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Significance of Serum Uric Acid and Lactate Dehydrogenase as An Indicator of Severity in Acute Amyloid Leukemia

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ABSTRACT

Objective: To estimate the serum level of uric acid in severe acute amyloid leukemia and to measure the high lactate dehydrogenase levels contributing in severity of acute amyloid leukemia. **Study Type:** It was Cross Sectional comparative study. **Methodology:** Out of 90 individuals of age 5 to 15 years, the mean age of participants in group A, group B, and group C was 10.53 ± 2.5, 10.5 ± 2.47 and 10.13 ± 2.501 respectively in Sheikh Zaid Hospital Lahore and Mayo Hospital Lahore. Blood uric acid and lactate dehydrogenase was evaluated by standard techniques spectrophotometer in the laboratory. All data collected was subjected to SPSS version 23. A relationship of serum uric acid and lactate dehydrogenase was calculated to see their significance in predicting the severity of disease subjected to statistical analysis. The quantitative variables like age were presented as mean ± SD. Prevalence was analyzed by Anova test, f value ≤ 0.005 will be taken as significant. **Results:** In Group A, 43.3% were males and 56.7% females, with a mean age of 10.53 years. Group B had 46.7% males and 53.3% females, with a mean age of 10.50 years, while Group C had 46.7% males and 53.3% females, with a mean age of 10.13 years. Significant differences were observed in uric acid, LDH, and WBC levels among the groups ($p = 0.000$). The ANOVA test confirmed a strong association among all groups. **Conclusion:** In conclusion, monitoring serum uric acid, LDH levels and WBC count is crucial in assessing the prognosis and mortality risk in patients with acute leukemia, particularly AML. Elevated LDH levels serve as a valuable prognostic indicator, especially in guiding treatment decisions and risk assessment for leukemic candidates.

INTRODUCTION

The term "leukemia" refers to malignant conditions of the hematopoietic stem cell compartment that are characterized by an accumulation of white blood cells in the bone marrow and peripheral circulation (Yamauchi et al., 2013). Myeloid cell cancer known as acute myeloid leukemia (AML) is characterized by the explosive growth of leukemic blasts that build up in the bone marrow and invade the entire body (Yamauchi et al., 2013). Acute myeloid leukemia (AML) is a multifaceted and severe hematological malignancy defined by the rapid proliferation of aberrant myeloid cells in the bone marrow, leading to decreased blood cell generation and infiltration into multiple tissues.(Arber, 2018; Behrmann et al., 2018). Clinical management of AML necessitates accurate prognostic indicators to guide treatment decisions and improve patient outcomes (Sekeres et al., 2020).

The elderly are more susceptible to developing acute myeloid leukemia (Waggoner M et al 2020) by which Males are somewhat more likely than females to get AML (Sharma et al.). In order to assess the prognosis of leukemia, biochemical tests such serum lactate dehydrogenase (LDH) activity and uric acid concentration have simultaneously grown in significance (Wang et al., 2021). In recent years, the role of serum uric acid (SUA) and lactate dehydrogenase (LDH) as potential indicators of disease severity in AML has garnered significant attention in the medical community (Udgiri et al.).

In AML, several prognostic factors have been identified, including age, performance status, cytogenetic abnormalities, and molecular mutations (Gbadamosi et al., 2018). In recent years, serum uric acid (SUA) and lactate dehydrogenase (LDH) have emerged as potential prognostic factors in AML. Serum uric acid (SUA) is a byproduct of purine metabolism, and LDH is an enzyme that is found in many tissues, including the liver, kidneys, and muscles (Nunes, 2018). Elevated SUA levels have been associated with an increased risk of relapse and death in AML patients. SUA is a byproduct of purine metabolism, and purines are essential for DNA synthesis. Therefore, elevated serum uric acid (SUA) levels may reflect increased cell proliferation, which is a hallmark of cancer (Chen & Meng, 2022).

