

A Prospective Study on the Levels of Serum Uric acid & Serum lactate dehydrogenase in patients suffering from Leukaemia

Sonal Agarwal

Associate Professor, Department of Pathology, RVRS Medical College, Bhilwara, Rajasthan, India.

Received: 18-07-2022 / Revised: 12-09-2022 / Accepted: 01-10-2022

Corresponding author: Dr. Sonal Agarwal

Conflict of interest: Nil

Abstract

Background: An early diagnosis & timely treatment can play an important role in improving the prognosis & quality of life in leukaemic patients. Estimation of serum uric acid & serum lactate dehydrogenase in patients suffering from leukaemia have emerged as acceptable markers in monitoring the prognosis of such cases especially when treatment is ongoing.

Aims: Estimation of Serum uric acid & lactate dehydrogenase levels in leukemic patients.

Material & Method: The present study recruited 60 patients who were diagnosed as leukaemic (acute or chronic, lymphoid or myeloid) patients of either sex, admitted in Department of Medicine of our Hospital from Dec 2021 to May 2022. Patients with previous history of chemotherapeutic drugs & who didn't give consent were excluded. For all the patients complete blood count, Hb%, serum lactate dehydrogenase and serum uric acid levels were estimated. Correlation between Serum uric acid & lactate dehydrogenase levels with total leucocyte count was assessed.

Results: Maximum patients were within 21-30 years age range, mean±SD being 41.67±18.24 years with 57% males & 43% females. The commonest type of leukaemia was chronic myeloid (54%), followed by acute myeloblastic (22%), chronic lymphoblastic (13%) and acute lymphoblastic type (11%). High Hb% was observed in chronic lymphoblastic type & lowest in acute lymphoblastic leukaemia. Mean total leucocyte count observed was 48660 (mm³). Low total leucocyte count was observed in acute type of leukaemia while higher values in chronic leukaemias. Mean serum uric acid was found to be 7.83±1.82 mg/dl with 64% of patients having concentration >7.2 mg/dl. Statistically significant difference was observed in the mean serum uric acid concentrations within different types of leukaemia (p<0.05). Mean LDH level was 801.07±202.54 IU/L. In 89% of study subjects Serum LDH was above normal range i.e., >460 IU/L. Statistically significant difference was noted between all the different types of leukaemia, when comparing mean LDH levels except between AML & CML (p>0.05). A strong correlation between increased total leucocyte counts and mean serum uric acid & lactate dehydrogenase levels were observed (p<0.05).

Conclusion: Serum uric acid & serum lactate dehydrogenase levels were found to important & significant prognostic markers within patients suffering from leukaemia. The serum levels significantly increased with total leucocyte counts & thus independently assess the deteriorating prognosis in such patients.

Keywords: serum uric acid, serum lactate dehydrogenase, leukaemia, Total leucocyte count.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Leukaemias are fatal malignant disorders characterized by increased numbers of white blood cells in the bone marrow and peripheral blood. [1]

Leukaemias are classified as either acute or chronic depending on clinical course and lymphoblastic or myeloblastic depending on the cell line predominantly involved. The four types of leukaemia are acute myeloblastic leukaemia (AML), acute lymphoblastic leukaemia (ALL), chronic myeloblastic leukaemia (CML) & chronic lymphoblastic leukaemia (CLL).

AML shows male preponderance. ALL is a predominant disease occurring in children, with highest incidence at 2- 6 yrs. of age. A second peak incidence can occur in elderly. CLL & CML occur mainly in Middle Ages & elderly. [2]

Uric acid a biological substance has been found to be raised in malignancies explained by rapid cell turn-over of malignant cells. It is major catabolic product of purine nucleosides adenosine and guanosine. Catabolism of dietary nucleic acid results in conversion of purine to uric acid directly. [3]

Uric acid is an antioxidant in the extracellular environment. It acts as a scavenger of oxygen radicals & reduce carcinogenic reactive oxygen species. [4] As a pro-oxidant, it has pro-oxidative effects in the intracellular environment. [5] Uric acid contributes to Tumorigenesis by entering normal cells and promoting tumor cell proliferation, migration, and survival, mediated by ROS and inflammatory stress. [6]

