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Serum lactate dehydrogenase level in childhood acute lymphoblastic leukemia

Shaimaa Saad Abdul Zahra, Entisar Hadi Al-Shammary, Ishraq Muneam Hameed[1]

Abstract:

BACKGROUND: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. It accounts for one-fourth of all childhood cancers and 72% of all cases of childhood leukemia.

OBJECTIVE: The objective was to evaluate the significant increase in serum lactate dehydrogenase (LDH) enzyme levels in patients with ALL with respect to patients' characters, clinical presentation, and patients' induction outcome.

PATIENTS AND METHODS: A prospective study had been conducted during the period from November 1, 2017 to October 31, 2018, included 86 patients newly diagnosed ALL patients under the age of 15th years, admitted to the pediatric hemato-oncology unit in the Child's Central Teaching Hospital the data were collect from the patients, included , age , sex, clinical presentation, investigation and induction outcome of ALL patients to undergo analysis of study.

RESULTS: Of a total (86) ALL patients started induction therapy, only (75/86) of them completed induction phase of therapy and those were enrolled in analysis of this study, while (11/86) did not complete induction therapy and excluded from the study (because 10 died, and one patient loss follow-up during induction). The mean age was 4.7 years. The male-to-female ratio was 1.26:1. LDH level ranged from 100 to 1995 U/L. There was a significant association between LDH level at day 0 and each of age and ALL risk group and no association with gender, hepatomegaly, splenomegaly, lymphadenopathy, central nervous system status, and induction outcome (remission/no remission). The mean of LDH levels at diagnosis was highly elevated in patients with ALL (726 ± 422 U/L); the response to induction treatment was observed by the significant decrease in mean LDH level (324 ± 201 U/L) at day 28th of treatment *P* value (0.0001).

CONCLUSIONS: The serum LDH level was highly elevated at diagnosis in the majority of ALL patients and decreased significantly in response to chemotherapy. The estimation of serum LDH level is easy, and available, so it may be a helpful tool in evaluating the clinical aspect of the disease, the response to induction chemotherapy.

Keywords:

Acute lymphoblastic leukemia, induction, lactate dehydrogenase

Department of Hemato-Oncology, Child's Central Teaching Hospital, [1]Department of Nepherology, Al-Karama Teaching Hospital, Baghdad, Iraq

Address for correspondence:
Dr. Entisar Hadi Al-Shammary, Department of Hemato-Oncology, Child's Central Teaching Hospital, Baghdad, Iraq.
E-mail: entisaralhaider@yahoo.com

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Introduction

All is the most common malignancy in children. It accounts for one-fourth of all childhood cancers and 72% of all cases of childhood leukemia.[1] The peak incidence of ALL occurs between 2 and 5 years of age.[2,3] The incidence of ALL is higher among boys than girls, and this difference is greatest among pubertal children.[4] There are geographic differences in the frequency and age distribution of ALL. This geographic variation may reflect in part the distribution of different immunologic and cytogenetic ALL subtypes.[5] LDH exists in many different cell systems and subsequent to tissue or cell damage, serum LDH levels

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may be elevated.[6] It is not clear whether the increased serum levels of LDH commonly found in cancer patients reflect greater production and release of the enzyme by malignant cells.[7] A relationship between neoplasia and increased LDH levels has been reported by many workers in both human and animal tumors.[6]

Markedly elevated level of LDH is recorded in the majority of patients with ALL and is suggestive of increase cell proliferation and turnover and number of white blood cell (WBC) during remissions or relapses of the disease.[6,8] On the other hand, it was suggested that elevated serum LDH may relate to total leukemia cell mass.[9] Early measurement of serum LDH can be used in identifying a group of standard-risk ALL patients with a high relapse hazard.[10] Following induction therapy with archived complete remission, serum LDH level decreases, and when tumor growth recurrent as the patient relapse, serum LDH level rises again.[11]

Aim of the study

The aim was to evaluate the significant increase in serum lactate dehydrogenase (LDH) enzyme levels in patients with acute lymphoblastic leukemia (ALL) with respect to patients' characters, clinical presentation, and patients' induction outcome.