Serum uric acid (SUA) is also a pro-inflammatory molecule, and inflammation has been linked to cancer progression. Serum uric acid (SUA) can also contribute to oxidative stress, which is a state of damage caused by free radicals. Oxidative stress has been implicated in cancer development and progression (Jelic et al., 2021). Elevated LDH levels are also associated with an increased risk of death in AML patients. This is thought to be due to the fact that LDH is released into the bloodstream when cells are damaged or die. Therefore, elevated LDH levels may reflect the extent of tumor burden and tissue damage (Cure & Cure, 2020).

Typical degrees of uric corrosive in people range from 2.5-7.0 mg/dL and 1.5-6.0 mg/dL, separately. Uric corrosive is a finished result of purines digestion and is heterocyclic natural compound that is available in pee and blood and delivered in the kidneys, liver, digestive system, and vascular endothelium. Uric acid protects neuronal cells and promotes brain development by inducing inflammatory responses (Saeed et al., 2022). Serum lactate dehydrogenase (LDH) values are used to predict the prognosis of AML (Xiao et al., 2021).

Similarly, LDH, an enzyme involved in cellular respiration and energy production, has gained recognition as a crucial marker of cellular damage and metabolic dysregulation in various malignancies, including AML (Al Ageeli, 2020). Lactate dehydrogenase (LDH) and erythropoietin levels are expanded in AML patients, as are liver boundaries, renal boundaries (counting uric acid). In AML more, elevated levels of youthful forebear cell expansion bring about elevated degrees of purine catabolism, which raises blood uric corrosive levels. Therefore, high serum levels of uric acid may serve as a biomarker for disease aggressiveness and a prognostic indicator in AML patients (Coiffier et al., 2008; Saeed et al., 2022).

Serum uric acid levels in patients with AML were examined in serum urine, plasma. However, serum and plasma are more relevant than other electrochemical sensors for uric acid detection, such as nonporous gold modified electrodes (Sukanya & Mohanan, 2018). Furthermore it has been discovered that even a tiny quantity of the LDH enzyme released from the injured tissue has the power to raise the LDH enzyme to higher levels (Anitha et al., 2022).

The combination of serum uric acid and lactate dehydrogenase as complementary biomarkers holds significant promise in accurately assessing the severity of acute amyloid leukemia (AML), guiding risk stratification, and tailoring personalized treatment strategies for patients. Understanding the dynamic relationship between these biomarkers and disease progression is paramount in enhancing the clinical management and overall prognosis of acute amyloid leukemia (AML) patients.

MATERIAL AND METHODS

It was a cross sectional comparative study. The sample was collected from Sheikh Zaid Hospital Lahore and Mayo Hospital Lahore from January 2024 to June 2024. The sample size was 90 individuals aged 30 to 50 years which were statistically estimated by using 5% level of significance. The total samples in the study were divided into three groups with 30 individuals. The sample size for the study was calculated based on the following formula:n = (Z^2 * P * (1-P)) / E^2 , for this study, the sample size was calculated as: n = 90 in each group. The blood uric acid and lactate dehydrogenase were evaluated using a **spectrophotometer** in the laboratory with the help of a kit. The kit used for the evaluation of serum lactate dehydrogenase was the **LDH (P -L)** kit with normal reference values. The kit contained the uric acid reagent and uric acid standard for the evaluation of serum uric acid. The blood samples were processed using standard techniques and the results were obtained using the kit (Luo et al., 2002).

The study consists of three groups, Group A was the control group comprising of 30 normal individuals without leukemia but will be tested for serum uric acid and lactate dehydrogenase. Group B was comprising of 30 individuals suffering from severe leukemia with high uric acid taken from medicine OPD of sheikh Zaid hospital and Mayo hospital Lahore and Group C was comprise of 30 individuals suffering from severe leukemia with high lactate dehydrogenase taken from medicine OPD of sheikh Zaid hospital and Mayo hospital Lahore. Blood samples were analyzed by using spectrophotometer-uv of the patients with acute amyloid leukemia with WBC count taken as a standard of severity ≥ 50,000 per micro liter by using enzymatic kit supplied by pharmaceutical.

