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Original Article

Oncology Section

Significance of Serum Lactate Dehydrogenase in Childhood Acute Lymphoblastic Leukaemia

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ABSTRACT

Introduction: Acute Lymphoblastic Leukaemia (ALL) is the most common childhood malignancy accounting for approximately 30% of childhood malignancies. The incidence rate of leukaemia in various parts of India varies from 0.3-1.2%. Lactate Dehydrogenase (LDH) is a pyridine-linked enzyme which is involved in metabolism of glucose in normal tissue. In leukaemic cells, there is loss of coordination of glycolytic sequence and tricarboxylic acid cycle, which leads to increased utilization of glucose. As there is high cell turnover, this leads to increased cell burden and high levels of serum LDH in ALL and the increase is much more than other haematological malignancies barring Burkitt's lymphoma.

Aim: To study the level of LDH in ALL cases at the time of diagnosis in comparison with Non-ALL cases.

Materials and Methods: Fifty five cases of ALL and 23 cases of Non-ALL haematological malignancies as control were evaluated based on clinical manifestations, haematological parameters, peripheral blood picture and bone marrow findings. Serum LDH was estimated at the time of presentation by Cobas 6000, a photometrically automated system. Statistical analysis was done using SPSS version 20.

Results: In our study, high serum LDH levels were seen in 89.1% (49) cases and normal levels in 10.9% (6) cases. High blast percentage i.e., >20% on peripheral smear (65.5%) was associated with high serum LDH level. On correlation of serum LDH with peripheral smear blast percentage, a p-value of <0.05 was obtained which shows a significant correlation.

Conclusion: Serum LDH level can be considered as a simple cost-effective tool in the presumptive evaluation of childhood Acute Lymphoblastic Leukaemia. LDH in combination with Uric acid helps in detecting tumour lysis syndrome at an early stage thereby aiding in early management.

Keywords: Lactate dehydrogenase, Leucocyte, Leukaemia

INTRODUCTION

ALL is the most common childhood malignancy accounting for approximately 30% of childhood cancers. The age-adjusted incidence is 1.6 per 10,000 persons per year and the median age group is 13 years of age [1,2]. The incidence rate of leukaemia in various paediatric centres in India varies from 0.3 to 1.2% [3].

LDH is a pyridine-linked enzyme which is normally seen in tissues. The main function of LDH is that it helps in reduction of free pyruvate to lactate in glycolysis. In gluconeogenesis it converts lactate to pyruvate. Both these cycles are involved in the metabolism of glucose [3]. In ALL, there is a high cell turnover rate which leads to increased leukaemic cell burden and increased serum LDH levels [4].

These cells have unique metabolism due to which there is increased utilization of glucose compared to normal tissue because of lack of coordination of glycolytic sequence and tricarboxylic acid cycle [5]. High serum LDH level is positively correlated with increased leukocyte count and low platelet count. The increased levels of serum LDH is due to increased rate of cell proliferation and cell turnover. This can be useful in categorization of ALL patients as those with high and low risk at the time of presentation [6].

The estimation of serum LDH is being included in routine workup in cases of acute leukaemia by many clinicians as it helps in diagnosis and prognosis of childhood ALL at initial stages of diagnosis and treatment.

In this study, LDH levels are correlated with peripheral blast count i.e., to validate LDH levels as a measure of the disease burden. LDH levels of ALL are compared with that found in other haematological malignancies with high blast counts such as Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML) in blast crises.

MATERIALS AND METHODS

The prospective study was conducted from January 2013 to January 2016; in which 55 cases of ALL and 23 non-ALL haematological malignancies were obtained [AML (n=17), CML in blast crises (n=6)] were evaluated. Non Hodgkin's Leukemia, anaemia and Multiple myeloma cases were excluded for the study.

Ethical approval was obtained from the institutional ethics committee after which, the study was commenced. Individual patient consent was taken from the consultants and samples were sent to our lab for investigations.

