



## Original Article

# Correlation with serum Lactate dehydrogenase level and Hematological parameters before and after induction of remission in childhood Acute lymphoblastic leukemia- A prospective study

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### Abstract

The relationship between serum LDH (lactate dehydrogenase) and the course of neoplasia had been well established in different studies. It might be a promising tool as assessing serum is easy, readily available and cheap in the prognosis of childhood Acute Lymphoblastic Leukemia (ALL). This study is aimed to evaluate the role of serum LDH before and after induction of remission in childhood ALL. This study was conducted at the Department of Pediatrics, Rajshahi Medical College Hospital, and Rajshahi for a period of two years. Total 30 children aged from 1-12 years newly diagnosed cases of ALL were included. Each patient underwent clinical evaluation and relevant investigations. All information was recorded in a separate case record form. Collected data were analyzed using the statistical software SPSS 23. Mean age of the studied children was  $5.03 \pm 3.17$  years. Male children were 66.7% and female children were 33.3%. Mean value of serum LDH was significantly lower at 29<sup>th</sup> days of induction of remission compared to the value before chemotherapy ( $432.40 \pm 310.52$  U/L vs.  $829.10 \pm 345.58$  U/L,  $p < 0.05$ ). Mean peripheral blast cell also reduced after chemotherapy ( $30.03 \pm 16.41\%$  Vs.  $0.37 \pm 0.96\%$ ). Pearson correlation model showed strong positive correlation between LDH level and bone marrow blast cell at both before and after chemotherapy ( $r > +0.75$ ,  $p < 0.001$ ). This study observed significant reduction of LDH after chemotherapy and positive linear relation with peripheral blast cells.

**Key words:** Blast cell, Chemotherapy, Hematology, Proliferation, Cell turnover.

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### Introduction

The most common hematological malignancy that affects lymphocytes, causing excessive infiltration in reticuloendothelial system is acute lymphoblastic leukemia (ALL). Patients' bone marrows with ALL have too many blast cells that thrust out normal white blood cells. With the paucity of

enough normal lymphocytes, the body has to face difficulties in fighting infections (St. Jude Children's Research Hospital 2020).

ALL representing more than one-fourth of all pediatric cancers.<sup>1</sup> Annually around 3000 children in the USA are diagnosed with ALL of 0-14 years of age<sup>2</sup> similar to worldwide incidence. However,

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it has been questioned whether the incidence may be less in low-income countries.<sup>3</sup> There is a slight male preponderance with white than black children and, which is most pronounced for T-cell ALL. ALL incidence peaks at 2-3 years of age and subsequently decreases with age. In India, the incidence of leukemia in various pediatric centers varies from 0.3 to 1.2%.<sup>4</sup> In Bangladesh, the age-standardized incidence rate of cancer is 7.8 per million children per year for children (0–14 years) in 2011–2014. Leukemia (18 %) is the second most common childhood cancer. ALL is by far the most common type of leukemia (86 %) in our country.<sup>5</sup>

ALL in children is a curable disease. After starting treatment remission occurs in about 98% of children within weeks. About 90% of those children can be cured. Current 4-years event-free survival rates are 61% in India,<sup>6</sup> and over 78% in Lebanon.<sup>7</sup> demonstrating that pediatric ALL is curable even in low-income countries.

Categorization of ALL as high and low risk at the time of presentation is a very much crucial task. LDH is a pyridine-linked enzyme normally seen in tissues. LDH 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.<sup>8</sup> In ALL, due to high cell turnover rate there is increased leukemic cell burden and increased serum LDH levels.<sup>9</sup> Due to unique metabolism of these cells there is increased utilization of glucose compared to normal tissue because of lack of coordination of glycolytic sequence and TCA cycle.<sup>10</sup> High serum LDH level is positively correlated with increased leukocyte count, lower blast cell DNA indices, lower platelet count and a larger spleen size. Due to increased rate of cell proliferation and cell turnover there increased levels of serum LDH. Biochemical estimation of serum LDH quantitatively shows a simpler and more objective measurement of tumor volume. This can be a useful parameter in categorization of ALL patients as those with high and low risk at the time of presentation.<sup>11</sup>

The estimation of serum LDH is being included in routine workup because it helps at initial stages of diagnosis, treatment and prognosis of childhood ALL.<sup>12</sup> Till now, there is a few such studies of serum LDH level estimation as an enzymatic tool for the presumption of childhood ALL as well as response to chemotherapy during induction of remission in Bangladesh. Thus the current study was carried out in a tertiary care hospital to correlate serum LDH with the clinical, hematological and biochemical parameters of ALL.