Individuals suffering from severe acute amyloid leukemia with high serum uric acid and lactate dehydrogenase were included. Normal individuals / non-diseased, patients having other diseases as diabetes, hypertension etc and patients taking antibiotics or antiviral medications were excluded. The Patient records

were taken from sheikh Zaid hospital and Jinnah hospital Lahore. The individuals included in groups were identified on the basis of their record and information taken from the Performa. These patients in experimental and control groups was asked to give their written consent personally to donate a blood sample for testing. All data collected was subjected to SPSS version 23. A relationship of UA and LDH were calculated to see their significance in predicting the severity of disease subjected to statistical analysis. The quantitative variables like age was presented as mean ± SD. Prevalence was analyzed by ANOVA test, f value ≤ 0.005 were taken as significance.

RESULTS

The results indicates that in Group A, 43.3% were males and 56.7% were females, with a mean age of 10.53 years. The mean uric acid level was 4.99, LDH level was 178.10, and WBCs level was 7.82. Group B had 46.7% males and 53.3% females, with a mean age of 10.50 years. The mean uric acid level was 7.68, LDH level was 472.47, and WBCs level was 47.80. In Group C, 46.7% were males and 53.3% were females, with a mean age of 10.13 years. The mean uric acid level was 8.17, LDH level was 569, and WBCs level was 53.9. The comparison showed differences in uric acid levels (4.99 in Group A, 7.68 in Group B, and 8.17 in Group C), LDH levels (178.10 in Group A, 472.47 in Group B, and 569 in Group C), and WBCs levels (7.82 in Group A, 47.80 in Group B, and 53.9 in Group C) among the groups. The Anova test was applied and it shows significant association among all groups as p = 0.000 (≤ 0.05).

Table 1

Comparison of Uric acid level among Group A, Group B and Group C.

	Mean	N	Std. Deviation	Minimum	Maximum	Sig.
Uric Acid Level Group A	4.9967	30	.65151	4.10	6.20	
Uric Acid Level Group B	7.6800	30	.82186	6.20	9.30	0.000
Uric Acid Level Group C	8.1667	30	.62219	7.20	9.90	

In the comparison of group, A, B and C with equal number of 30 participants, the mean of uric acid in A was (4.99 ± 0.65) compared to group B and C which was (7.68 ± 0.82) and (8.16 ± 0.622) respectively. The standard deviation of uric acid level was 0.65, 0.82 and 0.62 in group A, B and C respectively. The Anova test was applied and it shows significant association among all groups as p = 0.000 (≤ 0.05).

Table 2

Comparison of LDH level of Group A, Group B and Group C.

	Mean	N	Std. Deviation	Minimum	Maximum	Sig.
LDH Level (U/L) Group A	178.1000	30	19.25035	141.00	231.00	
LDH Level (U/L) Group B	472.4667	30	42.22496	401.00	562.00	0.000
LDH Level (U/L) Group C	569.1333	30	41.62868	469.00	669.00	

In the comparison of group, A, B and C with equal number of 30 participants, the mean of LDH level in A was (178.1 ± 19.25) compared to group B and C which was (472.4 ± 42.22) and (569.1 ± 41.62) respectively. The standard deviation of LDH level was 19.25, 42.22 and 41.62 in group A, B and C respectively. The Anova test was applied and it shows significant association among all groups as p = 0.000 (≤ 0.05).

Table 3

Comparison of WBC's level of Group A, Group B and Group C.

	Mean	N	Std. Deviation	Minimum	Maximum	Sig.
WBCs Level (mg/dL) Group A	7.8200	30	2.01980	3.30	10.10	
WBCs Level (mg/dL) Group B	47.8097	30	5.94809	33.21	59.60	0.000
WBCs Level (mg/dL) Group C	53.9030	30	3.87146	48.55	63.50	

In the comparison of group A, B and C with equal number of 30 participants, the mean of WBC'S level in A was 7.82 compared to group B and C which was 47.80 and 53.90 respectively. The standard deviation of WBC's level was 2.01, 5.94 and 3.87 in group A, B and C respectively. The Anova test was applied and it shows significant association among all groups as p = 0.000 (≤ 0.05).