Lactate dehydrogenase (LDH), a pyridine-linked enzyme is present in cell cytoplasm of all human tissues. It has function in metabolism of glucose catalyzing the reduction of free pyruvate to lactate during the last step of glycolysis, as well as the lactate to pyruvate during

gluconeogenesis. [7] Highest levels are observed in liver followed by skeletal muscle, heart and kidney. LDH activity is present in all cells of the body and is invariably found in the cytoplasm of the cell. Leakage of the enzyme from even a small mass of damaged tissue increases the serum activity of LDH to a significant extent. As cells get damaged LDH is released in blood. In malignancies, increased tissue destruction takes place thus, elevated serum LDH levels can be noted. This has been supported in studies done by Emad A Al-Saadoon et al. [8], Saharia GK et al [9] & Sharma K et al [10].

In order to have a better prognosis repeated investigations & bone marrow examination, biochemical tests need to be undertaken to keep a check on the prognosis, Serum LDH & uric acid levels have gained considerable attention in this regard as being cost effective & easily available. Thus, this study was undertaken with the basic objective of estimation of Serum LDH & uric acid levels in leukemic patients.

Material and Methods

The present study recruited 60 patients who were diagnosed as leukaemic (acute or chronic, lymphoid or myeloid) patients of either sex, admitted in Department of Medicine of our Hospital from Dec 2021 to May 2022. Patients with previous history of chemotherapeutic drugs & who didn't give consent were excluded. An approval sought from institutional ethics committee & written informed consent taken from patients. For all the patients CBC, TLC, Hb% serum LDH and serum uric acid levels were estimated.

Parameters studied:

1. Serum uric acid levels –The Quantification of the levels of serum uric acid was undertaken using a semiautomatic analyser. Normal

reference values taken were serum 3.5-7.2 mg/dL in males 2.6-6.0 mg/dL in females.

2. Serum LDH levels - The Quantification of the levels of serum LDH was undertaken using a semiautomatic analyser. Normal reference values taken were 230- 460 U/L at 37 °C.
3. Correlation between Serum uric acid & LDH levels with TLC.

Collection of blood sample: Under aseptic precautions 3ml of blood was collected from antecubital vein of study subjects with disposable needle & syringe. The blood was allowed to clot for 30 minutes in a clean dry test tube and centrifuged at 3000 rpm for 3 minutes. The separated serum was used to quantify serum LDH and serum uric acid levels. Serum with slightest evidence of hemolysis was discarded.

Statistical Analysis

The collected data was tabulated in excel spreadsheet & put to statistical analysis. The data was expressed as mean and standard deviation & percentage. Association between the various parameters was analyzed using Chi-square test. P value <0.05 was considered statistically significant.

Results

Out of 60 leukaemic patients maximum patients were within 21-30 years age range, mean±SD being 41.67±18.24 years with 57% males & 43% females. The commonest type of leukaemia was CML (54%), followed by AML (22%), CLL (13%) and ALL (11%). High Hb% was observed in CLL type & lowest in ALL. Mean TLC observed was 48660 (mm³). Low TLC values were observed in acute type of leukaemias while higher values in chronic leukaemias. Mean serum uric acid was found to be 7.83±1.82 mg/dl with 64% of the leukemic patients with serum uric acid concentration >7.2 mg/dl.

Maximum rise in serum uric acid levels were observed in AML followed by CML, ALL and CLL type. Statistically significant difference was observed in the mean serum uric acid concentrations within different types of leukaemia (p<0.05). On Chi square correlation analysis at 95% confidence interval, comparing mean serum uric acid levels within different types of leukaemias. Statistically significant difference was noted between all the different types of leukaemias, when comparing mean serum uric acid levels except between ALL & CLL. (p>0.05).