Both the ALL and non-ALL haematological malignancies were diagnosed based on the clinical manifestation and haematological parameters, peripheral blood picture and bone marrow findings. Serum LDH level was estimated by Cobas 6000 system based on UV assay determined photometrically by measuring the increase in absorbance of NADH. Lactate dehydrogenase catalyses the conversion of L-lactate to pyruvate. During this process, NAD is reduced to NADH, which is then measured. The rate of the NADH formation is directly proportional to the catalytic activity of LDH [7,8]. Serum LDH level of 150-250 IU/L is considered normal.

The peripheral blood films and bone marrow aspirate stained with Leishman stain for morphological studies and cytochemical (Periodic Acid Schiff (PAS), Myeloperoxidase, Sudan Black B (SBB) stains were reviewed [9]. The diagnosis of ALL was confirmed by flow cytometry.

The collected data was statistically analysed and results were obtained. Clinical and morphological characteristics were expressed as median and percentage. Chi-square test and Fisher's exact test were used to test the correlation between LDH levels and blast count variables as well as LDH levels between ALL and non-ALL haematological malignancies. Statistical Package for Social Sciences (SPSS) version 20.0, IBM was used to analyse the data. A p-value <0.05 was considered statistically significant.

Parameters	N	Mini-mum	Maxi-mum	Mean	Std. deviation	Median
LDH IU/L	55	189	6741	1292.11	1532.209	599.00
BLAST % ON PS	55	0	99	42.00	34.170	40.00
TLC IN /cu.mm	55	700	136800	15041.82	22117.838	7500.00

[Table/Fig-1]: Individual parameters expressed with mean, median and standard deviation.

	Diagnosis	N	Mean	Std. deviation	Minimum	Maximum
LDH	ALL	55	1292.1091	1532.20917	189.00	6741.00
	AML	17	556.3529	510.94324	190.00	1780.00
	CML	6	537.1667	301.25299	147.00	876.00

[Table/Fig-2]: Correlation of serum LDH levels between ALL and non-ALL cases.

RESULTS

Our study included 55 cases of ALL and 23 non-ALL haematological malignancies; the latter served as controls. Serum LDH levels were recorded at the commencement of treatment. Males were more common and constituted 63.6% of the ALL cases. Median age group in the study was 5 years with blast percentage being 99. Serum LDH levels was high in 89.1% (n=49) cases. Normal levels were observed in 10.9% (n=6) cases where blast percentage was less than 20% in the smear at the time of diagnosis. Blast population on peripheral smear consisted of >20% in 65.5% (36) cases and <20% in 34.5% (19) cases. The TLC was high in 40% (22) cases and in the normal range in 60% (33) cases. The mean of the individual parameters is listed in [Table/Fig-1].

LDH levels correlated significantly with peripheral smear blast percentage ($p < 0.01$). When serum LDH levels were cross-tabulated with TLC, 40% cases of high total leukocyte count showed high LDH levels but 40% of cases with normal total leukocyte count also showed high serum LDH levels. Statistical correlations showed a p-value of >0.05 indicating that serum LDH levels were not significant when correlated with raised TLC count alone. Correlation of serum LDH levels between ALL and non-ALL cases is shown in [Table/Fig-2].

The mean serum LDH levels in 55 ALL and 23 non-ALL haematological malignancies were 1292.11±1532.21 and 556.35±510.94 respectively. The p-values in both ALL and Non-ALL were < 0.05 by Fisher's test. High levels of serum LDH (1000 U/L) was more often significantly associated with ALL cases than non-ALL cases by chi-square test ($p<0.05$).

DISCUSSION

In our study serum LDH levels were elevated in 89.1% of cases of ALL with the blast percentage exceeding 20% in 65.5% of cases. Al-Sadoon EA et al., showed moderate elevation of LDH (562IU/L) in ALL cases [10]. Our cases show elevated LDH up to 1292 IU/L which is slightly higher as compared to these studies. As compared to AL-Sadoon EA et al., our cases showed mildly elevated serum LDH in non-ALL haematological malignancies [10]. Total leukocyte count and values did not show any statistical correlation in our study.

