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RESEARCH ARTICLE

VALUE OF CIRCULATING SERUM BIOMARKERS CEA AND LDH IN PATIENTS WITH COLORECTAL CANCER

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ABSTRACT

Introduction: Cancer is an abnormal growth of cells which tends to proliferate in an uncontrolled way and in certain cases depending upon the stage, cancer may metastasize involving adjacent organs and lymph nodes. Worldwide colorectal cancer is the 3rd most common cancer in men and 2nd most common cancer in women. In India the annual incidence rate of colorectal cancer in men is 4.1 to 4.4 per 1,00,000 people and in women it is 3.9 per 1,00,000 people. Tumor markers have an important role in all aspects of cancer care and have a momentum in early diagnosis, prognosis and screening for malignancy in asymptomatic groups.

Objective: The aim of the study is to correlate the values of Lactate Dehydrogenase (LDH) and Carcinoembryonic antigen (CEA) in colorectal cancer patients.

Material and Methods: This was a case control study of clinically diagnosed 100 colorectal cancer patients and 100 age and sex matched healthy controls were studied. Colorectal cancer patients were diagnosed by clinically and histopathologically.

Results: The mean LDH levels (189.83 ± 22.97 vs 173.66 ± 54.35, p< 0.007) and CEA levels (7.30 ± 3.350 vs 1.40 ± 0.625,p<0.001) are significantly higher in colorectal cancer patients as compared with controls.

Conclusion: Serum lactate dehydrogenase (p<0.007) and Carcinoembryonic antigen (p<0.001) are elevated in colorectal cancer patients. CEA levels were significantly higher in colorectal cancer patients and showed positive sensitivity to remain the marker of choice in monitoring colorectal cancer.

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INTRODUCTION

Cancers are characterized by unregulated cell growth, tissue invasion, and metastasis. The vast majority of human cancers are characterized by multiple genetic abnormalities, each of which contributes to the loss of control of cell proliferation and differentiation and the acquisition of capabilities, of tissue invasion and neo angiogenesis (Dan, 2011). As the cancer grows it begins the process of metastasis, shedding thousands of cells per day into the blood and lymphatic system that can cause cancers to form in distant locations into adjacent lymph nodes, peritoneum and distant organs. Colon cancers most commonly spread first to local lymph nodes before travelling to distant organs. Once local lymph nodes are involved, spread to the liver, the abdominal cavity, and the lung are the next most common destinations of metastatic spread (American Cancer Society, 2014). Many monoclonal antibodies (mAb) have been identified in the last 15 years since the advent of hybridoma methodology. Antibodies which detect colon cancer-associated antigens have made a place for themselves as an essential, non-invasive diagnostic tool for the clinicians. Carcinoembryonic antigen was first described in 1965 by Gold and Freedman (Michael, 2001). CEA is an oncofetal glycoprotein present in the gastrointestinal tract and body

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fluids of the embryo and fetus. This 200 (kda) antigen is also present in certain adult gastrointestinal cells, including the mucosal cells of the colorectum, and small amounts are also present in blood (Bigbee, 2003). Gold and freedman identified an antigen which was detected in only cancer and embryonic tissue; it was given the name carcinoembryonic antigen (CEA). Lactate dehydrogenase: (LDH) an enzyme that catalyzes the conversion of lactate to pyruvate. As cells die, their LDH is released and finds its way into the blood. Normal LDH levels vary with age, being higher in childhood due to bone growth. Nearly every type of cancer, as well as many other diseases, can cause LDH levels to be elevated. Therefore, this marker cannot be used to diagnose a particular type of cancer. LDH levels can be used to monitor treatment of some cancers.

MATERIALS AND METHODS

The present study was conducted in the department of Biochemistry of SGT Medical College, Hospital and Research Institute, Gurgaon Haryana. This case controlled study enrolled 100 colorectal cancer patients. Patients in age 20-70 years attending out patients department of Medicine and Surgery. A total of 100 colorectal cancer patients were compared with 100 age and sex matched healthy controls. A written informed consent was also taken from the cases with detailed history and other baseline investigations apart from tumor staging investigations. This study includes those patients who were diagnosed histopathologically after a colonoscopy guided biopsy. Venous blood sample were collected after overnight fasting using aseptic technique and serum was analyzed for biochemical parameters LDH and CEA. All parameters were quantitatively estimated in serum by using enzyme-linked immunosorbent assay (ELISA).