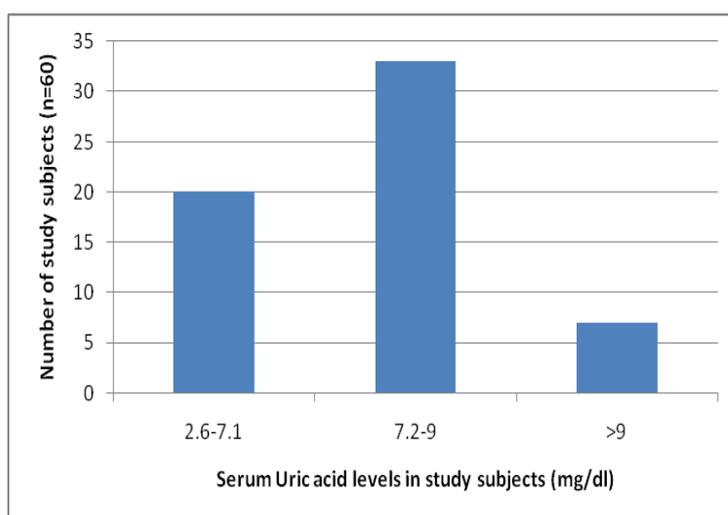


Figure 1: Distribution of subjects in relation to Serum uric acid levels

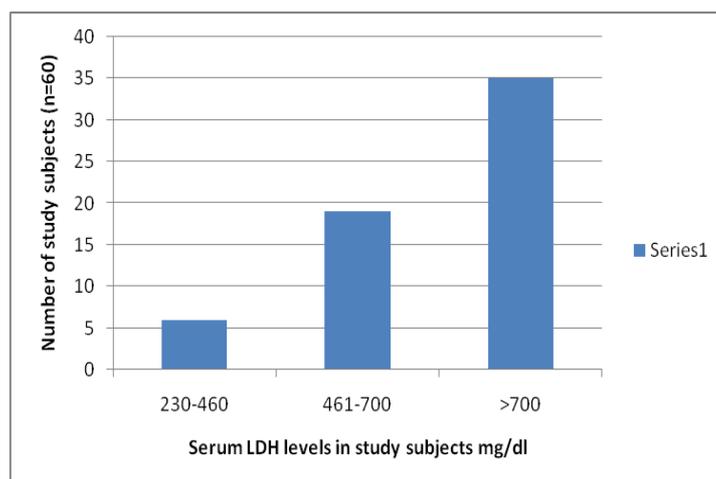


Figure 2: Distribution of subjects in relation to Serum LDH levels

Mean LDH level in the study subjects was 801.07 ± 202.54 IU/L. In 89% of study subjects Serum LDH was above normal range i.e., >460 IU/L. On Chi-square correlation analysis at 95% confidence interval, comparing mean serum uric acid levels within different types of leukaemias. Statistically, significant difference was noted between all the different types of leukaemias, when comparing mean serum LDH levels except between AML & CML. ($p > 0.05$).

A strong correlation between increased TLC levels and mean serum uric acid & LDH levels were observed ($p < 0.05$). Also, the notable association between serum uric acid and serum LDH was observed which was statistically significant.

Discussion

In the present study, maximum patients were within 21-30 years age range, mean \pm SD being 41.67 ± 18.24 years with 57% males & 43% females. Similarly in another study done by Sharma K et al 2020.[10] mean age of patients was 42.98 ± 20.44 years with male preponderance. Other similar studies were Saharia GK et al [9], AK Siraj et al [11], S. Ghosh et al [12] and Yiu A et al [13].

In the present study, commonest type of leukaemia was CML (54%), followed by AML (22%), CLL (13%) and ALL (11%).

High Hb% was observed in CLL type & lowest in ALL. Similarly, Sharma K et al 2020 study observed 52% CML & 12 % ALL cases. [10]

Mean TLC observed was 48660 (mm^3). Low TLC values were observed in acute type of leukaemias while higher values in chronic leukaemias. Similar observations noted in Sharma K et al study 2020. [10]

Mean serum uric acid was found to be 7.83 ± 1.82 mg/dl with 64% of the leukemic patients with serum uric acid concentration >7.2 mg/dl. Similarly, in Sharma K et al study 2020, mean serum uric acid levels of 7.69 ± 1.02 mg/dl were observed.[10] Saharia GK et al noticed mean levels to be 8.92 mg/dL with 83.3% of patients having levels above the normal range. Noted higher serum uric acid level in this study could be explained by increased turnover of malignant cells resulting in increased nucleic acid catabolism & purine catabolism .[9]

In the present study, maximum rise in serum uric acid levels were observed in AML followed by CML, ALL and CLL type. Statistically significant difference was observed in the mean serum uric acid concentrations within different types of leukaemia ($p < 0.05$). On Chi square correlation analysis at 95% confidence interval, comparing mean serum uric acid levels within different types of leukaemias.