Serum LDH level is almost always estimated among the patients with neoplasm, especially in hematological malignancy. It is an established fact that LDH has a favourable relationship with different tumour. High elevation in lactate dehydrogenase was found in patients with acute lymphoblastic leukemia and related with increased cell proliferation and turnover. The determination of serum lactate dehydrogenase activity has received attention in several medical fields as a diagnostic and prognostic tool, as because it is minimal invasive, readily available and cost-effective. It is also evidenced that, an elevation of lactate dehydrogenase is associated with leukocytosis, cytopenias and also associated with relapse in ALL. Thus it may be a promising tool in the diagnosis and prognosis of childhood ALL. Therefore, this study was conducted to evaluate the diagnostic and prognostic significance of serum lactate dehydrogenase level in the presumption and the response to chemotherapy during the induction of remission in childhood acute lymphoblastic leukemia.

### **Objective of the Study**

To evaluate the level of serum lactate dehydrogenase with hematological parameters before and after induction of remission in childhood acute lymphoblastic leukemia.

### **Materials and Methods**

This is a Prospective observational study done at Department of Pediatrics, Rajshahi Medical College Hospital from July 2019 to June 2021. Newly diagnosed 30 cases of ALL aged 1 to 12 year of either gender, willing to participate and

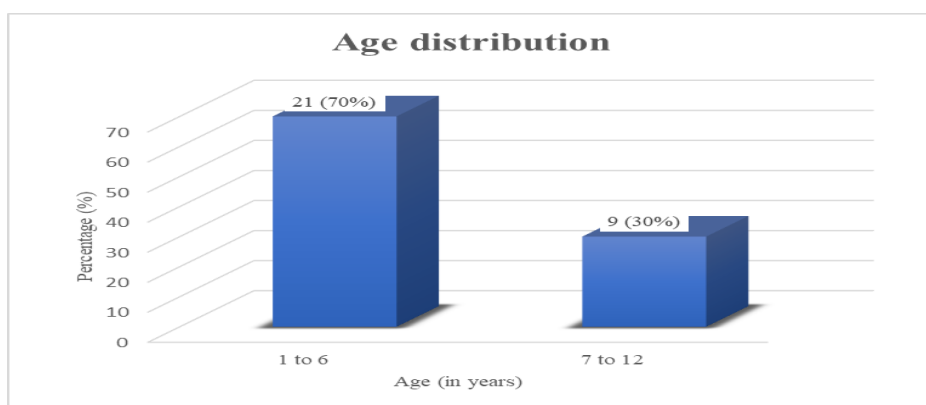
who were admitted during the study period were selected. Chemotherapy was given to all patients with acute lymphoblastic leukemia according to UK ALL 2003 protocol. Severely ill patients received any previous chemotherapy and any sign

of hemolysis were excluded from the study. Clinical data was collected, relevant investigations were done. In this study, 'p' considered as % of incidence or prevalence.

## Results

The results of the study are arranged in table and figure. Details of the study result are described below.

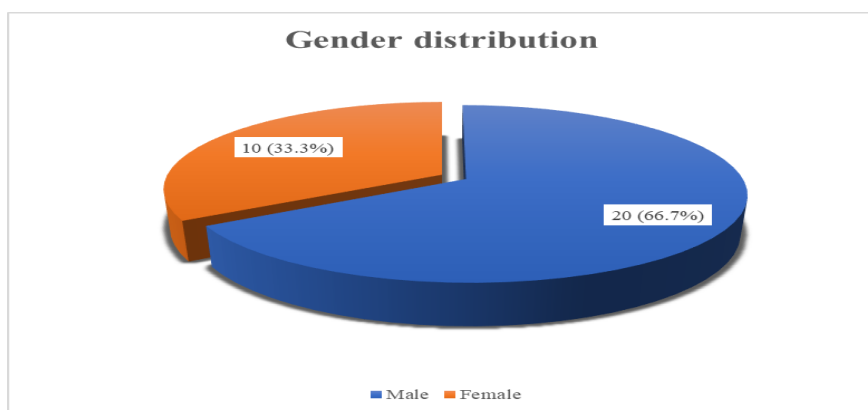
### Age distribution



**Figure-1 Age distribution of patients (n=30)**

1-6 years of age (70%) 7-12 years of age (30%), Mean age of all patient was  $5.03 \pm 3.17$  years (1-12 year) with majority belonged to 1-6 years of age (70%).

