



THE ROLE OF LDH AND LDH/ALBUMIN RATIO IN PEDIATRIC ACUTE LEUKEMIA

Paediatrics

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ABSTRACT

Background: Lactate dehydrogenase(LDH) is one of the major enzymes that is found in animals and humans and plays an important role in gluconeogenesis. According to clinical analysis, this enzyme is distributed in all organs but majorly found in the liver. LDH is measured in blood and body fluids that include the cerebrospinal fluid, pleural fluid, ascitic fluid etc. LDH/albumin ratio has been studied in various gastrointestinal(GI) malignancies. **Aim:** The study aims to analyze the role of LDH and LDH/albumin in pediatric acute leukemia cases **Method:** The study was conducted over a period of 1 year in pediatric (aged <15 years) patients with newly diagnosed acute leukemia. The diagnosis of acute leukemia was determined by bone marrow morphology and immunophenotyping. The association between LDH and LDH/albumin ratio with various clinical and laboratory parameters was studied. **Results:** A total of 153 patients were included. Mean age of the patients was 6.30 (SD=3.76). The most common age group was <6 years (51.3%). Male and female patients involved in the study were 59.1% and 40.9% respectively. A high LDH was found in 86.7% of children at diagnosis. The study found no significant associations of LDH or LDH/albumin with age, gender. However, analysis has found that LDH (IU/L) and LDH/albumin have a statistically significant association with bulky disease, uric acid and white blood cell(WBC) counts at presentation ($p < 0.05$). **Conclusion:** High LDH levels associated with leukocytosis co-relates with tumour burden. It is an easily available tool to assess disease status and can be utilised to monitor for tumour lysis syndrome. However, further studies are needed to establish its association with outcomes and also explore role of LDH/albumin ratio.

KEYWORDS

LDH, LDH/albumin ratio, pediatric, acute leukemia

INTRODUCTION

Lactate Dehydrogenase (LDH) is a protein and plays an important role in gluconeogenesis¹. It functions as checkpoint for glucose restoration during gluconeogenesis and single-stranded DNA metabolism². It is found in almost all the body tissues including the blood, heart, brain and lungs but majorly distributed in liver. LDH provides useful information on various health parameters in individuals. The level of LDH is correlates with the severity of damage to the tissues and a high cell turnover. The major causes of high LDH level include anemia, liver disease, muscle injury, myocardial damage and various infections³. Isoenzyme testing can localize the organ involved. LDH isoenzymes are five types each one specific to one organ. On tissue damage, LDH is released into blood stream or body fluids. It can be analysed in serum or other body fluids like cerebro-spinal fluid, pleural fluid and peritoneal washings.

In malignancies, high LDH is caused due to activation of gluconeogenesis pathway in cancer cells. Xiao et al found high serum LDH associated with poorer overall survival in acute myeloid leukemia⁴. LDH is used as an effective tool in monitoring disease in certain malignancies and hematopoietic stem cell transplant⁵. LDH/albumin ratio has been studied in various gastrointestinal(GI) malignancies^{6,7}. In this study we intend to look for association of LDH and LDH/albumin ratio with presentation and outcomes in pediatric lymphoblastic leukemia.

AIM

To analyze the role of LDH and LDH/albumin in pediatric acute leukemia cases.

METHODS AND MATERIAL

Study Subjects

All pediatric patients (aged upto 15 years) newly diagnosed with leukemia were included in the study. The diagnosis and type of acute leukemia was determined by immunophenotyping and cytogenetics on bone marrow or peripheral blood. Serum sample for LDH was collected at presentation. The baseline clinical characteristics, other

biochemical parameters, cytogenetics were collected as per proforma. All patients were treated as per modified UK ALL protocol. Data hence obtained analysed. Experiments involving human subjects were conducted according to the Declaration of Helsinki: the study was approved by the Ethics Committee. All patient enrollments were voluntary and with informed consent.

Sample Collection

Blood samples were drawn from all patients, and then they were allowed to clot then centrifuged to obtain serum sample. Serum samples were isolated and stored, until analysis, at 2-8°C for up to 48 hours or for prolonged storage aliquot and kept at -20 °C.

Statistical Analysis

Quantitative data were presented as mean and standard deviation or median and range. The quantitative data were examined by Kolmogorov Smirnov test for normality. For comparison between two groups, student t-test test (for non-parametric data) was used. For comparison between more than two groups, one way ANOVA test (for nonparametric data) was used. The spearman correlation coefficient (r) was used for measuring the relationship between two variables. Statistical analysis was performed using SPSS version 26 (SPSS Inc., Chicago, IL, USA). Significance was set at $p < 0.05$.

RESULTS

A total of 153 patients were enrolled in the study. The mean age of the patients was 6.30 years (SD=3.76). The age-wise distribution was as follows 51.3 % in <6 years, 29.9% in 6-10 years and >10 years constituted 18.8%. Of the study population, male were 59.1% and females were 40.9% female.

