

Significance of Serum Alkaline Phosphate and Lactate Dehydrogenase on Diagnosis and Prognosis of Gastrointestinal Cancer

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Abstract:

The roles of enzymes especially alkaline phosphate (ALP), lactate dehydrogenase (LDH) in carcinogenesis in relation to disease activity have shown useful in estimating the extent and prognosis of malignant tumor in the digestive organ. Keeping this in consideration, the study was conducted on 140 subjects either sex out of which 35 normal adults and 105 gastrointestinal (GI) cancer patients. The follow up study was further undertaken and values of serum ALP and LDH of the same patients before and after surgery were recorded. The study showed that higher elevation of serum ALP levels in gastric malignancy than normal control group. Similarly LDH level in different GI cancer patients increased significantly ($p < 0.01$) than the normal control group. The study suggests that levels of ALP and LDH can be used for monitoring the success of treatments as well they would be useful indicators for diagnoses and prognoses of gastrointestinal cancer.

Keywords: - Alkaline phosphate, Lactate dehydrogenase, gastrointestinal cancer, Tumor marker.

Introduction

Cancer is a second largest killer disease after coronary heart disease in the developing countries and leading cause of deaths worldwide.^[1] Cancer of gastrointestinal tract is one of the common malignancies in the United State, United Kingdom, Japan and Soviet Union.^[2] In India, gastrointestinal group cancer is the third largest group of cancer.^[3] They categorized 28.70 per cent uro-genital, 28.37 per cent oral pharyngeal and laryngeal and 13.31 per cent gastrointestinal cancer. Sabharwal et al.^[4] recorded the percentage incidence of malignant tumors in various parts of the gastro intestinal tract. They concluded that rectum and anal were the most susceptible sides with 28.28 per cent incidence of cancerous tumor followed by colon and oesophagus each with 25.25 per cent malignancy, whereas, stomach and small intestine were comparatively less affected sharing 7.07 and 5.05 per cent incidence. Age and sex play an important role in gastro intestinal malignancy. Prabhakar et al.^[5] and Sharma et al.^[3] estimated 70 to 80 per cent gastro intestinal tract are susceptible to cancer in 40 per cent population age group varying between 30 to 60 years.

Alkaline phosphate (ALP) is present in all tissue of the body but with the liver, placenta being especially richer. The ALP of the normal adult comes primarily from the liver. Its level may be helpful in the evaluation of metastases. In liver metastases the serum ALP levels shows a better correlation with other liver tests. Similarly, lactate dehydrogenase (LDH), an enzyme of the glycolytic pathway, is released as a result of cell damage. It has been demonstrated in variety of cancers that include liver; non-Hodgkin's lymphoma, acute leukemia, breast colon, stomach and lung cancers. The serum LDH level has been found to correlate with tumor mass in solid tumors and provide a prognostic indicator of disease progression.^[6,7]

Keeping this in view the present study was under taken to determine the quantitative value and sensitivity of ALP and LDH as biochemical indicator to diagnosis and prognosis of malignancy in gastrointestinal tract namely oesophagus, stomach and colon. The present study was under taken to compare the serum ALP and LDH levels in patients with cancer of the gastrointestinal tract (oesophagus, stomach and colon) with normal subjects and variation of serum ALP and LDH levels after surgery.

Material and Methods

This study was carried out in Department of Biochemistry at SMS, Medical College Jaipur. Patient blood samples were collected from Gastrology and Surgery Department of SMS, Hospital Jaipur. The study population included 140 subjects either sex was under taken of which 35 normal adults were having no symptoms of any disease and the rest 105 gastrointestinal cancer patients admitted in the wards of Gastrology and Surgery Departments, SMS Hospital, Jaipur. Of these there were 37, 30 and 38 patients distinguish had esophagus, stomach and colon cancer respectively. At the time of their admissions the patients were found suffering from different types of GI malignancy as evidence by clinical as well as histopathological observation. 80 patients did not find their treatments continuously for various reasons. In fact only 25 patients remained for follow up studies as schedule for their complete treatments.

Fasting blood samples were collected from anti-cubical vein of healthy control and gastro intestinal cancer patients before and after surgery in plain vials. The blood was allowed to clot at room temperature and serum was separated after centrifuging. The serum samples were stored at -200C until analysis.