Table 4

Post Hoc Test

Multiple Comparisons							
Tukey HSD							
Dependent Variable	**(I) gender**	**(J) gender**	**Mean Difference (I-J)**	**Std. Error**	**Sig.**	**95% Confidence Interval**	
						Lower Bound	**Upper Bound**
Uric Acid Level	GROUP A	GROUP B	-2.68333*	.18178	.000	-3.1168	-2.2499
		GROUP C	-3.17000*	.18178	.000	-3.6035	-2.7365
	GROUP B	GROUP A	2.68333*	.18178	.000	2.2499	3.1168

	GROUP C	GROUP C	-.48667*	.18178	.024	-.9201	-.0532
		GROUP A	3.17000*	.18178	.000	2.7365	3.6035
		GROUP B	.48667*	.18178	.024	.0532	.9201
LDH Level (U/L)	GROUP A	GROUP B	-294.36667*	9.29333	.000	-316.5264	-272.2069
		GROUP C	-391.03333*	9.29333	.000	-413.1931	-368.8736
	GROUP B	GROUP A	294.36667*	9.29333	.000	272.2069	316.5264
		GROUP C	-96.66667*	9.29333	.000	-118.8264	-74.5069
	GROUP C	GROUP A	391.03333*	9.29333	.000	368.8736	413.1931
		GROUP B	96.66667*	9.29333	.000	74.5069	118.8264
WBCs Level (mg/dL)	GROUP A	GROUP B	-39.98967*	1.09998	.000	-42.6125	-37.3668
		GROUP C	-46.08300*	1.09998	.000	-48.7059	-43.4601
	GROUP B	GROUP A	39.98967*	1.09998	.000	37.3668	42.6125
		GROUP C	-6.09333*	1.09998	.000	-8.7162	-3.4705
	GROUP C	GROUP A	46.08300*	1.09998	.000	43.4601	48.7059
		GROUP B	6.09333*	1.09998	.000	3.4705	8.7162

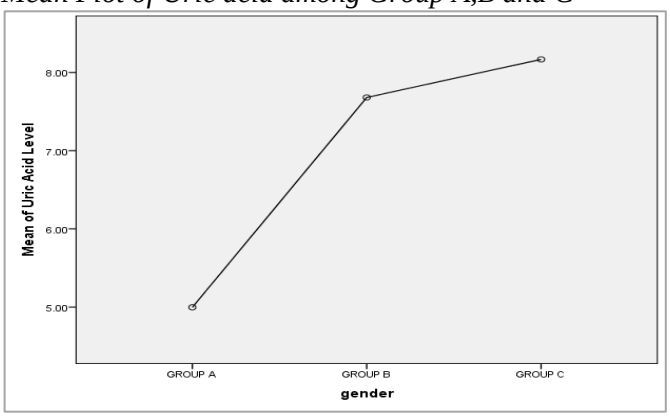
*. The mean difference is significant at the 0.05 level.

The table 4 shows results Post Hoc statistical analysis comparing three groups (A, B, and C) on multiple factors (uric acid level, LDH level, WBCs level). Tukey's HSD method was used to account for multiple comparisons and ensure reliable results.

- **Uric Acid Level:** There is a significant difference in uric acid level between GROUP A and GROUP B (mean difference: -2.68) and between GROUP C and GROUP B (mean difference: -3.17). This suggests that GROUP B has a lower uric acid level compared to both GROUP A and GROUP C.
- **LDH Level:** There is a significant difference in LDH level between all three groups. GROUP A has a significantly lower LDH level compared to both GROUP B (mean difference: -294.37) and GROUP C (mean difference: -391.03). GROUP B also has a significantly higher LDH level compared to GROUP C (mean difference: 294.37).
- **WBCs Level:** There is a significant difference in WBCs level between all three groups. GROUP A has a significantly lower WBCs level compared to both GROUP B (mean difference: -39.99) and GROUP C (mean difference: -46.08). GROUP C also has a significantly lower WBCs level compared to GROUP B (mean difference: 39.99).