The majority of patients were B-Acute lymphoblastic leukemia (ALL) making up 76.6% of the study cohort. A mediastinal mass was found in 14.9% of patients with T-ALL. Bulky disease was found in 57.1% patients. The range and average of various laboratory parameters in as given in table 1

Table 1: Mean and Range of various Parameters

(N=153)	Minimum	Maximum	Mean	Standard Deviation
WBC at presentation	670	648000	46731.36	94422.5
LDH	155	9462	726.3	932.2
Uric Acid	1.80	9.30	4.6	1.6
LDH/Alb	41.75	2490.00	205.2	265.7

LDH was elevated in 86.9% of the children with acute leukemia. However, there was no statistically significant association with age and gender. A statistically significant association was found between LDH levels and LDH/albumin, with WBC count, bulky disease and uric acid levels. Pearson correlation showed a significant positive association between WBC and LDH and also between WBC count and LDH/albumin ratio ($p < .05$).

Table 2: LDH and various parameters

Parameters	LDH<313	LDH>313	P value
Age			
• <6yrs	23	56	0.609
• 6-10yrs	17	29	
• >10yrs	08	20	
Gender			
• Male	26	64	0.338
• Female	22	41	
Bulky disease			
• Yes	26	61	0.001
• No	22	44	
Uric acid			
• High	1	32	0.001
• Normal	19	101	
WBC at diagnosis			
• < 11000	32	45	0.001
• >11000	16	60	

Table 3: LDH/Albumin Ratio and various parameters

	LDH to Albumin ratio			P-value
	<150	150-300	>300	
Age				
• < 6yrs	53	15	10	0.358
• 6-10 yrs	26	08	12	
• > 10yrs	16	06	07	
Gender				
• Male	53	19	18	0.631
• Female	42	10	11	
Bulky disease				
• Yes	53	15	20	0.015
• No	42	14	09	
Uric acid				
• Normal	60	25	16	0.001
• High	11	08	13	
WBC at diagnosis				
• < 11000	58	14	05	< 0.001
• >11000	37	15	24	

DISCUSSION

Lactate dehydrogenase (LDH) is one of the major enzymes that found in animals and humans that plays an important role in the gluconeogenesis pathway. It is ubiquitously present in all organs but majorly found in the liver. A high level of the LDH is associated with the aggressive disease and high tumor burden portending worse overall survival and progression free survival. LDH, a beta-2 macroglobulin is considered as an effective clinical tool to evaluate the risk and prognosis of patients with different disease.

In the current study of LDH in pediatric acute leukemias, 153 patients were enrolled in a study period of 18 months. Male female ratio was 1.44. LDH was found to be elevated in 86.9% of our study cohort. An Indian study by Murali N et al found LDH levels elevated in 89.1% of cases with ALL⁵. Mean LDH value in current study was 726 ± 932.2 and average LDH albumin ratio was found to be 205.2 ± 265.7 . These results are similar to findings of Zahra et al. they reported mean LDH values of 726 ± 422 U/L⁹.

In the same study the authors showed age > 10 years having an

association with LDH. But not with gender or hepato-splenomegaly. Pui et al had showed a significant association of LDH with splenomegaly¹⁰. However in the current study, LDH levels showed no association with age and gender. However, LDH showed a positive correlation with WBC counts at diagnosis, uric acid levels and bulky disease. A high LDH in acute leukemia is probably secondary to tissue damage, a high cell turnover in the marrow and tumour lysis. Also due to the high proliferative state malignant cells switch to gluconeogenesis for their energy needs.

Hafiz et al reported high LDH levels at diagnosis in hematological malignancies similar to current study¹¹. They also found significant decrease in levels with normalisation of blood cells as response to treatment. They found a positive correlation between LDH and white blood cells and bone marrow blasts. However subsequent LDH levels were not monitored in the current study.

In the present study, 96% of patients with hyperuricemia had high LDH levels. LDH and LDH/albumin showed significant association with uric acid levels. Thus children with high WBC and bulky disease with elevated LDH levels need to be monitored for tumour lysis syndrome (TLS). Apiyo et al found that elevated LDH levels >500 iu/l and bulky disease were significant predictors of TLS¹².

LDH/albumin ratio is well studied in adults with GI malignancies. High LDH/albumin ratio has been shown to be associated with poor prognosis in gastric and colon cancers^{6,7}. Albumin is a surrogate marker for the nutritional status in children. We tried to see its association with various parameters in acute leukemia. A significant association of LDH/albumin was found with WBC and uric acid.

CONCLUSION

High LDH levels co-relates with tumour burden. It is an easily available tool to assess disease status and can be utilised to monitor for tumour lysis syndrome. However, further studies are needed to establish its association with outcomes and also explore role of LDH/albumin ratio.

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