ORIGINAL ARTICLE

High Level of Serum Lactate Dehydrogenase : A Diagnostic Marker of Childhood Acute Lymphoblastic Leukaemia

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Abstract:

By the estimation of serum lactate dehydrogenase (LDH), one may assume the diagnosis of childhood acute lymphoblastic leukaemia (ALL). This case control study was aimed at evaluating the level of serum LDH at the initial presentation and to establish it as a diagnostic marker in childhood ALL. The study was carried out in the Paediatric Haematology and Oncology unit, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, during the period from January 2004 to December 2004 on 69 subjects with age ranging from birth to 15 years irrespective of sex. The study subjects were grouped into group I : ALL (44) and group II : healthy control (25). At the initial presentation, haematological investigations (Hb percentage, total WBC, platelet count and blast cell percentage) and measurement of serum LDH were done in both groups. But only in ALL patients bone marrow blast cell percentage was done at the initial presentation. At admission, mean ± SD of serum LDH level in ALL patients and healthy controls were 2091.98 ± 1073.20 and 362.32 ± 89.69 U/L respectively. It was found that serum LDH levels were markedly elevated (more than 900 IU/L) in 36 (82%) and moderately elevated (upto 900 IU/L) only in eight (18%) ALL patients at the initial presentation, and a very high serum LDH level was common in children with ALL at diagnosis and indicated a total tumour load. Serum LDH level was significantly raised in ALL patients than in control group (P< 0.001). So, the measurement of serum LDH can be accepted as a good and reliable enzymatic diagnostic marker of childhood ALL.

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Introduction:

Leukaemia is characterized by persistent and enormous production of immature white blood cells. It is responsible for an overwhelming majority of the childhood malignancies. The incidence of leukaemia in various paediatric centres in India varies from 0.3 to 1.2 %[1]. ALL in children is a highly curable disease. Now a days, the cure rate in western countries lies between 70 and 80%[2]. There is a good relationship between neoplasia and increased serum LDH level. LDH levels were

moderately elevated (up to 900 IU/L) in many cases of acute leukaemia, irrespective of their cell type. Markedly elevated (more than 900 IU/L) levels of LDH were recorded in the majority of patients with ALL and were suggestive of increased cell proliferation and turnover[3].

A definite and consistent shift in the pattern of molecular form of LDH has been found in a large series of malignant human neoplasms as compared to benign tumours and normal controls[4]. The serum LDH was abnormally raised in 90% of patients with acute leukaemia. It is thought that the determination of serum LDH activity has received attention in several medical centres both as an investigative tool and as a clinical laboratory procedure because of the promise it has shown in the diagnosis of childhood ALL[5]. Quantitative biochemical estimation of serum LDH provides a simpler and more objective measurement of tumour volume. Such measurement should be included in the evaluation of the patients with ALL[6]. Higher serum LDH levels were associated with higher leukocyte counts, lower blast cell DNA indices, lower platelet counts and a larger spleen size. Patients with highest LDH levels (greater than 1000 U/L) were most likely to be non-responsive to treatment, whereas those with lowest levels (less than 300 IU/L) had the minimum risk of failure ($P<0.001$). The measurement of serum LDH is useful in risk assessment or stratification of ALL patients. Early measurement of serum LDH level could be useful in identifying a group of standard risk ALL patients with a high relapse hazard[7]. There was a good relationship between serum LDH level and the course of neoplasia and the degree of dissemination of the neoplastic process[8]. A definite relationship was found between initial serum LDH level and the extent of the tumour[9].

Serum LDH is almost certainly produced by the tumour cells. Its concentration rises during tumour growth. Serum LDH level has significant correlation with the total tumour burden[10]. Serum LDH level which may reflect the mass of tumour present and it is lowest in patients with localized disease. High proliferation with high cellular turnover rate could explain the markedly elevated levels of serum LDH in untreated patients with large tumours[11].

Till now, there is no such study of serum LDH estimation as a diagnostic marker of childhood ALL in Bangladesh, but it is proposed by many workers in different situations that LDH level is a dependable diagnostic tool for childhood ALL. As the estimation of serum LDH is easy, readily available and economic, we can assume the diagnosis of childhood ALL by its high level at the initial presentation through this measurement. So, with this background it was decided to conduct this study to see serum LDH level in children with ALL at the time of diagnosis.