Among the non-ALL cases, 6 cases of CML in blast crises also showed mildly elevated serum LDH while a study by Kornberg and Polliack showed marked elevation of serum LDH in cases of CML in blast crisis [9]. Though Flanagan GM et al., showed elevated serum LDH in all these cases of CML [11], it is not known how many cases presented with blast crisis. In comparison with non-ALL cases, serum LDH activity was highest in ALL cases, a feature which concurred in all three studies.

In a study done by Hafiz and Mannan, a significant correlation of LDH and bone marrow blast percentage was not found on day 14 of induction while LDH showed a marked reduction on day 28 [12]. In the present study, correlation between serum LDH with treatment response and platelet counts was not done. Blast percentage on day 8 and day 28, total leukocyte count and platelet count were taken as parameters to assess treatment response.

Serum LDH estimation was done at the time of presentation in our study while in that by Hafiz and Mannan [12], serum LDH was estimated at the time of presentation at day 14 and day 28 of chemotherapy.

Based on the higher levels of serum LDH in ALL cases as compared to other malignancies, we can infer that there is higher cell turnover and proliferation in ALL.

LIMITATION

Limitations of the study include less number of patients and lack of follow up to stratify the risk in patients with high LDH.

CONCLUSION

Serum LDH level can be considered as a sensitive and simple cost effective tool in correlating the diagnosis of childhood Acute Lymphoblastic Leukaemia with the simultaneous evaluation of other haematological parameters. This study shows that serum LDH can help in assessing the tumour burden at the initial presentation.

REFERENCES

[1] Greer JP, Arber DA, Glader B, List AF, Means RT, Parashevas JF, et al. Wintrobe's Clinical Haematology; 13th ed. Wolters and Lippincott Williams and Wilkins, 2014; Ch.80, Pp.1616-35.

[2] Swerdlow SH, Campo E, et al. WHO classification of tumours haematopoietic and lymphoid tissue. International Agency for Research on Cancer (IARC), France; 4th ed, 2008;167-176.

[3] Gupte S. Pediatric Oncology. In: The short textbook of paediatrics. 9th ed. New Delhi, Jaypee Brothers, 2001; Pp. 438-51.

[4] Pui CH, Dodge RK, Dahl GV, Rivera G, Look AT, Kalwinsky D, et al. Serum lactic dehydrogenase level has prognostic value in childhood acute lymphoblastic leukaemia. Blood. 1985;66(4):778-82.

[5] Lehninger Al. Organ interrelationships in the metabolism of mammals. In: Lehninger Textbook of Biochemistry, New York: Worth, 2000:829.

[6] Cairo MS, Coiffier B, Reiter A, Youner A. Recommendations for the evaluation of risk and prophylaxis of tumour lysis syndrome in adults and children with malignant diseases: an expert TLS panel consensus. BJH. 2010;149:578-86.

[7] Van der Heiden C, Bais R, Gerhardt W. Approved recommendation on methods for the measurement of catalytic concentration of enzymes. IFCC method for lactate dehydrogenase. Eur J Clin Chem Clin Biochem. 1994;32:639-55.

[8] Schumann G, Bonora R, Ceriotti F. IFCC Primary reference procedures for the measurement of catalytic activity concentrations of enzymes at 37ºC- Part 3. Reference procedures for the measurement of catalytic concentrations of lactate dehydrogenase. Clin Chem Lab Med. 2002;40(6):643-48.

[9] Bain B J, Bates I, Laffan MA, Lewis SM. Dacie and Lewis Practical haematology; 11th ed;61-65, 318-324.

[10] Al-Sadoon EA, Al-Naama LM, Hassan JK. Serum Lactate dehydrogenase activity in children with malignant diseases. Baharain Med Bull. 2003;25(2):7.

[11] Flanagan NG, Ridway JC, Platt CC, Rowlands AJ, Whitson A. Lactic dehydrogenase estimation in haematological malignancies. Clin Lab Haematol.1989;11(1);17-26.

[12] Hafiz GM and Mannan MA. Serum lactate dehydrogenase level in childhood acute lymphoblastic leukaemia. Bangladesh Med Res Counc Bull. 2007;33:88-91.

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