SERUM LEAD LEVEL IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

MORSHED AKMA¹, AHMED T², CHOU_DHURY TR³, ISLAM S⁴

Abstract

Introduction: There are some reports where serum lead levels were measured and change in concentration of serum lead level was found among Acute Lymphoblastic Leukemia patients. The aim of this study was to determine serum lead levels in patients with ALL.

Methods: In this cross sectional study all children suffering from acute lymphoblastic leukemia ranging 2 to 12 years (30 patients) were evaluated for serum lead levels who were admitted at the Department of Pediatrics in DMCH, from February 2013 to January 2014. Serum measurements for lead were performed by Atomic absorption spectrophotometer in Analytical Chemistry Laboratory of Atomic Energy Centre Ramna, Dhaka.

Results: Among the 63 children there was no significant difference in age and sex between the patients and control. The mean serum lead level of Acute lymphoblastic Leukemia patient group (234.8±162.9 g/L) was significantly higher than that of the control group (23.6±12.6 µg/L). There was significant difference of serum lead level in children with ALL and control group (p<0.05).

Conclusion: From the findings of the study it can be concluded that there is significant difference between Acute Lymphoblastic Leukemia patient and normal control in terms of serum Lead (pb) level.

Key words: Children, Acute Lymphoblastic Leukemia, serum Lead.

Background:

Acute lymphoblastic leukemia (ALL) is one of the most common malignancies of childhood. Over the last decade or two, ALL has evolved and served as an ideal model for diagnosing and treating cancers in children as well as in adults. ALL is characterized by anemia, fatigue, weight loss, easy bruising, thrombocytopenia, granulocytopenia with bacterial infections, bone pain, lymphadenopathy, hepatosplenomegaly and sometimes spread to the central nervous system.¹ There are about 6,000 new cases of ALL in the United States each year.¹,² The exact cause of ALL is unknown, although several genetic and environmental factors are associated with it. Main environmental factor is radiation, namely prenatal exposure to x-rays or postnatal exposure to high doses of radiation. Certain genetic disorders such as Down Syndrome, Fanconi anemia, Bloom syndrome have an increased incidence of Acute Lymphoblastic leukemia.³

The term “heavy metal” assumes a variety of different meanings throughout the different branches of science. Although “heavy metal” lacks a consistent definition in medical and scientific literature, the term is commonly used to describe the group of dense metals or their related compounds, usually associated with environmental pollution or toxicity.⁴ Elements fitting this description include lead, mercury,
and cadmium. Although “heavy metal” toxicities are generally considered rare in mainstream medicine, less well-recognized is that chronic accumulation that may not achieve classical acute toxicity thresholds may nevertheless contribute to adverse health effects. For example, in the United States, children are exposed to lead in at least 4 million households. Children are particularly sensitive to lead intoxication, both acute and chronic, and there is no identified safe level of lead exposure in children. 

A specific toxic metal exerts its detrimental effect by selective mechanism. Lead can effectively inhibit cellular glutathione peroxidase reducing the effectiveness of this antioxidant defense system for detoxification. Many toxic heavy metals act as molecular “mimics” of nutritionally essential trace elements; as a result, they may compete with essential metallic cofactors for entry into cells and incorporation into enzymes. For example, lead is chemically similar to calcium. the exact mechanism of its carcinogenicity is not completely understood, although they can act as weak mutagens (cause DNA damage), can disrupt gene expression, and deregulate cell growth and development.