Materials and method:

This case control study was carried out on 69 subject of both sexes, age ranging from birth to 15 years who were admitted in the Paediatric Haematology and Oncology Unit of Bangabandhu Sheikh Mujib Medical University during the period from January 2004 to December 2004. Patients were stratified into Group-I: diagnosed case of ALL (44) who did not have any sign of haemolysis, were not severely sick and did not receive any previous chemotherapy and Group II: healthy control (25) who did not suffer from any kind of illness. The diagnosis of every patient of

ALL was made on the basis of clinical manifestation, complete blood count, peripheral blood film and the findings of bone marrow aspirate. All haematological tests, bone marrow study and biochemical test (serum LDH) were done in the laboratory of Paediatric Haematology and Oncology Unit of Bangabandhu Sheikh Mujib Medical University. Diagnostic value of these children was assessed on the basis of serum LDH at the initial presentation. Cut off value of serum LDH was taken as 900 IU/L. Upto 900 IU/L was considered as moderately elevated and more than 900 IU/L was considered as markedly elevated level[3].

Under all aseptic precautions, 3 ml of venous blood was drawn from the antecubital vein by using a disposable syringe and then blood was transferred into a clean, dry, plain test tube and allowed to clot, and then centrifuged and clear serum was formed. Then 20 μl of serum was mixed thoroughly with 1 ml of reagent and was kept at a temperature of 37^{0}C and the mixture was transferred into the RA-50 Chemistry System using at 340 nm wave length and reading was taken exactly after two minutes. Collected raw data were organized into a statistical format and appropriate statistical analysis was done. All continuous data were expressed as mean (±SD). The values were analyzed statistically with paired 't' test. 'p' value of <0.05 was taken as minimum level of significance.

Results:

At admission, mean (±SD) of serum LDH level in ALL patients and healthy controls were 2091.98 (±1073.20) and 362.32 (±89.69) U/L respectively. Serum LDH level was very high and significantly raised in ALL patients than control group (p<0.001) (Table-I).

Discussion:

Acute lymphoblastic leukaemia (ALL) is responsible for an overwhelming majority of the childhood malignancies. It is one of the most common health problems in this country and also in the developed countries. With the availability of advanced diagnostic techniques and improved therapeutic and supportive care, cure rate in childhood cancer has considerably improved[1]. The determination of serum LDH level is an important concern in children with ALL at the initial presentation. Serum LDH level estimation at appropriate time gives us presumption of the disease, tumour load, increased cell proliferation and turnover rate [3].

To evaluate the diagnostic value of serum LDH in children with ALL, 69 subjects were studied. Among them, 44 (64%) were with ALL and 25 (36%) were healthy control. At admission, mean ± SD of serum LDH level in ALL patients and healthy control subjects were 2091.98 ± 1073.20 and 362.32 ±89.69 U/L respectively. In this study, at initial presentation, serum LDH level was

Table-I: Comparison of serum LDH level between ALL patients and control group at admission

Group	Serum LDH U/L Mean ± SD (Range)	't' Value	'p' Value
ALL (n-44)	2091.98 ± 1073.20 (405-6150)	10.63	<0.001
Control (n-25)	362.32 ± 89.69 (213-532)		

significantly raised in ALL patients than that in control group ($p<0.001$). These findings were consistent with the findings of Korberg and Polliack, when they showed that marked elevation of serum LDH level was highly suggestive of ALL[3]. The findings showed a good correlation with another study done by Erickson and Morales, when they found an abnormal rise of serum LDH level in patients with acute leukaemia[5].

These observations are also consistent with Wroblewski, when he observed that serum LDH level was increased in many patients with leukaemia. He also observed that the patients of ALL who are untreated or therapeutically resistant maintained an elevated serum LDH level[8].

The findings of this study were also consistent with those of Hsieh et al, when they found that the serum LDH activity generally followed the tumour growth or it increased with tumour ages[12].

It was found that serum LDH level was markedly elevated (>900 IU/L) in 36 (82%) and moderately elevated (upto 900 IU/L) only in eight (18%) of ALL patients at the initial presentation. So, the measurement of serum LDH level can be accepted as a reliable enzymatic tool for the diagnosis of childhood ALL.

From the present study, it can be presumed that high serum LDH level is common in children with ALL at the initial presentation and it can be used as a rough indicator of the total tumour mass. Therefore, it is suggested that serum LDH level can be accepted as a good and reliable diagnostic marker of childhood acute lymphoblastic leukaemia.

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