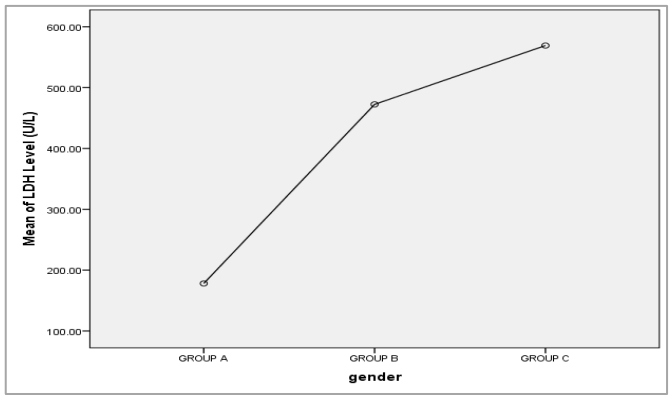
Graph 1

Mean Plot of Uric acid among Group A,B and C



Graph 2

Mean Plot of LDH levels among Group A,B and C



Graph 3

Mean Plot of WBC samong Group A,B and C

Overall , the results in mean plot graphs revealed significant differences among all three groups as , Group B has a lower uric acid level compared to groups A and C. Group A has a lower LDH level compared to groups B and C, and group B has a higher level than C. Group A has a lower WBCs level compared to groups B and C, and group C also has a lower level than B.

DISCUSSION

Jumaah MH et al., in 2021 whether hematopoietic lacking cell transplantation (HSCT) is connected with gigantic changes in serum UA levels in patients with hematological issues. Whether hematopoietic undifferentiated cell transplantation (HSCT) is associated with stepped changes in serumU A levels in

hematological patients. The results of the study supported level of serum biomarkers (blood urea, creatinine) for patients with AML (58.82+1.49 1.831+0.05 8.34+0.15 mg/dl, respectively) were significantly higher (p< 0.01) in comparison to the control (31.10 Beyond that, the LDH' level was found to be significantly higher (p< 0.01) in the AML group (657.72±80.76 U/L) as compared to the control group (166.05±6.15 U/L). The results of a comparison between our study and another show standard deviation of LDH levels in groups A, B, and C as ~19.25, ~42.22 and ~41.62 respectively. On the other hand , the average of uric acid in A was 4.99 and the rest were 7.68 and 8.16 in comparison (Jumaah et al., 2021).

Saeed U et al., in 2022 performed Proficient electrochemical detecting of uric corrosive as potential biomarker in intense myeloid leukemia patients. The result showed, Ce-MOF-400 °C-GCE had the higher power of electricity than Ce-MOF-GCE. The Ce-MOF-400 °C-GCE is optimized for uric acid determination with respect to different concentrations, different scan rates and also in varying pH in 0.1 M PBS. Whereas in our study, standard deviation of uric acid level was found to be 0.65, 0.82, and 0.62 in group A, B, and C, respectively. It reveals that there is a higher association of uric acid level patients with acute myeloid leukemia (Saeed et al., 2022).

Abdalla AA et al., in 2016 to assess the level of AST, ALT, urea and creatinine among Sudanese patients with acute lymphocytic leukemia.Abbala AAA and colleagues, in 2016, to evaluate the serum activity of AST, ALT, urea and creatinine among Sudanese patients with acute lymphocytic leukemia. The study provided us with data showing significance in the rise of the levels of AST, ALT, urea, and creatinine among patients with acute lymphocyt The mean±SD was 73.0±42.2 U/L, 85.1±34.8), 40.9±22.8 and 1.4±0.88 mg/dl of ALL patients and was 32.5±8.5 U/L, 25.2±7.6, 29.2±9.1(Abdalla & Akasha). In contrast with our study, the mean of WBC'S level in A was 7.82 compared to group B and C which was 47.80 and 53.90 respectively. The standard deviation of WBC's level was 2.01, 5.94 and 3.87 in group A, B and C respectively .

Fikry MEW et al., assessed the degree of lactate dehydrogenase (LDH) in intense leukemia and researched its clinical importance with other hematological and clinical boundaries. Lactic dehydrogenase (LDH) level as well as platelets were set for examination - the analysts expressed. Concerning the LDH level, it is particularly raised in intense leukemia patients and ended up being the tremendous contrast between the benchmark group and the patient gathering, it is more critical increment also in the intense lymphoblastic leukemia bunch contrasted with the intense myeloid leukemia bunch (p< 0.001). In comparison to our study, the level of glomerular filtration (LDH) was on the rise with 178.1 in group A and had also increased in the next group which was 472.4 in group B and 569.1 in group C. The lactate dehydrogenases represented as a secondary enzymatic treatment tool make them differential diagnostic markers especially with different types of leukemia (Abdalla & Akasha, 2018).

