ISSN- O: 2458 - 868X, ISSN –P: 2458 - 8687

International Journal of Medical Science and Innovative Research (IJMSIR)

IJMSIR : A Medical Publication Hub

Available Online at: www.ijmsir.com

Volume – 3, Issue –1, February - 2018, Page No. : 210 - 213

CEA levels in colorectal carcinoma, correlation with the tumor staging, and CEA as independent predictor of prognosis of colorectal cancers.

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Introduction

Cancers are characterized by unregulated cell growth, tissue invasion and metastasis[1]. When an excrescence has defined boundaries, grows slowly in an unregulated fashion but without tissue invasion, it is as benign neoplasm. Manifold genetic abnormalities are the attributions of the majority of human cancers each of which contribute in varied ways and proportions eventually culminating in several things such as differentiation, acquisition of capabilities of tissue invasion, neo-angiogenesis as well the loss of control over cell proliferation[1] .Nearly all cancers are believed to originate from a single cell; this colonal origin is a distinguished feature which differentiates between neoplasia and hyperplasia[1]. For the evolution of a tumor from normal to a fully malignant tumor, multiple internally additive mutational events are required. In terms of molecular genetics, colon cancer is probably one of the most multivalent cancer[1]. The additive effects of genetic mutations, leading to progressively disordered local DNA replication and paced colonocyte multiplication, are believed to be the pre-emptive causes of colon cancer[2]

Different cancer staging systems are used worldwide. The current and most clinically useful staging for colorectal cancer is tumour-node-metastasis (TNM) classification of the American Joint Committee on Cancer (AJCC) and the International union for cancer control.[6] TNM staging provides more veracious rendering of the depth and nodal involvement of the tumour. In TNM staging T stage describing the size and depth of penetration, N stage involvement of regional lymph nodes and M stage presence or absence of distant metastasis. Several screening tests have been developed to reach an early diagnosis of colorectal cancer, as well as adenomas. Gold and Freedman identified an antigen which was detected in only cancer and embryonic tissue; it was given the name carcinoembryonic antigen (CEA).[3] Thirty years after the initial detection in serum, CEA is one of the most widely used tumour markers worldwide and certainly the most frequently used marker in colorectal cancer.[4] CEA is used for detecting recurrence and prognosis of colon cancer, increased levels may precede clinical evidence of recurrence by as much as 6 months.[5]

Aims and objectives

To evaluate CEA levels in colorectal carcinoma, correlation with the tumor staging,and CEA as independent predictor of prognosis of colorectal cancers.

Material and Methods

The present study was conducted on 100 subjects of colorectal cancer patients in the department of Biochemistry, Faculty of Medical Science SGT University Budhera Gurugram Haryana. The total number of subjects was 200 which were divided into two equal groups: Group (1) included 100 colorectal cancer patients which were diagnosed histopathologically after a colonoscopy guided biopsy. Group (2) included 100 age and sex matched healthy controls. A written informed consent was also taken from the cases. Ethical Clearance was obtained from SGT University Ethical Committee. Colorectal cancer patients included in this study were subjected to the following: Full history and complete clinical examinations, patients with biopsy of colorectal cancer tissues for histopathological examinations to confirm the diagnosis and staging. Venous 5 ml blood sample was collected using aseptic techniques. Serum was separated from the blood by centrifugation at 3000 rpm for 10 mints. Serum was stored at -80 ^{0}C until analysis. The repeated thawing and freezing of serum was avoided. Serum samples were analyzed for CEA. CEA were quantitatively estimated in serum by using enzyme-linked immunosorbent assay (ELISA)

Results

The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were summarized in the form of means and standard deviations. The present study was conducted on 100 colorectal cancer patients in the age group 23-75 years. The mean age group of colorectal cancer patients was 52.9 ± 10.54 and control was 48.7 ± 11.04 no significant p value (Table 1). Among the 100 patients 75 (75%) were male and 25 (25%) were female. Similarly in the case of 100 healthy controls 69 (69%) were male and 31 (31%) were female (Table 2).

Significant differences was observed in CEA of colorectal cancer patients stage of IIB when compared with stage IIA (5.91 ± 1.324 vs 4.63 ± 3.47, p<0.001). Mean CEA levels between stage III and IV of colorectal cancer patients showed significant increase in stage IV (10.12 ± 2.969, p<0.001).

Table 1: Showing correlation of CEA marker with stage of disease

Stage	N	Mean	SD	P-value
IIA	29	4.63	3.471	<0.001*
IIB	8	5.91	1.324	
III	40	7.89	1.953	
IV	23	10.12	2.969	

In our study majority of patients (N=40) fall in the stage III group CEA was elevated in all stages but the elevation was more in stage IV group (10.12 ± 2.969). (Table 1)

Discussion

Colorectal cancer (CRC) is a multifactorial disease with dietary lifestyle and environmental exposures on one hand and genetic predispositions on the other hand. The risk of CRC begins to increase above the age 50 to 55 years. (American cancer society 2010)[7]. In the present study, the mean age of CRC patients was 52.9 years (p<0.787). Maximum incidence was between groups 23 to 75 years. Studies done by Youssef EMI et al (2013)[8] and EI Bolkieny et al (2006)[9]reported the mean age of CRC

patients in Egypt was 50.63 years and 51 years respectively. Our results are also similar with those of Ruhina shirin et al (2014)[10] as they concluded mean age in colorectal cancer was 50.4. A slightly higher mean age of 55 years in CRC patients was reported by Ibrahim et al (2011)[11] .However, in Western countries CRC is considered the disease of elder population. Max et al (2005)[12] reported the mean age of CRC patients about 65 years in the western countries. Serum tumor markers (STMs) are chemical substances generated by the reactions of the human body to certain tumors or are expressed and synthesized by genes in tumor cells and include glycoproteins, isoenzymes or peptide hormones which may reveal the presence of cancer Lumachi F et al (2012)[13] and Panzhang et al (2016)[14]. Increased serum levels of STMs are significantly associated with certain tumor types. Thus, the elevation of STM levels in human serum can be useful for early diagnosis of cancer or recurrence for monitoring the curative effect of chemotherapy. (Lumachi F 2012)[13]. In the present study, the patients with stage IV colorectal cancer showed significantly elevated levels of CEA marker in comparison to other stages of disease whereas Chen CC et al (2005)[15], Park IJ et al (2009)[16] reported elevated levels of CEA, in stage II of disease to have significantly poorer prognoses. The study of Reiter W et al (2000)[17], Liska A et al (2007)[18], Landmark G et al (1995)[19] demonstrated that CEA levels have prognostic impact in all colorectal patients but without significant between stage differences. Our results are in accordance with Polat E et al (2014)[20] as they reported concentration of CEA were significantly higher in patient group ($p<0.001$) and were significantly higher in stage III and IV than stage II. Our study match with M Stojkovic et al (2017)[21] as they also reported statistically significant difference in the levels of serum CEA between different disease stages of colorectal cancer.

Conclusion: Serum levels of CEA may be useful to predict tumoral extension, and also for the prognosis regarding stages of colorectal cancer patients. CEA is an independent prognostic factor of survival in colorectal cancers with lymph node metastases.CEA is the marker useful for monitoring patients with colorectal cancer.

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