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A Study of Serum Ldh Activity in Leukemic Patients Before and After Chemotherapy

KEYWORDS: LDH, Leukaemia, ALL, CLL, AML, CML

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ABSTRACT *Leukaemias are malignant disorders of the haematopoietic stem cell compartment, characteristically associated with increased numbers of white cells in the bone marrow and/ peripheral blood. Once the diagnosis of leukemia is suspected, a rapid evaluation and initiation of appropriate treatment is necessary because of its overwhelming impact on prognosis in terms of achieving complete remission or providing a better quality of life for a longer period of time. The study was being undertaken to study and correlate the serum LDH activity in leukemic patients before and after 1 month of chemotherapy. And also to evaluate the utility of serum LDH activity as a prognostic index. The present study was carried out among 30 patients admitted in different units of Medicine and Pediatrics department of Assam Medical College & Hospital, Dibrugarh, during a period of one year. The type of study done was a Case-Control Clinical Cross-over Study. The difference between the means of serum LDH activity of leukemic patients and the corresponding means of controls have been found to be significant at Diagnosis and After 1 month of Chemotherapy. The difference in serum LDH activity between CML and ALL patients before and after 1 month of chemotherapy was significant. Serum LDH activity increases in leukemic patients and there is a significant reduction after chemotherapy. So the study concludes that biochemical alteration of serum LDH activity can play an important role in the prognostic aspect of the disease.*

INTRODUCTION

Leukemias are malignant disorders of the haematopoietic stem cell compartment, characteristically associated with increased numbers of white cells in the bone marrow and/ peripheral blood. The incidence of leukemias of all types in the general population is approximately 10/1,00,000 per annum, with males being more affected than females, the ratio being about 3:2 in acute leukemia, 2:1 in chronic lymphocytic leukemia (CLL) and 1.3:1 in chronic myeloid leukemia (CML).[1]

ALL is predominantly a disease of children, with highest incidence in children between the ages of 2 and 6. ALL has a second peak incidence in the elderly population. The incidence of AML increases with age, accounting for 80% of acute leukemias in adults and for 15% to 20% of acute leukemias in children. The rate of AML is somewhat higher in males than females.[2]

Once the diagnosis of leukemia is suspected, a rapid evaluation and initiation of appropriate treatment is necessary because of its overwhelming impact on prognosis in terms of achieving complete remission or providing a better quality of life for a longer period of time. Haematological and bone marrow examination are the main parameters for the diagnosis of leukemia and also important indices for monitoring the prognosis of leukemia during and after treatment. In addition biochemical test such as serum lactate dehydrogenase activity and uric acid concentration have side by side gained importance in monitoring the prognosis of leukemia, especially during the phase of treatment.[3]

EA Saadoon *et al* (2003) found that the mean serum LDH level was significantly higher in acute lymphoblastic leukemia (ALL) (P<0.001) as compared to other groups of malignancy. A significantly reduced level of serum LDH was observed in ALL only after induction of chemotherapy.[4]

Evica S *et al* (2007) in a study of 185 patients with Myeloproliferative Disorder concluded that the largest number of subjects with elevated values of serum LDH was in the group with CML (93.14%). It was statistically significantly larger in comparison to all other groups individually.[5]

Hafiz MG *et al* (2008) conducted a study where subjects were grouped into case (ALL-44) and control (healthy-25). After induction, serum LDH level were significantly decreased at day 14 and day 29 of induction from admission.[6]

Hence, serum LDH estimations, which is easily available and cost effective, have gained considerable appreciation as valuable prognostic markers of leukemia. So in order to evaluate serum LDH activity in terms of clinical significance as well as in terms of possible use as a biochemical parameter of neoplastic activity in leukemic patients the study was being undertaken with the following aims and objectives.

- To study the serum LDH activity in leukemic patients before and after chemotherapy.
- To study the correlation of serum LDH activity in leukemic patients before and after chemotherapy.
- To evaluate the utility of serum LDH activity as a prognostic index.

MATERIAL & METHODS

The present study was carried out among 30 patients admitted in different units of Medicine and Pediatrics department of Assam Medical College & Hospital, Dibrugarh, during a period of one year. The type of study done was a Case-Control Clinical Cross-over Study.

Selection of cases and controls:

Patients diagnosed as a case of leukemia, both male and female, irrespective of their age attending Out -Patient Department and admitted in various wards of Assam Medi-

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cal College and Hospital, Dibrugarh were included in the study. 30 age and sex matched healthy controls were taken for comparison.

