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EVALUATION OF SERUM FERRITIN LEVELS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

[1]Dr Anam, [2]Dr Rizwan Rabbani, [3]Dr Zeeshan Ahmad

[1]Independent Medical College Faisalabad

[2]Senior Registrar, Services Hospital Lahore

[3]Saidu Medical College Swat, Khyber Medical University, Peshawar

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Abstract:

Objective: *Acute lymphoblastic leukemia (ALL) is the most common malignancy in children. Although the increase in serum ferritin levels in many forms of malignancies is known, the growing pattern with different stages of ALL has not yet been explained.*

Aim: *To assess serum ferritin, uric acid and LDH in patients with acute lymphoblastic leukemia.*

Place and Duration: *In the Pediatric Unit II and Pediatric Oncology department of Jinnah Hospital Lahore for one year duration from March 2019 to March 2020.*

Material and method: *This is a case-control study. 80 ALL patients were registered in this study, for a total of 160 cases; and 80 healthy gender issues as controls. All test results were statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0.*

Results: *In this study, 160 selectees, 80 ALL patients, 42 patients (52.5%) were men, and 38 reminders (47.5%) were women. The mean age in the group of cases was 17.6 ± 5.6. The control group included 80 healthy people aged (17.8 ± 12.1) and sex (52.5% men, 47.5% women). Statistically significant positive correlations were found between the number of serum ferritin levels in blast cells (r = 0.735, p <0.0001) and uric acid (r = 0.618, p <0.0001) and LDH (r =) in ALL patients. 0.570, p <0.0001).*

Conclusion: *ALL was associated with high serum ferritin. Serum ferritin levels were significantly correlated with various stages of the disease and had a positive linear correlation with serum uric acid, LDH and blast number, so serum ferritin can be used as prognostic markers for ALL.*

Key words: *serum ferritin, acute lymphoblastic leukemia, blood.*

Corresponding author:

Dr Anam,

Independent Medical College Faisalabad

QR code

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INTRODUCTION:

Acute lymphoblastic leukemia (ALL) is the most common malignancy in children and occurs in about 2-4 out of 100 children under 15 years of age. Over the past 40 years there has been a significant improvement in results for ALL patients. Before the start of effective chemotherapy for cancer about 40 years ago, ALL was equally lethal, and most children survived only 2-3 months after diagnosis. However, currently around 60% of children with this disease are in full remission 5 years after their initial diagnosis; Many of these children treat themselves. The clinical onset of ALL is usually acute, but a small percentage of cases can develop insidiously within a few months. Symptoms and signs are associated with leukemia cell load and bone marrow replacement and lead to cytopenia. The most common symptoms are fever (caused by infection secondary to leukemia or neutropenia), fatigue and drowsiness (due to anemia), pain and bleeding diathesis (associated with thrombocytopenia). Patients with precursor ALL / LBL from T cells often have mediastinal mass with or without pleural effusion, which can lead to respiratory disorders and other symptoms of superior vena cava syndrome. Common areas of extra medullary involvement include lymph nodes, liver, spleen and meninges, while less often ALL can leak into the orbital tissues, testicles, tonsils and tonsils. Cell death and nuclear cleavage of the malignant colon produce large amounts of nucleic acid, purines (adenine and guanine) are converted to uric acid by destroying purines, causing hyperuricemia. Basically, an increase in LDH is observed in tumor lysis syndrome, probably due to anaerobic glucose metabolism. Serum LDH levels are usually elevated in lymphoproliferative disorders, LDH values have prognostic value in patients with non-Hodgkin's lymphoma and is widely used to evaluate treatment response and control tumor recurrence. Iron also inhibits host defense, allowing cancer cell proliferation and functioning as a nutrient for unlimited cancer cell proliferation. Iron was carcinogenic in animal models, and in some studies, iron stores were positively associated with the risk of certain cancers in humans, including the colon and liver. Iron is particularly worrying because the body is still absorbed, even if the reserves are sufficient. Patel et al. Patients with various hematological cancers were examined to determine the relationship between changes in serum ferritin levels and the clinical status of patients. Serum ferritin levels have been significantly increased in patients with Hodgkin's disease, non-Hodgkin's lymphoma, multiple myeloma, explosion crisis caused by chronic myelogenous leukemia, acute myelogenous leukemia and ALL patients. Serum ferritin levels reflect acute phase reactions and are generally associated with iron storage. Other recent studies suggest that ferritin replaces advanced disease and affects relapse because high serum ferritin predicts overall survival and relapse-free survival after autologous stem cell transplantation in lymphomas. In patients not treated with ALL, the average serum ferritin concentration was about 15 times higher than normal in this age group. Circulating ferritin levels during chemotherapy were higher than in the pre-treatment period. There was no correlation between ferritin levels and remission time in patients still receiving chemotherapy. The increase in circulating ferrite during chemotherapy may be due to the increased release of damaged leukemia cells. Chemotherapy can also damage other cells containing ferritin, but the lack of correlation with serum transaminase activity does not make major liver parenchymal cells. Similarly, unlike high serum ferritin and aplastic anemia, the lack of correlation reduces the likelihood that this is due to increased reserves. Low serum ferritin levels found in long-term survivors of ALL suggest that ferritin levels may be a useful indicator for predicting relapse and as a prognostic symptom. Acute lymphoblastic leukemia is the most common malignancy in children. Treatment includes induction of chemotherapy for a long period of time. During treatment, prognostic requirements increased to ensure complete elimination of the malignant clone and to avoid excessive chemotherapy. Cytogenetic tools are so expensive that we analyzed serum ferritin as a prognostic factor and its relationship to the severity of malignancy due to the percentage of outbreak and the correlation of uric acid and lactate dehydrogenase with serum levels. To our knowledge, there is very little research on this type of cancer; The purpose of this study is to provide more evidence of the relationship between serum ferritin and ALL.