Patients and Methods

A prospective study had been conducted during the period from November 1, 2017 to October 31, 2018, over a period of 1 year, included 86 patients newly diagnosed precursor B cell ALL patients under the age of 15th years (ALL-L3 and T-cell ALL were excluded from the study), who admitted to the pediatric hemato-oncology unit in the Child's Central Teaching Hospital. He data were collect from the patients, included , age , sex, clinical presentation, investigation and induction outcome of ALL patients to undergo analysis of study. Physical examination was performed, the liver and the spleen considered hepatomegaly and splenomegaly if enlargement ≥5 cm below the costal margin and axillary and cervical lymph nodes considered enlarge if >1 cm and inguinal lymph nodes >1.5 cm. Patients stratified into standard and higher risk group as follows standard risk, WBC <50,000/ml and age 1–9.9 years; high risk, WBC ≥50,000/ml or age ≥10 years.[12] The patients with complete remission (CR) have no evidence of leukemia when evaluated by physical examination and hematologic assessment of peripheral blood and bone marrow (lymphoblasts fewer than 5% in bone marrow).[13] Serum LDH levels were determined at the time of diagnosis (at day 0 before starting chemotherapy) and at end of induction (day 28 of induction). The range of serum LDH level was 90–190 U/L (the cutoff level of serum LDH was 200 U/L, levels above that were considered to be elevated).

Statistical analysis

Patients' data were analyzed by using (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp) program, Database and statistics program for public health to estimated *P* value. Qualitative data are expressed as frequency and percentage, quantitative data as mean and median. $P < 0.05$ is considered statistically significant.

Results

A total (86) ALL patients were enrolled in this study, 11 of them did not complete induction phase (10 of them died, and one patient lost follow-up during induction), the remaining (75) patients completed induction phase and achieved CR. The most common age group was 1.1–9.9 years; the male-to-female ratio was 1.26:1.

The gender, age and risk groups, clinical findings, and central nervous system (CNS) status of the patients are described in Table 1.

This study demonstrates that there was a significant association between LDH level at day 0 and each of ALL risk groups and age (*P* value 0.0001, and 0.0001). There is no significant association between LDH level at day 0 and sex, hepatomegaly, splenomegaly, leukocyte

Table 1: Descriptive data of 86 acute lymphoblastic leukemia patients at diagnosis

Item	Subtype	*n* (%)
ALL group	Standard group	60 (70)
	Risk group	26 (30)
Age group (years)	≤1	6 (7)
	1.1-9.9	72 (83.7)
	≥10	8 (9)
Sex	Male	48 (55.8)
	Female	38 (44.2)
Hepatomegaly (cm)	≥5	54 (62.8)
Splenomegaly (cm)	≥5	45 (52.3)
CNS positive	Positive by cytospin	6 (7)
LAP	Positive	25 (62)

ALL=Acute lymphoblastic leukemia, CNS=Central nervous system, LAP=Leukocyte alkaline phosphatase

Table 2: Correlation between serum lactate dehydrogenase level at day 0 and patient character

Item	Subtype	*n*	LDH mean (SD) day 0	*P*
ALL	Standard risk	60	616 (427)	0.0001
	High risk	26	970 (324)	
Sex	Male	48	707 (406)	0.4
	Female	38	743 (462)	
Age group (years)	≤1	6	1005 (398)	0.0001
	1.1-9.9	72	644 (395)	
	≥10	8	1225 (352)	

ALL=Acute lymphoblastic leukemia, SD=Standard deviation, LDH=Lactate dehydrogenase

alkaline phosphatase (LAP), and CNS status (*P* value not significant) as shown in Tables 2 and 3.

The serum level of LDH at date of diagnosis (day 0 of induction therapy) and after completed induction phase of chemotherapy (day 28 of induction therapy) for (75/86) patients who complete induction therapy and achieved complete remission. The response to treatment was observed by the decrease in LDH level. This decrease was statistically highly significant (*P* value 0.0001), as described in Table 4.