Statistically significant difference was noted between all the different types of leukaemias, when comparing mean serum uric acid levels except between ALL & CLL. ($p > 0.05$). Similar results noted by Sharma K et al 2020 where statistically significant difference noted between the four types of leukaemia ($p < 0.001$). A strong correlation was noted between increased TLC levels (11000-100000 and above 100000 TLC Levels) & mean serum uric acid.¹⁰ Although Yamauchi et al. observed only 14.3% of the patients with hyperuricemia, the higher uric acid concentrations reflect burden of AML blasts or proliferating potential.^[14]

In a study conducted in 1,180 patients with AML Tsimberidou et al. evaluating the prognostic factors noted higher uric acid levels & LDH to be >1.5 -times above normal range indicating these parameters to be independent predictors of poor prognosis in more than 60 yrs. of age.¹⁵ In chronic granulocytic leukaemia, high uric acid production is due to increased nucleic acid "turnover" and the attendant enhancement of de novo purine biosynthesis. In CLL, "recycling" of polynucleotides is associated with normal uric acid production. ^[16]

In the present study, mean LDH level was 801.07 ± 202.54 IU/L. In 89% of study subjects Serum LDH was above normal range i.e. >460 IU/L. In Saharia et al study, mean LDH concentration was 774.2 IU/L, with 96.6% of patients in the above normal range. Highly significant difference in the mean value of serum LDH concentrations observed at diagnosis time between the leukemic patients and control group ($p < 0.0001$) with significant reduction after one month of chemotherapy. ^[9] Accordingly, Sharma K et al noted mean LDH levels to be 794.07 ± 227.62 IU/L with 90% of leukaemic cases with LDH levels above normal range ($230-460$ IU/L).¹⁰ Similar results obtained by Emad A Al-Saadoon et al ⁸ and Hafiz MG et al.¹⁷ Higher LDH

levels indicate increased cell destruction due to cytokine activity resulting from under rapid proliferation and immaturity of tumor cells. Physiological stress affects altered enzyme production rate or defect in the permeability of the cell membrane.^[7]

On Chi square correlation analysis at 95% confidence interval, comparing mean serum LDH levels within different types of leukaemias. Statistically significant difference was noted between all the different types of leukaemias, when comparing mean serum LDH levels except between AML & CML ($p > 0.05$). Maximum increase in serum LDH levels were noted in ALL, followed by CML, AML CLL type. Similar results noted by Kornberg and Polliack et al ¹⁸ & Sharma K et al^[10].

A strong correlation between Serum uric acid levels & Serum LDH levels with TLC counts was observed which can be explained by the rapid rate of cell turn over in leukaemics. Similar observations noted by Golam H et al ^[19] and Emad et al ^[8].

Conclusion

Leukaemia presets with high mortality and morbidity & extant as a major challenge to the clinicians. Timely diagnosis & intervention may prolong the life expectancy of patients. Laboratory evaluation of Serum uric acid and LDH levels are readily accessible to determine the prognosis of disease. AML type of leukaemia with high TLC had highest elevated serum uric acid levels followed by CML. Highest elevated serum LDH levels were observed in ALL type followed by CML. Thus, patients presenting with raised TLC along with hypercellular bone marrow and elevated serum uric acid and LDH levels have poorer prognosis in comparison to other leukaemia patients.