RESULTS

The present study was conducted on 100 colorectal cancer patients in the age group 23-75 years. Colorectal cancer patients were diagnosed histopathologically after a colonoscopy guided biopsy. In our study the mean age of colorectal cancer patients was 52.9 years ($p < 0.787$, 52.9 ± 10.54) (Table1). As compared to healthy controls, colorectal cancer patients showed significant increase in mean LDH level (173.66 ± 54.55 vs 189.83 ± 22.9, $p < 0.007$) (Table 2). Mean of CEA in colorectal cancer patients was significantly higher than healthy controls (7.30 ± 3.350 vs 1.40 ± 0.625, $p < 0.001$) (Table 2).

Table 1. Showing mean age (years) among cases and controls

Age (years)	N	Mean	SD	Range	P-value
Cases	100	52.9	10.54	23-75	0.787
Controls	100	48.7	11.04	20-63	

Table 2. Comparison based on LDH and CEA among cases and controls

Parameter	Cases		Controls		P-value
	Mean	SD	Mean	SD	
LDH	189.83	22.97	173.66	54.35	0.007*
CEA	7.30	3.350	1.40	0.625	0.001

DISCUSSION

Cancer is an abnormal growth of cells which tend to proliferate in an uncontrolled way and, in some cases metastases occurs if not diagnosed early and intervened (Dan, 2007). Colorectal cancer is a dreadful health problem worldwide. Carcinogenesis is a long, complicated and incremental process. Epithelial cells which are affected by abnormal acceleration under genetic impact lead to the creation of new clones, unrecognized by the suppressor genes that are probably damaged to recognize these changes at DNA level, so that different cells produce cells of new lineage which will form new tumors (Zora Vukobrat-Bijedic, 2013). Globally more than 40% of the CRC cases are constituted by the cancer of ano-rectum its incidence peaks between the age of 60 to 70 years, while in patients below 40 years its occurrence is rare (Ruhina Shirin, 2014). The risk of CRC begins to increase above the age 50 to 55 years. (American cancer society 2010) in the present study, the mean age of CRC patients was 52.9 years (American Cancer Society Cancer Facts and figures for African Americans, 2010). Maximum incidence was between 23 to 75 years. In agreement with the present study results, Youssef EMI *et al* (2013) and EI Bolkieny *et al* (2006), reported the mean age of CRC patients in Egypt was 50.63 years and 51 years respectively. A slightly higher mean age of 55 years of CRC patients was reported by Ibrahim *et al* (Ibrahim, 2011). However, in Western countries CRC is considered the disease of elder population. Max *et al* (2005) reported the mean age of CRC patients about 65 years in the west. In many malignancies LDH level have been found to be increased. In our study serum lactate dehydrogenase (LDH) levels are elevated in colorectal cancer patients ($p<0.007$) which are similar with various authors Sabrina Hundt *et al* (2007) and Marc *et al* (1991) also found that serum LDH levels were high in colorectal cancer patients. Caputo *et al* (2015), reported that LDH level was in the normal range in 56.2 % of non metastatic colorectal cancer patients and concluded that preoperative serum levels of LDH alone failed to demonstrate a prognostic role in a selected series of colorectal cancer patients. Authors concluded that, preoperative serum levels of LDH alone failed to demonstrate a prognostic role in a selected series of colorectal cancer patients. Carcinoembryonic antigen has taken center stage as a validated and guideline recommended tumor marker in colorectal cancer. In this study, CEA levels were significantly higher in CRC patients than healthy controls ($p<0.001$). The same results were reported by Zhao *et al* (2005), Grotowski *et al* (2001), Guadagni *et al* (1995), Youssef EMI *et al* (2013). A Spilla *et al* (2001) reported that CEA showed positive sensitivity and remain the marker of choice in monitoring colorectal cancer.

Conclusion

During last few years, many approaches have been reported to develop and evaluate noble blood parameters for the early detection of CRC. Currently, an ideal tumor marker for CRC is not available. Although, CEA is a well known tumor marker for CRC and remains the marker of choice in monitoring colorectal cancer as compared with LDH. Current guidelines recommendations CEA is the most important tumor marker for prognosis, detection of current disease as well as for treatment monitoring in all stages.

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