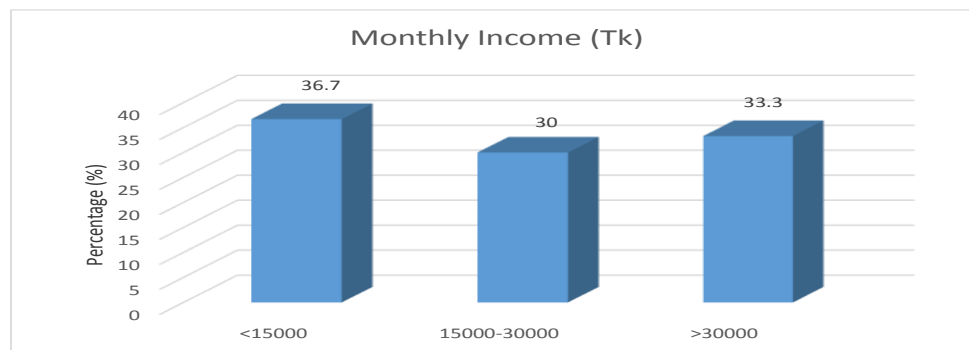
### Gender distribution



**Figure-2: Gender distribution of patients (n=30)**

Male (66.7%) female (33.3%) Greater part of the patients was male (66.7%) with a male: female ratio 2:1.

### Socioeconomic status



**Figure-3: Monthly family income of study patients (n=30)**

Monthly family income <15000 tk. (36.7%) 15000 -30000 tk., (30%) >30000 tk. (33.3%) , maximum patients was below 15000 taka (36.7%).

**Table-1 Distribution of study subjects according to clinical manifestations (n=30)**

Clinical manifestation*	Frequency	Percentage (%)
Fever	30	100
Anemia	30	100
Mild	8	26.7
Moderate	17	56.7
Severe	5	16.7
Hepatomegaly	27	90
Splenomegaly	20	66.7
Hepatosplenomegaly	17	56.7
Lymphadenopathy	18	60
Bleeding manifestation	12	40
Bony tenderness	9	30

\*multiple response

Besides, fever and anemia maximum patients of this study had hepatomegaly (90%) followed by splenomegaly (66.7%), lymphadenopathy (60%), bleeding manifestation (40%) and bony tenderness (30%). In addition, 17 patients (56.7%) had both hepatosplenomegaly.

**Table-2: Distribution of hematological parameters among study patients before chemotherapy (n=30)**

<b>Biomarker</b>	<b>Mean±SD</b>	<b>Minimum</b>	<b>Maximum</b>
S. LDH (U/L)	829.10±345.58	265	1653
Total WBC count (10 <sup>9</sup> /L)	44.45±63.72	2.50	343
Platelet count (10 <sup>9</sup> /L)	73.83±55.60	4	232
Peripheral blast cell (%)	30.03±16.41	5	53
Bone marrow blast cell (%)	59.47±18.76	8	80

**Table-3: Distribution of hematological parameters among study patients after chemotherapy at 29 days of induction of remission (n=30)**

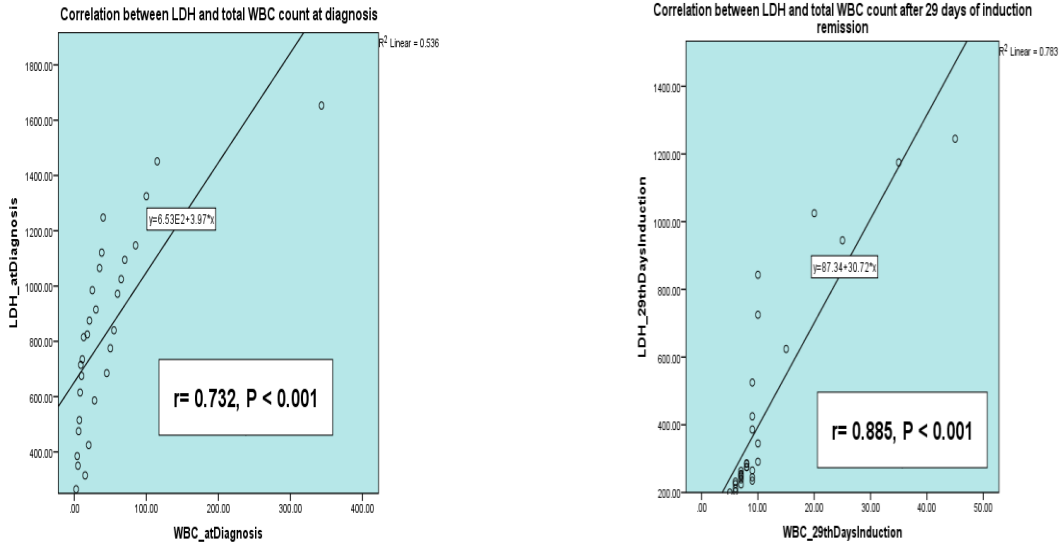
<b>Biomarker</b>	<b>Mean±SD</b>	<b>Minimum</b>	<b>Maximum</b>
S. LDH (U/L)	432.40±310.52	200	1245
Total WBC count (10 <sup>9</sup> /L)	11.23±8.94	5	45
Platelet count (10 <sup>9</sup> /L)	153.83±36.83	55	192
Peripheral blast cell (%)	0.37±0.96	0	4
Bone marrow blast cell (%)	2.77±2.34	0	10