Discussion

A prospective study was involving a sample of 86 ALL patients. This study found that patients with high-risk group ALL had a higher LDH level at diagnosis than standard risk group ALL with a significant *P* value (0.0001) which was similar to Hiçsönmez *et al*.[14] study; this finding may be related to that the patients with high risk ALL had most likely greater bulk of the disease than standard-risk ALL. In the present study, females show higher LDH levels at diagnosis as compared to males which was statistically not significant *P* value (0.4), Pujari *et al*.,[15] agree with us while Pui *et al*.[10] disagree. In this study, we found a significant association between age and LDH level at diagnosis, patients with age group ≥10 years had higher LDH levels than other age groups with significant *P* value (0.0001), a finding similar to Pujari *et al*.,[15] who found there was a significant trend in LDH levels with respect to age *P* value (<0.001) while Pui *et al*.,[10] found that there was no association between LDH level and age. The current study found no significant association between LDH level at diagnosis and hepatomegaly, splenomegaly, LAP, and CNS status *P* value 0.4, 0.6, 0.1, and 0.9, respectively. The Pui *et al*. study shows no significant association between LDH level at diagnosis and hepatomegaly, while higher LDH level at diagnosis had a larger spleen size *P* value (0.04).[10]

Table 3: Correlation between serum lactate dehydrogenase level at day 0 and patient clinical finding

Item	Subtype	*n*	LDH mean (SD) day 0	*P*
Hepatomegaly	Yes	54	751 (436)	0.4
	No	32	676 (421)	
Splenomegaly	Yes	45	743 (418)	0.6
	No	41	966 (446)	
LAP	Yes	25	838 (423)	0.1
	No	61	676 (412)	
CNS status (cytospin)	Positive	6	730 (332)	0.9
	Negative	80	722 (438)	

SD=Standard deviation, LDH=Lactate dehydrogenase, CNS=Central nervous system, LAP=Leukocyte alkaline phosphatase

Table 4: Correlation between lactate dehydrogenase level according to induction time for 75 acute lymphoblastic leukemia patients

Item	Mean (SD)		*P*
	LDH day 0	LDH day 28 after remission	
LDH (U/L)	726 (422)	324 (201)	0.0001

SD=Standard deviation, LDH=Lactate dehydrogenase

This study found that the mean of LDH levels among ALL patients at diagnosis was highly elevated (726 ± 422 U/L); these results were consisted with results obtained from Pui *et al*.,[10] Pujari *et al*.,[15] Pandit *et al*.,[16] Kornberg and Polliack,[6] D'Angelo *et al*.,[17] Hiçsönmez *et al*.[14] and Ghosh *et al*.[18] The results could be explained as LDH levels will be elevated due to tissue damage, leukemic cell lysis, and rapid cell turnover. Furthermore, increased cellular LDH activity reflects a shift toward anaerobic metabolism and increased glycolysis in the cytoplasm of malignant cells. In the present study, the response to induction treatment was observed by the significant decrease in mean LDH level (324 ± 201 U/L) on day 28th of treatment which was a statistically significant *P* value (0.0001). All the patients in this study got a CR after induction of chemotherapy. These results regarding LDH level were similar to those obtained from Pandit *et al*.,[16] Hafiz and Mannan,[11] AL-Saadoon *et al*.[19] ($P < 0.01$), Hafiz *et al*.[20] ($P < 0.001$), and Bien and Balcerska.[21] These observations were explained in that the patients with ALL on presentation had high LDH levels and with the institution of induction therapy enzymatic activities dropped gradually till normalization this was coincidental with clinical and hematological remission.

Conclusions

The serum LDH level was highly elevated at diagnosis in the majority of ALL patients decreased significantly in response to chemotherapy. There was a significant association between LDH level at diagnosis and each of ALL risk groups and age. The estimation of serum LDH level is easy, and available, so it may be a helpful tool in evaluating the clinical aspect of the disease, the response to induction chemotherapy.

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Conflicts of interest
There are no conflicts of interest.

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