The test for measuring the ALP was carried on semi auto analyzer (Spin react Bio lab) and Radiant diagnostic kit was used for this. Total serum LDH activity assayed by spectrophotometrically, determining the rate of oxidation of

NADH at 370C by measuring the change in absorbance at 340 nm with semi auto analyzer (Spin react Bio lab). For this reagents and methodology of spin react LDH kit were used.^[8] Statistical significance was tested by student's t –test and paired t –test. $P < 0.05$ and $P < 0.01$ were considered significant highly significant, respectively.

Result

Alkaline phosphate (ALP)

Table 1. Exhibit the mean value of serum alkaline phosphate (ALP) of normal and gastrointestinal cancer patients. The mean value of ALP in normal cases is 198.45 U/L where as in the case of oesophagus, stomach and colon cancer patients these values are 326.04, 377.07 and 372.62 U/L, respectively. It can be seen that there is highly significant ($p < 0.01$) increase in the levels of ALP as compared to normal (control) groups. Higher elevation of serum ALP levels in gastric malignancy than normal control group can be seen in Fig. 1. Mean value of serum ALP relating to follow up study presented in Table 2 indicate that there is significant ($p < 0.01$) decrease in ALP level in case of oesophagus, stomach and colon cancers patients after their treatments. However, in case of colon cancer cases there was significant decrease ($p = 0.045$) in ALP level at 5 %. Further, it can be noted (Table 2 and Fig. 2) that after treatments of different gastrointestinal cancer patients ALP level were decreased from 351.71 to 303.86, 380.60 to 320.41 and 372.3 to 346.39 U/L in case of oesophagus stomach and colon cancers patient, respectively.

Table: 1 Mean value of serum alkaline phosphate (ALP) in normal group and gastro-intestinal cancer patients

S. No.	Subject	No. of cases	Mean±SE (U/L)	Range µg/dl		CI (p = 0.01) µg/dl		Compared to normal	
				Min.	Max.	Lower	upper	t-test	p-value
1	Normal (control)	35	198.45±3.9	155.0	250.0	193.40	203.49	-	-
2	Oesophagus cancer	37	326.04±7.7	250.1	400.5	316.08	335.99	14.47	< 0.01
3	Stomach cancer	30	377.07±8.4	273.5	430.5	366.22	387.91	20.15	< 0.01
4	Colon cancer	38	372.62±7.9	270.3	453.4	362.43	382.83	19.21	< 0.01

Table: 2 Serum alkaline phosphate (ALP) levels in GI cancer patients before and after treatment

S. No.	Subject	No of cases	Alkaline phosphate levels		Paired t-value	p-value
			Before treatment	After treatment		
			Mean ±SE (U/L)	Mean ±SE (U/L)		
1.	Normal (control)	35	198.45±3.91	-	-	-
2.	Oesophagus cancer	8	351.71±12.01	303.86±14.41	6.285	<0.01
3.	Stomach Cancer	7	380.60±12.80	320.41±15.48	3.782	<0.01
4.	Colon Cancer	10	372.79±13.30	346.39±14.19	1.892	0.045

Lactate dehydrogenase (LDH)

Mean value of serum lactate dehydrogenase of normal group and gastro intestinal cancer patients is exhibited in Table 3. The mean value of normal control group is 288.68 U/L whereas in oesophagus, stomach and colon cancer patients these are 477.98, 402.25 and 410.18 U/L, respectively. LDH

level in different GI cancer patients increased significantly (p <0.01) than the normal control group. At CI (p <0.01) lower and upper values of LDH lie between 284.76 to 292.57 in normal cases while these values are lying between 463.48 to 492.48, 384.36 to 420.13 and 395.18 to 425.21 U/L in oesophagus, stomach and colon cancer patients, respectively.

