



Comparison of ALP and LDH levels and role in depicting prognosis in metastatic colorectal carcinomas

Dr. Sajad Ahmad Bhat¹, Dr. Tabinda Ayub Shah², Dr. Mir Nadeem^{3*}, Dr. Basit Rafeeq⁴, Dr. Gumarova Zhannat⁵

¹ Assistant Professor, Department of Biochemistry, West Kazakhstan Marat Ospanov State Medical University, Aktobe, Kazakhstan

² Senior Resident, Department of Medicine, GMC Srinagar and Associated Hospital, University of Kashmir, India

³ Assistant Professor, Department of Medicine, SGT Medical College and Research Centre, Haryana, India

⁴ Department of International Affairs, West Kazakhstan Marat Ospanov State Medical University, Aktobe, Kazakhstan

⁵ Associate Professor, Department of Chemistry, West Kazakhstan Marat Ospanov State Medical University Kazakhstan, Aktobe, Kazakhstan

*Corresponding Author: Dr. Mir Nadeem

Abstract

Introduction: Cancers are characterised by unregulated cell growth, tissue invasion and metastasis. Colorectal cancer is the third most commonly diagnosed malignancy in men (663,000 cases, 10%) and second in women (5710, 000 cases, 9.4%) worldwide as per data available till 2014 by ICMR. Lactate dehydrogenase (LDH) an enzyme that catalyses the conversion of lactate to pyruvate. LDH is released as cells die and finds its way into the blood. Nearly every type of cancer, as well as many other diseases, can cause LDH levels to be elevated. In metastatic colorectal cancer serum alkaline phosphatase (ALP) levels are frequently elevated. Elevation of ALP levels more than three times of normal range is considered significant for evaluation of colorectal hepatic metastases.

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. Full history and complete clinical examinations, patients with biopsy of colorectal cancer tissues for histopathological examinations to confirm the diagnosis. 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 °C until analysis. The repeated thawing and freezing of serum was avoided. Serum samples were analyzed for LDH and ALP levels. All parameters were quantitatively estimated in serum.

Result: The mean age group of colorectal cancer patients was 52.9 ± 10.54 and control was 48.7 ± 11.04 . As compared to healthy controls, colorectal cancer patients showed significant increase in mean LDH level (173.66 ± 54.55 vs 189.83 ± 22.9 , $p < 0.007$). ALP level showed highly significant differences in mean of colorectal cancer patients and healthy controls (118.28 ± 21.68 vs 72.08 ± 12.65 , $p < 0.000$)

Conclusion: The combined use of ALP and LDH may be support to predict the prognosis and metastasis of colorectal cancer patients.

Keywords: cancer, lactate, colorectal, alkaline phosphatase, metastasis

1. Introduction

Cancers are characterised by unregulated cell growth, tissue invasion and metastasis [1]. 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]. For the evolution of a tumour from normal to a fully malignant tumour, multiple internally additive mutational events are required. In terms of molecular genetics, colon cancer is probably one of the most multivalent cancers. About 15 % of sporadic colon cancers are believed to be caused by the mutations of the particular set of genes called 'mismatch repair genes' [1]. For a cell to progress from the normal to the fully malignant phenotype, it is believed that 5-10 additive mutations are necessary. Colorectal cancer is the third most commonly diagnosed malignancy in men (663,000 cases, 10%) and second in women (5710, 000 cases, 9.4%) worldwide as per data available till 2014 by ICMR [2]. Lactate dehydrogenase (LDH) an enzyme that catalyses the

conversion of lactate to pyruvate [3]. LDH is released as cells die 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 [3]. To identify colorectal cancer patients with high probability of having liver metastasis several investigators have tried to use serum tests. In metastatic colorectal cancer serum alkaline phosphatase (ALP) levels are frequently elevated [2]. Elevation of ALP levels more than three times of normal range is considered significant for evaluation of colorectal hepatic metastases. Increased ALP is seen in specific disorders, including malignant biliary obstruction, primary biliary cirrhosis, primary sclerosing cholangitis, and hepatic lymphoma.

2. 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. In this case control study patients attending SGT Hospital from 2014 to 2017 were included. 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. Venous 5 ml blood sample was collected using aseptic techniques. Serum was separated from the blood by centrifugation at 3000 rpm for 10 mins. Serum was stored at -80 °C until analysis. The repeated thawing and freezing of serum was avoided. Serum samples were analyzed for LDH and ALP levels. All parameters were quantitatively estimated in serum.

3. 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 summarised 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. 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 1). ALP level showed highly significant differences in mean of colorectal cancer patients and healthy controls (118.28 ± 21.68 vs 72.08 ± 12.65, p<0.000) (Table 1).

Table 1: 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*
ALP	118.28	21.68	72.08	12.65	0.000**

4. Discussion

Sequential accumulation of genetic alterations over time leads to gradual development of colorectal cancer⁴. The majority of cases (80%) are sporadic with genetic and environmental factors playing important role. Research of so many years from the procurable world data has shown that the reasons which are associated with carcinogenesis is the life style, the type of diet, smoking as well as the influence of the surrounding environment in which man lives and works⁴. All of these have significant impact on the evolution of the disease. Carcinogenesis is a long complicated and incremental process¹⁵. More than 40% of the CRC cases are constituted globally, in which incidence of ano- rectum peaks between the age of 60-70 years and in below 40 years its occurrence is rare. LDH level have been found to be increased in many malignancies. In our study statistically significant rise in lactate dehydrogenase (p<0.005) level of colorectal cancer patients was observed. Sabrina Hundt *et al.* (2007)⁶ and Marc *et al.* (1991)¹⁷ also observed that LDH level in CRC patients was higher, while as Caputo *et al.* (2015) found that serum LDH level was normal in 56.2% of non-metastatic CRC patients. LDH is increased in CRC

patients but alone it failed to demonstrate a prognostic role in a selected series of colorectal cancer patients. In colorectal rectal cancer patients serum alkaline phosphatase level was significantly higher (p<0.000). Similar findings were reported by Paul I *et al.* (1980)¹⁸ as authors found increased ALP concentration in 58-85% of patients with liver metastasis. These results were also found similar with the observation of M.Wasif *et al.* (2005)¹⁹ as they found ALP levels are frequently elevated in colorectal cancer patients with liver metastasis.

5. Conclusion

In this study both ALP and LDH are increased in colorectal cancer patients. LDH alone failed to demonstrate a prognostic role in a selected series of colorectal cancer patients. The combined use of ALP and LDH may be support to predict the prognosis and metastasis of colorectal cancer patients.

6. References

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