MATERIALS AND METHODS:

This is a follow-up study conducted in the Pediatric Unit II Pediatric Oncology department of Jinnah Hospital Lahore for one year duration from March 2019 to March 2020. A total of 160 patients were included in the study, 80 patients were diagnosed and in accordance with WHO criteria and 80 patients of the same age and control group were obtained. The sample size was calculated based on the sample size from the basic formula. People taking iron supplements or drugs affecting iron metabolism were excluded from the study. Prior to

the study, verbal consent was obtained from all participants or their parents. A venous blood sample (5 ml) was taken from each participant with aseptic measurements from an elbow vein. They were dosed into a 2.5 ml EDTA tube and immediately used for counting blood, preparing blood smears and forecasting serum ferritin. The remaining 2.5 ml was placed in a heparinized tube and used to assess serum uric acid and LDH. Blood mixed with EDTA was used for full blood counts using an automated hematology analyzer (Sysmex XT-2000I-Japan) within 1 hour after collection to minimize differences due to sample aging. Thin blood membranes were stained for PBP 2 testing: one was made with RAL Diff Quick stain, the other with MGG, as well as another sample and stained with SBB. The rest of the blood in EDTA was centrifuged for 3 minutes at 3200 rpm to obtain plasma, and then the resulting plasma was used to assess serum ferritin using an electro-chemiluminescent immunoassay using a Cobas e411 automated clinical chemical analyzer (Roche-Germany).

Heparinized blood was centrifuged at 3200 rpm for 3 minutes and the serum was collected in 1.5 ml Eppendorf tubes and stored for up to 7 days (at 2-8 ° C). Serum uric acid and LDH were then determined using an automated clinical cobas c311 chemical analyzer (Roche-Germany). Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 20.0. Summary statistics were used to summarize the characteristics of the surveyed population. The mean and standard deviation were calculated for numerical variables (age, blood counts, batch number, uric acid, serum ferritin and LDH). An independent sample T test was performed to compare serum ferritin levels between cases and controls. Pearson's correlation was used to assess the correlation between serum ferritin and other variables (uric acid, LDH and batch number). Analysis of variance was performed to compare serum ferritin levels in a patient group according to ALL grade using a unilateral ANOVA test. In all tests, p <0.05 was considered statistically significant.

RESULTS:

The study involved 160 people, 42 patients (52.5%) men and 38 people (47.5%) with an average age of 17.6 ± 5.6 years and other 80 healthy people (80). 17.8 ± 12.1) and gender (52.5% men, 47.5% women). The hematological parameters in the case group show a significant decrease in hemoglobin, red blood cell count and red blood cell count, as well as thrombocytopenia compared to the control group. While the total number of white blood cells has increased significantly, dominant blast cells indicate the acute phase of the disease (Table 1).

Table 1 Mean value of blood count parameters

Variables	RBCs (× 10^{12}/l)	Hb (g/dl)	PCV (%)	PLts (× 10^9/l)	WBCS (× 10^9/l)	Blast count (× 10^9/l)	Blast (%)
Case Group	2.9	8.2	25.8	54.4	157.1	151.4	87.6%
Control Group	4.9	13.4	40.0	268.2	7.0	0.0	0.0%

The mean values of serum uric acid, LDH and ferritin were higher in group conditions compared to the control group (Table 2) and showed a positive linear correlation using the correlation of explosions with ferritin, uric acid and LDH. Pearson's correlation coefficient ip <0.05 (Table 3).