**Table-4 Comparison of serum LDH level between before and after chemotherapy (n=30)**

	<b>At diagnosis</b>	<b>At 29 days of induction of remission</b>	<b>p value*</b>
S. LDH level (U/L)	829.10±345.58	432.40±310.52	<0.001

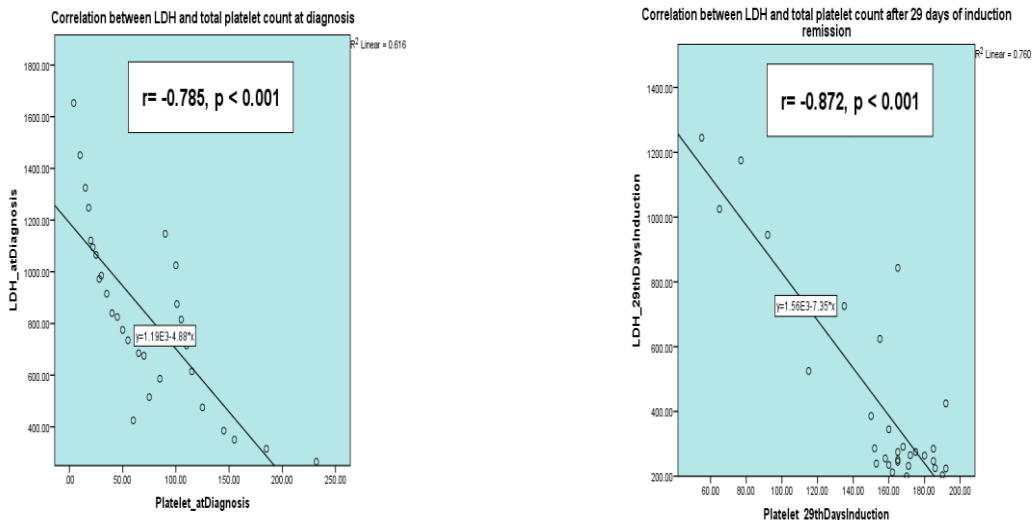
\*p value was determined by related samples Wilcoxon Signed rank test

Serum LDH level was significantly decreased after chemotherapy (at 29 days of induction of remission) compared to before chemotherapy level (p<0.001).



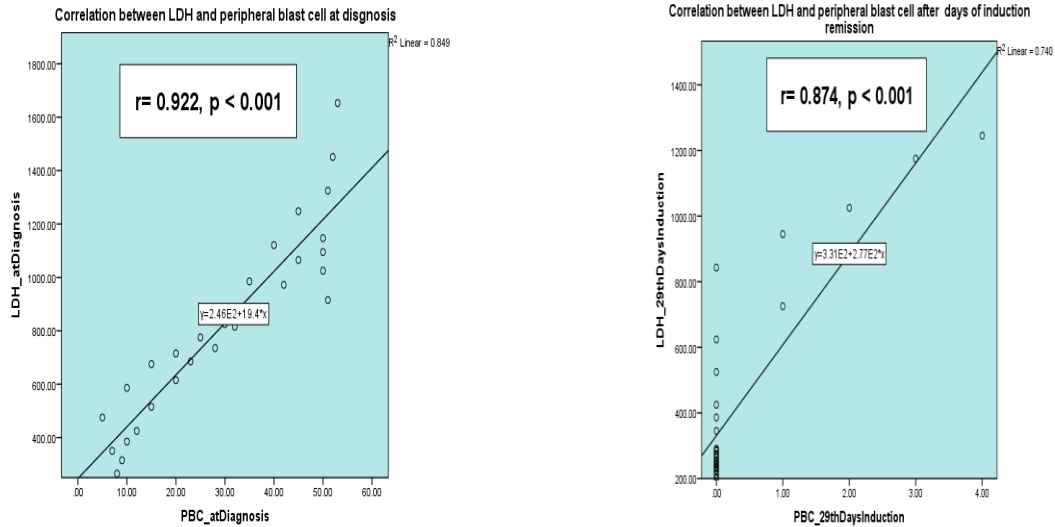
**Figure-4** Scatter diagram showing correlation between LDH and total WBC count at diagnosis & between LDH and total WBC count after 29 days of induction of remission of the respondents (n=30 in each group)