Table: 3 Mean value of serum lactate dehydrogenase (LDH) levels in normal (control) and gastro intestinal cancer patients

S. No.	Subjects	No. of cases	Mean± SE (U/L)	Range (U/L)		CI(p=0.01) (U/L)		Compared to Normal	
				Min.	Max.	Lower	Upper	t-stat	p-value
1.	Normal (Control)	35	288.68±.73	235.5	320.5	284.76	292.59	-	-
2.	Oesophagus cancer	37	477.98±11.25	356.0	689.0	463.48	492.46	15.84	<0.01
3.	Stomach cancer	30	402.25±13.88	250.5	505.1	384.36	420.13	8.57	<0.01
4.	Colon cancer	38	410.18 ± 11.67	253.5	525.0	385.13	425.21	9.70	<0.01

Serum LDH levels before and after treatments of gastro intestinal cancer patients are presented in Table 4. The LDH levels decreased highly significantly (p <0.01) in gastro intestinal cancer patients after their treatments. It can be noted that the mean value of LDH indicate decreasing trend as

496.48 to 375.70, 400.46 to 334.70 and 399.75 to 292.70 U/L in case of oesophagus, stomach and colon cancer patients, respectively. Decrease of LDH levels in different GI cancer patients after treatment can be seen in Fig. 2.

Table: 4 Serum lactate dehydrogenase level in gastrointestinal cancer patients before and after treatments.

S. No.	Subject	No of cases	Serum LDP levels		Paired t-value	p-value
			Before treatment	After treatment		
			Mean ±SE (U/L)	Mean ±SE (U/L)		
1.	Normal (control)	35	288.68 ± 3.04	-	-	-
2.	Oesophagus cancer	8	496.84 ± 34.88	375.70±19.06	6.285	<0.01
3.	Stomach cancer	7	400.46 ± 21.37	334.70 ±23.25	3.782	0.036
4.	Colon cancer	10	399.75 ± 28.61	292.70 ±15.43	1.892	< 0.01

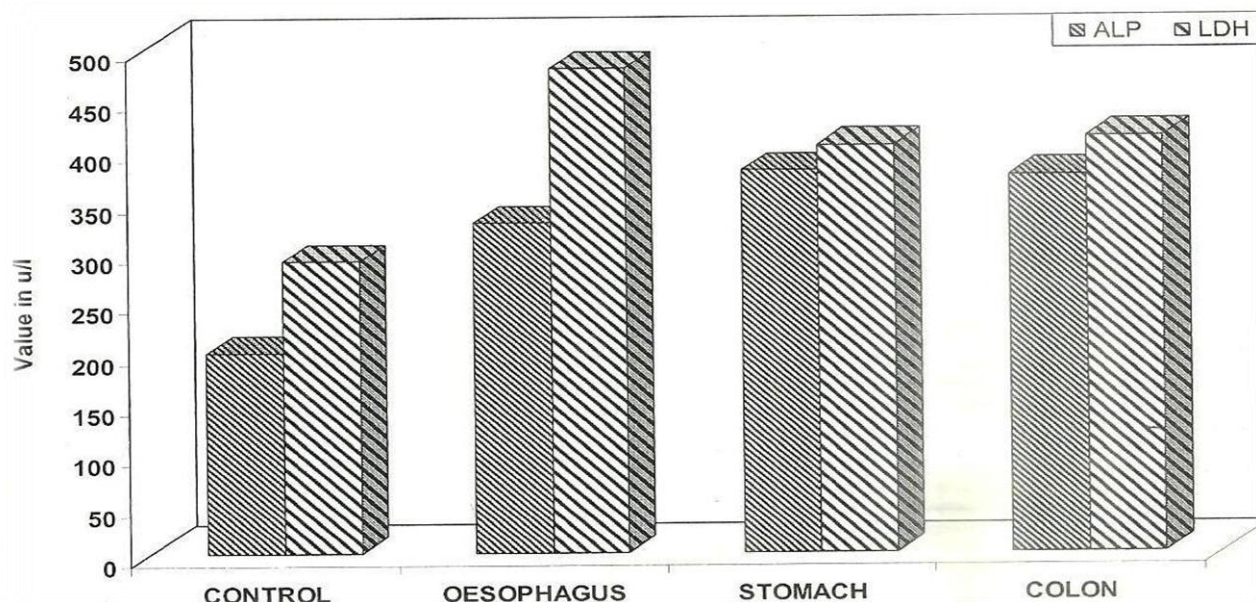


Fig.1 Lactate dehydrogenase and alkaline phosphatase level in normal and gastrointestinal cancer patients