References

1. Craig JIO, McClelland DBL, Ludlam CA. Blood disorders: Functional

- anatomy, physiology and investigations In Davidson's principles and practice of Medicine. 20th ed. Elsevier Publications, Chapter 24: 2007; 889.
- Harendra Modak, Suyamindra S Kulkarni, Kadakol GS, Hiremath SV, Patil BR, Umesh Hallikeriet al. Prevalence and Risk of Leukaemia in the Multi-ethnic Population of North Karnataka. *Asian Pacific J Cancer Prev.* 2011; 12:671-75
 - Teitz Textbook of Clinical Chemistry and Molecular Diagnostic. 4th ed, Elsevier Saunders, 2006:601, 803–805.
 - Jacob F, Reaman G H, Sposto R, Sensel MG. Treatment outcome and prognostic factors for infants with acute lymphoblastic leukaemia, *Journal of Clinical Oncology.* 1994;17:445.
 - Mathieu M, Artur Y, Aubry A, Bailly M, Braun JP, Bretauiere JP et al. Recommendations for determining the catalytic concentration of lactate dehydrogenase in human serum at +30 °C. *Ann Biol Clin.* 1982; 40:87-164.
 - Wakui M, Kuriyama K, Miyazaki Y, Hata T, Taniwaki M, Ohtake S, et al. Diagnosis of acute myeloid leukaemia according to the WHO classification in the Japan Adult Leukaemia Study Group AML-97 protocol. *Int J Hematol.* 2008;87:144–151.
 - Puc CH, Dodge R K, Dahl G V et al. Serum lactic dehydrogenase level has prognostic value in childhood acute lymphoblastic leukaemia. *Blood.* 1985; 66: 778-782
 - Emad A Al-Saadoon, Lamia M Al-Naama, Janan KH. Serum lactate dehydrogenase (LDH) activity in children with malignant diseases. *Bahrain Medical Bulletin.* 2003; 25:1-7.
 - Saharia GK, Barua LB, Bhattacharyya K. Utility of serum lactate dehydrogenase and uric acid concentrations as prognostic indices for leukaemia patients under chemotherapy in a tertiary care hospital of Assam. *Int J Health Sci Res.* 2015; 5(4):152-158.
 - Sharma K, Mehra V, Paul S, Singh P, Bagga PK & Sharma D. To study levels of serum lactate dehydrogenase and serum uric acid in patients suffering from Leukaemias. *International Journal of Clinical and Diagnostic Pathology* 2020; 3(1): 242-247
 - Siraj AK, Kamat S, Gutiérrez MI, Banavali S, Timpson G, Sazawal S *et al.* Frequencies of the major subgroups of precursor B-cell acute lymphoblastic leukaemia in Indian children differ from the West. *Leukaemia.* 2003; 17(6):1192-1193.
 - Ghosh S, Shinde SC, Kumaran GS, Sapre RS *et al.* Haematologic and immunophenotypic profile of acute myeloid leukaemia: An experience of Tata Memorial Hospital. *Indian J Cancer.* 2003; 40(2):71-76.
 - Yiu A, Van Hemelrijck M, Garmo H *et al.* Circulating uric acid levels and subsequent development of cancer in 493,281 individuals: findings from the AMORIS Study. *Oncotarget.* 2017; 8(26):42332-42342. doi: 10.18632 / oncotarget. 16198.
 - Yamauchi T, Negoro E, Lee S, Takai M, Matsuda Y *et al.* A high serum uric acid level is associated with poor prognosis in patients with acute myeloid leukaemia. *anticancer research.* 2013; 33:3947-3952.
 - Tsimberidou AM, Kantarjian HM, Wen S, O'Brien S, Cortes J, Wierda WG *et al.* The prognostic significance of serum β 2 microglobulin levels in acute myeloid leukaemia and prognostic scores predicting survival: Analysis of 1,180 patients. *Clin CancerRes.* 2008; 14:721-730.
 - Irwin H. Krakoff and M. earlbalis. Abnormalities of purine metabolism in human leukaemia. *Ann N Y Acad Sci.* 1964; 28:113:1043-52.
 - Hafiz MG, Rahman MM, Mannan MA. Serum lactate dehydrogenase as a prognostic marker of childhood acute

- lymphoblastic leukaemia. Mymensingh Med J. 2008; 17(2):169-173.
18. Kornberg A, Polliack A. Serum lactic dehydrogenase levels in acute leukaemia: Marked elevations in lymphoblastic leukaemia. Blood. 1980; 56:351-55.
19. Golam H Mannan. Serum lactate dehydrogenase level in childhood acute lymphoblastic leukaemia. Bangladesh Med Res Counc Bull. 2007; 33:88-91.