Table 4: Relation between serum level of CEA and CA 19-9 with age and sex

Parameter		CEA	CA 19-9
Age before 60 And after 60	P – value	0.02	0.017
Sex: Male and Female	P – value	0.288	0.854

- The table shows the means \pm SD and probability (P).
- t- Test was used for comparison.
- $P < 0.05$ is considered significant.

IV. Discussion

Colorectal cancer is one of the essential reason for cancer-related death ⁶. CEA is a well-known cell surface antigen expressed in large quantities in about 95 % of colorectal carcinoma that has been known to facilitate tumor progress and metastasis ³. Also, increased serum concentrations of CA19-9 have been described in combination with a range of gastrointestinal tumors including colorectal carcinoma ⁷ and it has been indicated that it may be helpful in the diagnosis and monitoring of patients with colorectal cancer ⁸.

In this study, the patients were divided into two groups, 29 patients being in stage I or II (Group A) and 21 patients in stage III or IV (Group B). The result showed that the serum levels of CEA and CA 19-9 were significantly increased in the cancer patients group compared to the control group, this agree with other researchers who found the level of these antigens in peripheral blood most often associated with irresistible disease ^{9, 10}. Another study done by Wang et al in 2014 found that; the levels of these markers were significantly higher in CRC patients compared to non-malignant colorectal disease (NMCD) ¹¹.

Results of this study, showed a significant correlation between CEA and CA 19-9 in advanced CRC. Likewise, a similar result reported by Mroczko B showed that the higher levels of CEA and CA 19-9 are seen in advanced CRC ⁹.

The results also showed significantly higher levels of CEA and CA 19-9 in patients over 60 years of age compared to patients below 60 years, but no relation between concentrations of these markers with sex. This results agree with those of Connie I. Diakos et al in 2014 ¹² who reported that CRC is largely a disease of the elderly, with a median age of 69 years at diagnosis and an increasing incidence with age. Same like our observation, Mroczko observed higher serum levels of CEA and CA 19-9 in males compared to females, but these differences were not significant. They reported also that the CA 19-9 levels were higher in patients who were over 60 years of age ⁹.

V. Conclusion

We conclude, serum concentrations of CEA and CA 19-9 can be helpful in the diagnosis and staging of colorectal carcinoma (CRC). These two markers (i.e. CEA and CA 19-9) are significantly increased in patients with CRC. Furthermore, these two markers in advanced stage of CRC showed more elevation than early stages

of the disease. Also, significant elevation of these two markers was noticed among patients above 60 years of age comparing to younger patients. We observed that the increase of these two markers in male patients is more than female patients. Final conclusion, we suggest these marker levels could be of great screening value in detection of CRC in its early stage.

VI. Recommendation

According to this study and regarding the high significance of increasing serum level of CEA and CA 19-9 in patients with CRC of both males and females, we recommend these tests to be included in the regular health checkup for males and females by age of 50 years old and above. Purpose of these investigations at this age period is to detect early arising of these two parameters which indicates deviation of health and to detect CRC in its earliest stage as much as possible. Early detection of CRC is of great importance and can be a lifesaving measurement.

On the other hand, we recommend this study to be repeated in different areas of Sudan as well as the globe to evaluate the extent to which different populations and different ethnic groups will give same results of our study. Furthermore, we are highly recommending for repeating this study with much larger number of cases to quantify the amount of CEA and CA 19-9 in patients with CRC and to match their levels with each stage of this cancer type (i.e. CRC).

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