Scatter diagram revealed a strong positive relation between LDH and total WBC count both before and after chemotherapy ( $r > +0.75, p < 0.001$ ).



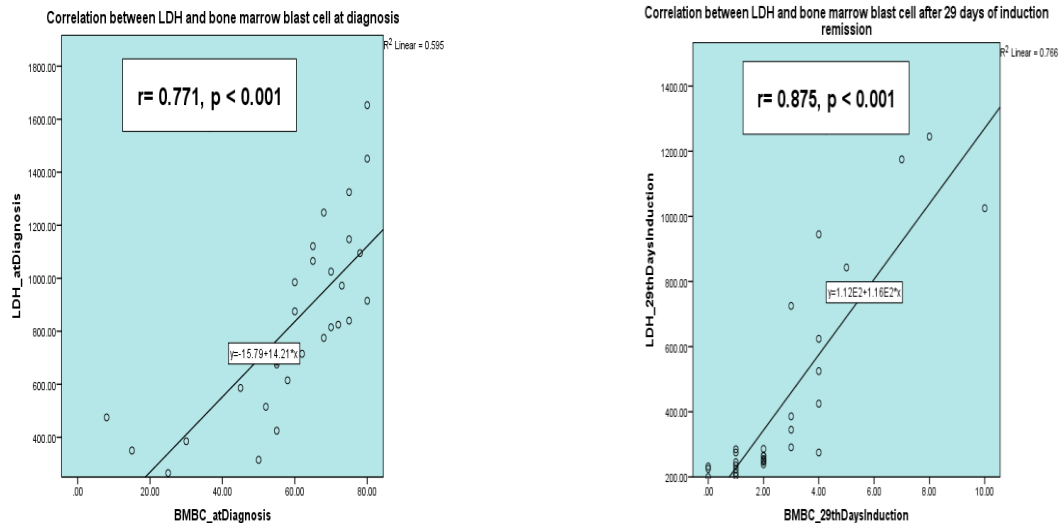
**Figure-5** Scatter diagram showing correlation between LDH and total platelet count at diagnosis & between LDH and total platelet count after 29 days of induction of remission of the respondents (n=30 in each group)

Scatter diagram revealed a strong significant negative relation between LDH and total platelet count both before and after chemotherapy ( $r < -0.75, p < 0.001$ ).



**Figure-6 Scatter diagram showing correlation between LDH and peripheral blast cell at diagnosis & between LDH and peripheral blast cell after 29 days of induction of remission of the respondents (n=30 in each group)**

Scatter diagram revealed a strong positive relation between LDH and peripheral blast cell both before and after chemotherapy ( $r > +0.75$ ,  $p < 0.001$ )



**Figure-7 Scatter diagram showing correlation between LDH and bone marrow blast cell at diagnosis & between LDH and bone marrow blast cell after 29 days of induction of remission of the respondents (n=30 in each group)**

Scatter diagram revealed a strong positive relation between LDH and bone marrow blast cell both before and after chemotherapy ( $r > +0.75$ ,  $p < 0.001$ ).

**Table-5:** Association of peripheral blast cell with serum LDH level at before and after chemotherapy (n=30)

Peripheral blast cell (%)	LDH at diagnosis		P <sub>1</sub> *	LDH at 29 days of induction of remission		P <sub>2</sub> **
	<1000 U/L	≥1000 U/L		<1000 U/L	≥1000 U/L	
At diagnosis	22.14±12.87	48.44±4.22	<0.001	27.59±15.45	52±1.0	<0.001
At 29 days of induction of remission	0	1.22±1.48	0.017	0.07±0.27	3±1.0	<0.001

\*P<sub>1</sub> value was determined by independent samples Mann-Whitney U test to compare peripheral blast cell % distribution with serum LDH level at diagnosis

\*\* P<sub>2</sub> value was determined by independent samples Mann-Whitney U test to compare peripheral blast cell % distribution with serum LDH level at 29 days of induction of remission

Peripheral blast cell percentage was significantly lower among patients those who had serum LDH <1000 U/L compared to serum LDH level ≥1000 U/L patients at both before and after chemotherapy.