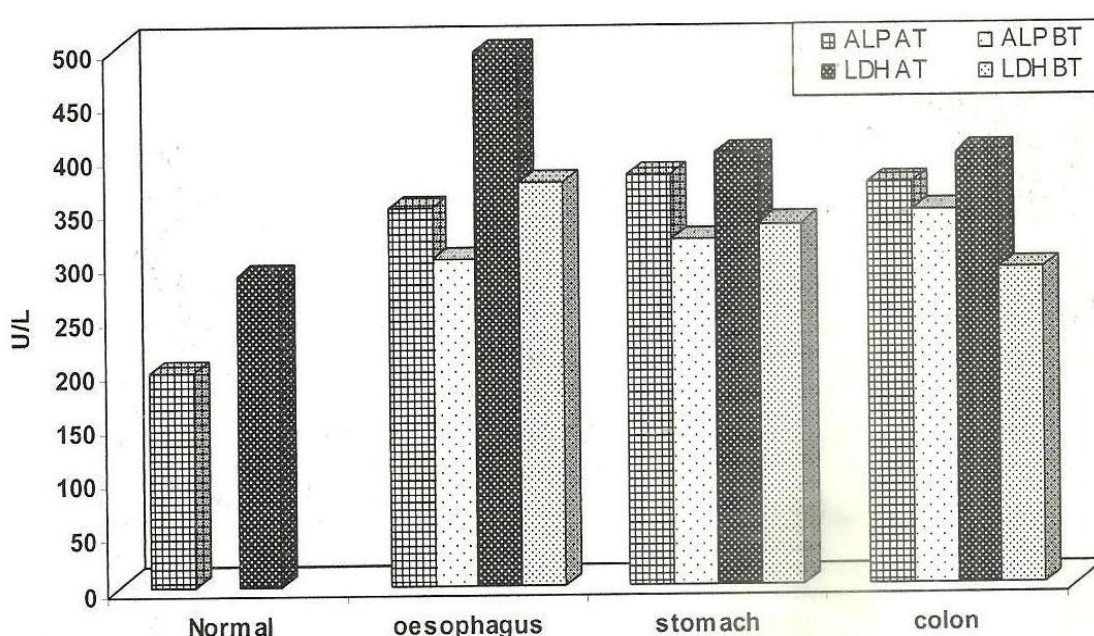


Fig.2 Serum alkaline phosphatase and lactate dehydrogenase level in different gastro-intestinal cancer patients before and after treatments

Discussion

The serum of normal subject and GI cancer patients were analyzed for ALP. Serum ALP exhibited a significant ($p < 0.01$) increase in gastric cancer patients as compared to normal subjects. The increase in ALP level in GI cancer patients may probably due to destruction of tissues facilitating the leakage of enzyme and their appearance in blood circulation. These observations are in agreement with the finding of Nigam et al.^[9] and Lavin et al.^[10] Harmenberg et al.^[11] in their study also observed an association between tumor progressions of colorectal carcinoma and raised serum ALP enzyme. Certain types of lungs carcinomas such as squamous cell and epidermoid and adenocarcinoma of alkaline phosphatase as reported by Sella et al.^[12] Similarly, Coombes et al.^[13] also reported the elevated levels of ALP in breast cancer patients. The levels of alkaline phosphatase decreased after the treatments of oesophagus, stomach and colon cancer patients but did not reach to the level of ALP as the normal control subjects maintained. The magnitude of this marker reduction may, however, reflect the degree of success of treatment of colorectal carcinoma and raised serum ALP enzyme.

Serum lactate dehydrogenase (LDH) is another enzyme which is produced increasing due to cancer cells. It was found that there was significant rise ($p < 0.01$) in serum LDH levels of different GI cancer patients as compare to normal subjects.

The malignant tumors usually exhibit high rate of glycolytic activity as result the glycolytic enzymes rose in accordance with tumor progression. The elevation of LDH is directly related to the high proliferation rate of tumor cells. The present findings are in good consistence with the findings of several researchers such as Taylor et al.^[14], Nigam et al.^[9] Galen et al.^[7] and Coombes et al.^[13] Kornbarg and Polliack.^[15] They also observed raised activities of serum LDH in cases of acute leukemia's, chronic myeloid leukemia's and lymphomas. Follow up study indicate that serum LDH level decreased significantly in GI cancer patients after their treatments but did not attain the LDH levels to the extent as the normal subjects hold^[16].

Conclusion

The result of present study suggests that levels of ALP and LDH can be used for monitoring the success of treatments as well they would be useful indicators for diagnoses and prognoses of gastrointestinal cancer.

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