Table 2 Mean value of uric acid, LDH and serum ferritin

Variables	Uric Acid (mg/dl)	LDH (U/L)	Ferritin (mg/l)
Case Group	7.4	699.0	510
Control Group	4.5	94.2	245

Table 3 Correlation of blast cells count with serum uric acid, LDH and ferritin levels

Variables	Mean value	Blast cells count (× 10^9/l)	Pearson correlation (r)	p-value
Uric Acid (mg/dl)	7.4	151.4	0.604	<0.0001
LDH (U/L)	699.0	151.4	0.783	<0.0001
Ferritin (µg/l)	510.0	151.4	0.735	<0.0001

The correlation of serum ferritin levels between cases and controls shows a significant difference when it is statistically analyzed by an independent sample T test (p <0.05) (Table 4).

Table 4 Correlation of serum ferritin levels between cases and controls

Variables	Case Group	Control Group	p-value
Serum Ferritin (µg/l)	510	245	<0.05

Serum ferritin levels correlate positively with serum uric acid levels (r = 0.618, p <0.0001) (Table 5).

Table 5 Correlation of serum levels of ferritin with serum levels of uric acid and LDH

Variables	Mean value	Serum Ferritin (µg/l)	Pearson correlation (r)	p-value
Uric Acid (mg/dl)	7.4	510	0.618	<0.0001
LDH (U/L)	818.0	510	0.570	<0.0001

Of the 80 ALL patients, there were 52 patients (65%) who were diagnosed with acute lymphoblastic leukemia at an early stage and increased TWBC and blast cell counts compared to other stages and had the highest serum uric acid levels. LDH and ferritin. There were 21 patients (26.3%) with a moderate increase in TWBC, blast cells, uric acid, LDH and serum ferrite in the relapse phase. The remaining 7 patients (8.8%) had remission, clinical status, and the hematological parameters were normal or nearly normal (Table 6).

Table 6 Frequency and the mean value for (TWBCs, blast, uric acid, LDH, and ferritin) within the different stage of the disease

Stage	Frequency (%)	TWBCs (× 10^9/l)	Blast (× 10^9/l)	Uric acid (mg/dl)	LDH (U/L)	Ferritin (µg/l)
Early	52 (65.0%)	432.7	216.4	10.3	1280.0	834.6
Recurrent	21 (26.2%)	48.4	39.2	7.6	624.0	497.8
Remission	7 (8.8%)	11.6	5.2	4.4	194.1	200.0

Serum ferritin levels increased significantly in patients at an early stage (mean = 834.6 ug / l) compared to relapses (mean = 497.8 ug / l) and remission (mean = 200 ug / l) using a one-way ANOVA test. (p <0.05) (Table 7).

Table 7 Difference in serum ferritin levels within three ALL groups

Variables	Early	Recurrent	Remission	p-value
Serum Ferritin (µg/l)	834.6	497.8	200	<0.05

DISCUSSION:

Acute lymphoblastic leukemia is a childhood cancer and accounts for over 50% of leukemia in this age group. In recent years, more emphasis has been placed on the status of iron and iron chelator, such as the cytotoxic effects of antiproliferative agents and apoptosis of induced cells in leukemia tumors, assuming that iron deficiency can control. induces the proliferation and apoptosis of various cancer cells. This study found a significant increase in serum ferritin levels in patients with acute lymphoblastic leukemia compared to healthy subjects, which was in line with the previous study by Jaina et al. 260 patients with ALL, mean ferritin 1081 were evaluated, and LDH prevalence was significantly higher. In another study by Zhang et al., Increased cell destruction, increased serum levels and increased serum ferritin levels, which in several cases with different types of malignancies have reported an increase in serum ferritin levels due to increased transferrin receptors in leukemia cells, these results they were Aulbert and it was in line with the work done by Schmidt. However, there is no agreement with the study of Chua et al., Who found that serum ferromagnetic inflammation is not associated with cancer risk or death due to cancer, these differences are examples and methods used to measure race, serum ferritin. In addition, our study shows that a change in serum ferritin levels at a normal level in patients with clinical remission and maximum increase in early stages shows a positive correlation. Directly with serum uric acid, LDH, white blood cell count and blast cells, the study was conducted by Jain et al. And Zhang et al. Although there are misunderstandings in the study, they agree with our results. They found that Ahlawat et al. They showed no correlation between serum ferritin and total white blood cell counts and the number of peripheral blood cracks. And this dispute is the method used

to measure differences in race, sample size and serum ferritin.

CONCLUSIONS AND RECOMMENDATIONS:

Although serum ferritin increases significantly in patients with early and recurrent acute lymphoblastic leukemia, it lowers to normal in patients with clinical remission. Therefore, measuring and monitoring changes in serum ferritin levels can be useful to easily and simply assess and predict disease in these patients.

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