## Discussion

Determination of serum lactate dehydrogenase (LDH) activity has received attention in several medical fields both as a tool of diagnosis and prognosis. As the estimation of serum lactate dehydrogenase is easy, readily available and economic, therefore, this study was conducted with an aim to evaluate the level of serum LDH before and after chemotherapy (at 29 days of induction of remission) in childhood ALL patients.

The average age (Table-1) of all patient (n30) was 5.03±3.17 years (1-12 year) with majority belong to 1-6 years of age (70%). Male gender (66.7%) was explicitly predominant with a male: female ratio 2:1 (Fig.-1). Previous studies also found male predominance with a peak incidence rate between 1 to 5 years of age among childhood ALL patients<sup>13, 14, 15, 16</sup> though the reason behind male majority is still unknown.

In this study, there was significant raised level of platelet at day 29 of induction from admission. Besides, peripheral and bone marrow blast cells were significantly decreased after 29 days of of induction compared to at admission level (Table-2&3). These findings were consistent with the findings of Hafiz and Mannan, where they observed no significant increase of platelet, peripheral and bone marrow blast cells after 14 days of induction as bone marrow was infiltrated with the blasts cell, but because of lympholysis following chemotherapy there was significant raised level of platelet at day 29 of induction from admission.<sup>12</sup>

In this study, mean serum LDH level (Table-4) was significantly decreased after chemotherapy (at 29 days of induction of remission) compared to before chemotherapy level (432.40±310.52 vs. 829.10±345.58, p<0.001). Besides, Pearson correlation model (Fig-4,5,6,7) showed that serum LDH had strong significant relation with total



WBC count, platelet count, peripheral and bone marrow blast cell at both before and after chemotherapy ( $p < 0.05$ ). These findings are comparable with several previous studies.<sup>12,13,17,18,19</sup> A Bangladeshi study where serum LDH was also significantly decreased after 29 days of induction compared to on admission level ( $2091.98 \pm 1073.20$  vs.  $701.70 \pm 420.17$  U/L), as well as significant correlation of serum LDH with each hematological parameter on both day of admission and 29<sup>th</sup> days of induction. Higher serum LDH level was associated with higher leukocytes counts, lower blast cell DNA indices and lower platelet count.<sup>12</sup> Another Bangladeshi study by also found strong significant correlation of serum LDH with total WBC count and blast count, with high initial serum LDH level  $1026.59 \pm 846.49$  U/L.<sup>13</sup> Higher LDH levels in ALL were associated with high leukocyte counts and blast cells ( $r = 0.46$ ,  $P < 0.01$ ), with a significantly reduced level of LDH after induction of chemotherapy ( $P < 0.01$ ).<sup>17</sup> Another observation of positive significant correlation of serum LDH activity with white blood cells and bone marrow blasts, while a negative significant correlation with total platelets.<sup>18</sup> The relation of serum LDH with total WBC and peripheral blast cell are comprehensible, as initial LDH gets high with high WBC count and quite understandably high initial blast cell count contributed to high initial WBC count. So, as the tumor load increased initial LDH also mounted up. This finding was further strengthened by the comparison of the mean blast cell count between the two groups of ALL- one containing higher ( $\geq 1000$  U/L) LDH and the other with that of the lower ( $< 1000$  U/L) LDH. The mean peripheral blast cell percentage was found significantly lower among patients with higher LDH compared to lower LDH level at both before and after chemotherapy (Table-5).

Therefore, based on my research findings, it could be inferred that serum LDH level might be a useful addition to routine morphologic and cytochemical methods for diagnostic as well as a prognostic tool in follow up the ALL children during their treatment, as detection of LDH

activity is comparatively easy to perform due to its availability and price.

## Conclusion

The average age of the children with ALL was 5 years along with clear male predominance. Significant reduction of LDH was observed at 29<sup>th</sup> days of remission chemotherapy. Moreover strong positive correlation between LDH level and bone marrow blast cell was observed before and after chemotherapy. So, serum LDH can be recommended as a tool to evaluate the prognosis of patients with ALL.

**Conflict of interest:** None declared

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