Lead toxicity is one of the most frequently reported unintentional toxic heavy metal exposures and the leading cause of single metal toxicity in children. Lead has no known beneficial function in human metabolism. Human environmental exposure is often through lead-containing paint, food stored in lead can liners, food stored in ceramic jars, or contaminated water (pipes cast in lead or soldered using lead solder). Inhalation of lead particulates is a primary route of occupational lead exposure, while oral ingestion is a primary form of exposure in the general population. Children absorb lead up to 8-times more efficiently than adults. Ingestion of deteriorating lead-based paint chips or dust is the primary source of lead exposure in children. Also, toys and other children’s products may contain lead or be painted with lead-based paint; Conditions that cause release of calcium from the bones (fracture, pregnancy, age-related bone loss) will also release stored lead from bones, thus allowing it to enter into the blood and other organs. Lead can leave the body through feces or urine. In children, low level (<10 µg/dL) lead exposure can result in several developmental disorders (accelerated skeletal growth, cognitive deficits, distractability, attention deficit hyperactive disorder and IQ decline, slowed growth and delayed sexual maturation) and higher levels (around 60-100 µg/dL) can manifest as colic.

There are few reports regarding increased lead level in patients with leukemia. In a previous study which was undertaken to assess the levels of zinc, cadmium, copper, lead showed insignificantly higher level of lead in ALL patients. Another study in Turkey showed significantly higher level of Lead (p<0.001) in children with ALL. Egyptian study stated that serum lead level was insignificant in leukemic patients than control. So far there was no previous study in Bangladesh regarding serum Lead level in ALL children. This study will be done on newly diagnosed ALL patients before starting induction therapy.

**Methodology**

This cross sectional and analytical study was done in Pediatric Hematology & Oncology Department, Dhaka Medical College Hospital from January 2013 to December 2013 (1 year).

Newly diagnosed patients of ALL in Pediatric Hematology & Oncology Department in Dhaka Medical College Hospital were selected as cases in this study on the basis of following selection criteria. In this study, 30 patients of newly diagnosed ALL who were admitted in Department of Pediatric Hematology & Oncology, Dhaka Medical College and Hospital and 33 age and sex matched healthy children were enrolled from January 2013 to December 2013. After enrollment the investigator was taken history, examined thoroughly and essential investigations done along with bone marrow examination, Immunophenotyping, LFT, RFT and infection screening. Diagnosis was confirmed by bone marrow examination and/or immunophenotyping. Patients who were previously diagnosed and treated or partially treated were excluded. Seriously ill patients and patients with other morbidity were also excluded. Consent was obtained from their parents. Data were collected by researcher himself in a pre-designed questionnaire. Physical examination was done to exclude any other illness. Blood samples (3mL) were drawn from patients by aseptic way & then allowed to stand for 15-30 minutes for formation of clot. Clotting was separated by ringing or rimming. The remaining fluid (serum) was
centrifuged and the supernatant fluid was used for serum lead determination. For long term storage specimens were kept below -20°C. Serum lead status was measured using flame atomic absorption spectrometry method (atomic absorption spectrophotometer, model no: Varian AA240FS, USA in Analytical Chemistry Laboratory, Chemistry Division of Atomic Energy Centre, Ramna, Dhaka). Serum samples were diluted (1:1) with de-ionized water. The viscosity of the diluted serum samples were then matched effectively with the working standard solution. The working standard solution was prepared by diluting a stock solution containing 1000mg/L of single element. A Varian (Varian, DuoAA240FS and AA280Z) atomic absorption spectrophotometer (AAS) equipped with fully integrated atomizers (viz. a burner system for flame atomization), used for doing analysis under the following conditions: Wave length: 213.9 nm, Slit width: 1.0, Lamp current: 5 mA, Flame type: Air/Acetylene, Air flow: 13.50 L/min, Acetylene flow: 2.00 L/min.

Serum Lead level: <100 µg/L was regarded as normal.

Age and sex matched children having same socio economic status and food habit from outpatient department for minor illness like cough, cold etc were taken as control.

After collection all data were checked and edited. then data were entered into computer with the help of software SPSS for windows program version 16.0 and double checked before analysis and analysis plan was developed keeping in view with the objectives of the study. Result on continuous measurement was presented on mean± SD (Min-Max) and results on categorical measurement were presented in number (%). Student t test has been used to find out the significance of the study parameters. Chi-square and one way ANOVA test has been used to find out the significance of the study parameters on categorical scale between two or more groups.