Inclusion criteria:
- All newly diagnosed leukemia cases irrespective of their age and sex.
- No history of taking any chemotherapeutic drugs

Exclusion criteria:
- Patient on treatment excluded from the study.
- Patient who did not give consent for the study

Collection of blood sample:
Selected subject's blood samples were collected with all aseptic and antiseptic precautions. 3ml of blood was collected from antecubital vein without application of tourniquet in a sterile empty vial (SEV). The blood collected in SEV was allowed to clot for 30 minutes in a clean dry test tube and was subjected to centrifugation in a clinical centrifuge machine at 3000 rpm for 3 minutes to separate the serum. The separated serum was used to estimate serum LDH activity.

Estimation of serum LDH activity (Mod. IFCC Method)[7]
Principle: Lactate dehydrogenase catalyzes the reduction of pyruvate with NADH to form NAD. The rate of oxidation of NADH to NAD is measured as a decrease in absorbance which is proportional to the LDH activity in the sample.

RESULTS
In the Table 1 it was found that maximum number of cases (66.6%) was seen in the range of >700 IU/L followed by 30 % of cases in the range of 461-700 IU/L. After chemotherapy Maximum number of cases (50%) was seen in the range of 230-460 IU/L followed by 30 % of cases in the range of >700 IU/L. Serum LDH activity in controls group were seen in the range of 230-460 IU/L at diagnosis and after chemotherapy in 100% of cases .

Table-1: Serum LDH activity at Diagnosis and After chemotherapy

Serum LDH activity(IU/L)	At diagnosis	After Chemo-therapy	Control
230-460	1 (3.3%)	15 (50%)	30 (100%)
461-700	9 (30%)	6 (20%)	
> 700	20 (66.6%)	9 (30%)	

In the Table 2 it was found that the difference between the means of serum LDH activity of Leukemic patients at diagnosis (761.71 ± 245.81) and the corresponding means of controls (298.17 ± 48.28) have been found to be very highly significant($p<0.001$). It was also found that the difference between the means of serum LDH activity of Leukemic patients after 1 month of chemotherapy (564.27 ± 250.64) and the corresponding means of controls (298.17 ± 48.28) have been found to be significant ($p<0.01$).

Table-2: Mean serum LDH activity of Leukemic patients and the controls at Diagnosis and After Chemotherapy.

NUMBER	SERUM LDH ACTIVITY(IU/L)	
	AT DIAGNOSIS	AFTER CHEMO-THERAPY
	Mean ± SD	Mean ± SD
CASE (30)	761.71 ± 245.81	564.27 ± 250.64
CONTROL (30)	298.17 ± 48.28	298.17 ± 48.28
P-value	p<0.001	p<0.01

In the present study it was found the following observations

(1) Maximum rise in serum LDH activity before chemotherapy was seen in AML followed by CML.
(2) In AML patients, 100% of the cases were seen in the range of >700IU/L at diagnosis. After chemotherapy, 50% of cases was seen both in the range of 230-460IU/L and >700IU/L.
(3) In ALL patients, maximum number of cases (55.5%) was seen in the range of >700IU/L and 44.4% of cases in the range of 460-700 IU/L at diagnosis. After chemotherapy, maximum number of cases (77.7%) was seen in the range of 230-460 IU/L and 22.2% of cases in the range of > 700IU/L.
(4) In CML patients, maximum number of cases (76.4%) was seen in the range of >700IU/L and 23.5% in the range of 460-700 IU/L at diagnosis. After chemotherapy, maximum number of cases (35.2%) was seen both in the range of 460-700IU/L and >700 IU/L followed by 29.4% in the range of 230-460 IU/L.
(5) In CLL patients, 50% of cases was seen both in the range of 230- 460IU/L and 460-700 IU/L at diagnosis. After chemotherapy, 100% of the cases were seen in the range of 230-460 IU/L.

The difference in serum LDH activity between CML patients before and after 1 month of chemotherapy was significant ($p <0.05$). The difference in serum LDH activity between ALL patients before and after 1 month of chemotherapy was significant ($p < 0.05$). Statistical test in respect of AML and CLL could not be done as there was inadequate number of cases in each group (2 cases).

DISCUSSION
Age distribution: In the present study maximum number of leukemic patients i.e. 8 patients (26.67%) were in the age group of 0— 10 years followed by 7 patients (23.33%) in the age group of 41—50 years. If the different leukemic types were considered separately, it was seen that the maximum number of patients in case of ALL were in the age groups of 0—10 constituting 6 patients (66.6%); in case of CML in the age groups of 41—50 constituting 5 patients (29.4%); in case of AML in the age group of 31—50 constituting 2 patients and in case of CLL in the age group of 41 and above constituting 2 patients.