M Geva et al., in 2021 in his study involving patients with acute leukemia, including acute myeloid leukemia (AML), serum LDH levels were significantly elevated compared to healthy controls. The study group consisted of 17 cases of ALL (9 were males and 7 were females, with mean age 34.4 ± 14.1years) , 33 cases AML(25 waren males and 8 were females, with mean age 43.3 ± 13.9 years) and 20 cases of healthy control(10 were males and 10 Seventy three samples were separated in to four groups according to age. While our research showed a balance between the mean age of group A (10.53+-2.5) and group B (10.5+- 2.47) ages for the former group were between 6 and 15 whereas for the latter the range was 6 to 15. On tHe other hand, group C had age that averaged at 10.13± 2.501 and their minimum age was 6 tallest ones being 15. Higher LDH levels were found in patients with acute lymphoblastic leukemia as well as non-LLZ patients. LDH is inversely associated with erythrocyte, and it evinces direct correlations with white blood cells and bone marrow blasts, as well as it decreases uric acid (Geva et al., 2021).

Zhenmu Jin et al., in 2021 conducted a study on COVID-19 patients revealed lower serum uric acid levels in severe cases compared to non-severe cases. In severe cases, higher LDH values showed a negative correlation with the oxygenation index. In this work we found a significant difference in serum albumin and prealbumin between the groups of patients with low and moderate severity (p<0.01), and we found a lower level of serum uric acid in the group of patients with severe form of the illness (p<0.05). However, in our study, the value of uric acid for group B was 7.68 and 8.16 for group C which was close to the result of another study where the mean of uric acid in their study was 4.99 (Jin et al., 2021).

Lyanger V et al., in 2021 conducted a studya and revealed Elevated WBC count is a common finding in leukemia, including acute amyloid leukemia. The leukemia cells can drive out normal blood cells in the bone marrow by succeeding over them, which increase the level of WBC. Differential examination made sense of on the distinctions that showed that LR were more neutrophil predominant(83% %vs.59%, p<0.01) and that "critical neutrophilia" (characterized as neutrophilia >90%) was 97% explicit (27% touchy) in distinctive LR from MM. Gentle eosinophilia (outright eosinophils >500/μL) and basophilia (outright basophils >200/μL) were 72% and 58% delicate and 80% and 95% explicit, separately, for MM. In examination with our review, the

mean of WBC'S level in A was 7.82 contrasted with bunch B and C which was 47.80 and 53.90 separately (Iyengar & Freed, 2021).

M Dwebi et al., in 2019 performed a study on patients with acute amyloid leukemia may exhibit significantly higher WBC counts compared to other types of leukemia or non-leukemic conditions. Hemoglobin9.6 g%, TLC474,300/mm 3 ,with immature Neutrophila combination totals, but considering the fact that CML is a relatively benign disease, it does not pose a serious risk to his major organs. On liver and kidney assignments heart tests were normal. Post-, PT/INR and APTT were not found to be significantly increased. Jantan's serum LDH was 859 and the serum uric acid count was 7. This is contradicting with an earlier study because we got similar results and calculated the standard deviation for group A, B and C that was 2.01, 5.94 and 3.87 (Dwebi & Cumber, 2019).

CONCLUSION

In conclusion, monitoring serum uric acid, LDH levels and WBC count is crucial in assessing the prognosis and mortality risk in patients with acute leukemia, particularly AML. Elevated LDH levels serve as a valuable prognostic indicator, especially in guiding treatment decisions and risk assessment for leukemic candidates. The study may be limited by a less time, potentially impacting the generalizability of the findings. Inconsistencies in how LDH levels are measured or recorded across studies could introduce variability and affect result comparability. Future studies should include a diverse range of patients with severe acute amyloid leukemia to ensure representation across different demographics, disease subtypes, and prognostic profiles. Perform multivariate analyses to account for potential confounding variables such as age, sex, comorbidities and treatment regimens that could influence the association between uric acid/LDH levels and disease severity.

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