**Results:**

In this study it was observed that male was found 17(56.7%) in case group and 21(63.8%) in control group. Female was 13(43.3%) in case group and 12(36.4%) in control group. The difference was not statistically significant (p>0.05) between two groups.

### Table-I

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Case (n=30)</th>
<th>Control (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6</td>
<td>19 (63.3%)</td>
<td>22 (66.7%)</td>
<td>0.781ns</td>
</tr>
<tr>
<td>7-12</td>
<td>11 (36.7%)</td>
<td>11 (33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

In history 21(70.0%) patients had fever, 17(56.7%) had generalized weakness, 13(43.3%) had pallor, 14(46.7%) had bleeding manifestation. Majority 6(20.0%) patients had skin bleeding manifestation.

### Table-II

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>Number of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anaemia</td>
<td>15</td>
<td>50.0</td>
</tr>
<tr>
<td>Palpable lymph nodes</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td>Purpuric rash</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td>Palpable liver</td>
<td>20</td>
<td>66.7</td>
</tr>
<tr>
<td>Palpable spleen</td>
<td>18</td>
<td>60.0</td>
</tr>
</tbody>
</table>

Majority 15(50.0%) patients had haemoglobin level 7-10 gm/d. 14(46.74%) had <7 gm/dl and 1(3.3%) had > 11 gm/dl.

### Table-III

<table>
<thead>
<tr>
<th>Serum lead level (µg/L)</th>
<th>Case (n=30)</th>
<th>Control (n=33)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;100</td>
<td>5</td>
<td>33</td>
<td>100.0</td>
</tr>
<tr>
<td>100-200</td>
<td>13</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>&gt;200</td>
<td>12</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>Mean± SD</td>
<td>234.8±162.9</td>
<td>23.6±12.60</td>
<td>.001s</td>
</tr>
<tr>
<td>(min-max)</td>
<td>(39.9-602)</td>
<td>(20-75)</td>
<td></td>
</tr>
</tbody>
</table>

Serum lead level of the patients was normal (< 100 µg/L) in 5(17.0%) and 33(100.0%) in control group. Mean serum lead level was found 234.8±162.9 µg/L in case group and 23.6±12.6 µg/L in control group. The difference was statistically significant (p<0.05) between two groups. Serum lead level was significantly high in children with ALL.
Discussion:
The present study focused on the serum lead level in acute lymphoblastic leukemia patients admitted in Department of Pediatric Hematology & Oncology, Dhaka Medical College and Hospital. In this study a total of 63 children were included. Of them 30 child were patients and 33 healthy control.

It was observed that majority 19(63.3%) in case group and 22(66.7%) patients in control group belonged to age 2-6 years respectively. The difference was not statistically significant (p>0.05) between two groups. 

Begum showed that the mean age of ALL was about 6 years±3.32 years Similarly, Margolin, et al. and Link and Weinstein found almost similar age range in their study. The above findings are comparable with the current study.

In our study male: female ratio was1.3:1 in ALL patients. Sabina and Antonella showed male to female ratio of 1.25 with anoverall male gender prevalence in their study. The above findings are comparable with the current study.

In this study majority 15(50.0%) patients had Hb% 7-10 gm/d, 14(46.74%) had <7 gm/dl and 1(3.3%) had > 11 gm/dl which is comparable with the study of Alexander FE and Ricketts T J where they showed Hb% frequently below 10 gm/dl in young patients of ALL. Demir C showed that serum Cu, Pb and Cd were significantly elevated (p=0.003, p<0.001, p<0.001, respectively) in ALL patients. M.K.Schwartz revealed serum Pb concentration was high in acute lymphoblastic leukemia compared to the control group. Lead was insignificantly elevated (p=0.038)in another study

There is significant difference of serum lead concentration in ALL patients (234.8±162.9 µg/L) with those of control (24.05 ±13.0 µg/L) in present study(P=<.001) which is comparable with findings of Demir C and M.K. Schwartz.

Conclusion:
In conclusion this study revealed that there is significant difference between Acute lymphoblastic Leukemia patient and normal control in terms of serum Lead (pb) level.

References