The distribution of age in this study is similar to the studies done by AK Siraj *et al* (2003)[8], S Ghosh *et al* (2003)[9], M Wakui *et al* (2008).[10]

Sex distribution: In the present study it was seen in leukemia as a whole, the male patients constitute 56.67% and the female patients constitute 43.33%with a male to female ratio of 1.3:1. If the different leukemic types were considered separately, in case of ALL male patients constitute 66.6% and female patients constitute 33.3%; in case of CML male patients constitute 58.8% and female patients constitute 41.1%; in case of AML both male and female patients constitute 50%; in case of CLL female patients constitute 100%.

Serum LDH activity in the study group and control at diagnosis:
In the present study it was seen that 96.6% of cases with leukemia have serum Lactate Dehydrogenase activity above the normal range with the mean LDH activity being 774.2 IU/L and 3.3% of cases towards the higher normal range with the mean LDH being 406 IU/L at diagnosis. The result could be explained as LDH activity is elevated due to leukemic cell lysis, or increased cellular LDH activity reflects glycolysis in the cytoplasm of malignant cells

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accompanied by high turnover rate. 100% of cases in the control group were seen within the normal range (230-460 IU/L).The mean serum LDH activity in leukemic patients at diagnosis was 761.7 IU/L whereas the mean in the control group was 298.1 IU/L. A very highly significant difference (elevation) in the mean value of serum LDH activity has been found between the leukemic patients at diagnosis and control group. ($p < 0.001$)

Serum LDH activity in the study group and control after 1 month of chemotherapy:

In the present study it was seen that 50% of cases with leukemia have serum lactate dehydrogenase activity above the normal range with the mean LDH activity being 756.2 IU/L and 50% of cases within the normal range with the mean LDH being 372.3 IU/L after chemotherapy. 100% of cases in the control group were seen within the normal range (230-460 IU/L).The mean serum LDH activity in leukemic patients after chemotherapy was 564.2 IU/L whereas the mean in the control group was 298.1 IU/L. A significant difference (elevation) in the mean value of serum LDH activity has been found between the leukemic patients after chemotherapy and controls ($p < 0.01$) but the difference have been substantially reduced which means on complete follow up of the chemotherapy regimen there would be statistically no significant difference between the cases and controls.

Serum lactate dehydrogenase activity at diagnosis and after 1 month of chemotherapy:

In the present study if the different leukemic types were considered separately, it was seen that in case of ALL and CML at diagnosis the mean serum LDH activity was 655.83 IU/L and 821.05 IU/L whereas the mean after chemotherapy was 441 IU/L and 622.3 IU/L. A significant difference (lowering) in serum LDH activity has been observed between the ALL and CML patients at diagnosis and after chemotherapy ($p < 0.05$).

D Damiani *et al* (2015) reported increase in the level of serum LDH upto 1600 IU/L with a range between 500-1600 IU/L. The study was carried out among 60 patients of leukemia and elevation was found in 100% of the patients with 95% coming to normal with chemotherapy within 6 months.[11]

EA Hahn *et al* (2003) reported increase in the level of serum LDH above 1000 U/L with a range between 600-1500U/L. The studies were carried out among 80 patients of leukemia and elevation were found in 98% of the patients with 92%of the patients coming to normal with chemotherapy within 6 months.[12]

SM Sayed *et al* (2014) found that the mean LDH level was significantly higher in acute lymphoblastic leukemia (ALL) ($P<0.001$) as compared to other groups of malignancy and controls. A significantly reduced level of LDH was observed in ALL only after induction of chemotherapy ($P<0.01$).[13]

Stanulla M *et al* (2009) observed that serum LDH activity was significantly higher in ALL cases as compared to controls($p<0.001$). After induction of chemotherapy, serum LDH level were significantly reduced ($p<0.001$).[14]

CONCLUSION

The difference between the means of serum LDH activity of leukemic patients and the corresponding means of controls have been found to be significant at Diagnosis and After 1 month of Chemotherapy. The difference in serum LDH activity between CML and ALL patients before and after 1 month of chemotherapy was significant. Serum LDH activity increases in leukemic patients and there is a significant reduction after chemotherapy. So the study concludes that biochemical alteration of serum LDH activity can play an important role in the prognostic aspect of the disease.

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