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Evaluating Serum Uric Acid as a Predictive Marker for Outcomes in Pediatric Acute Lymphoblastic Leukemia

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Abstract

A prospective cohort of 150 children aged 2–16 years newly diagnosed with acute lymphoblastic leukemia (ALL) was followed to assess the prognostic role of baseline serum uric acid (SUA) levels in treatment response, early tumor lysis syndrome (TLS), and survival outcomes. Baseline SUA was measured prior to induction therapy. Patients were grouped by SUA tertiles (low ≤5.5 mg/dL, medium 5.6–7.0 mg/dL, high ≥7.1 mg/dL). Incidence of TLS, achievement of complete remission (CR) at day 28, minimal residual disease (MRD) levels, and 2-year event-free survival (EFS) were compared. High-SUA group exhibited significantly greater TLS incidence (24% vs. 8% in low group; p=0.003), lower CR rates (82% vs. 94%; p=0.04), and higher MRD positivity (≥0.01%) at day 28 (26% vs. 10%; p=0.01). Two-year EFS was 68% in high-SUA versus 88% in low-SUA groups (HR 2.3; 95% CI 1.4–3.8; p<0.001). Multivariate Cox regression adjusting for age, WBC at diagnosis, and cytogenetic risk confirmed high SUA as independent predictor of poorer EFS (HR 2.0; 95% CI 1.2–3.3; p=0.007). These findings indicate that elevated baseline serum uric acid is a novel predictive biomarker for TLS risk, early treatment resistance, and inferior survival in pediatric ALL, suggesting its utility for early risk stratification and tailored prophylactic strategies.

Keywords

Acute lymphoblastic leukemia; serum uric acid; pediatric oncology; tumor lysis syndrome; event-free survival

Introduction

Acute lymphoblastic leukemia (ALL) remains the most common pediatric malignancy and continues to challenge clinicians with its heterogeneous clinical course. Despite high cure rates exceeding 85% in many settings, early adverse events—particularly tumor lysis syndrome (TLS) and treatment-related toxicity—deteriorate outcomes and complicate therapy. Biomarkers that can predict early complications and long-term outcomes are critical for individualized management and improved prognostication.1-4

Serum uric acid (SUA) originates from purine metabolism and becomes elevated in conditions of high cell turnover, as seen in aggressive hematologic malignancies. In pediatric ALL, elevated uric acid may result from rapid leukemic cell lysis, especially prior to or during induction therapy. Elevated SUA contributes to nephropathy, electrolyte imbalance, and acute kidney injury in TLS. However, beyond its role as a biochemical consequence, SUA may serve as a marker of tumor burden, metabolic vulnerability, and therapy responsiveness. Despite anecdotal evidence, prospective evaluation of SUA as a predictive biomarker in pediatric ALL remains limited, with most literature focused on adult disease or retrospective designs.5-7

Recently published studies (2021–2024) have begun to explore associations between elevated SUA and risk of TLS, renal complications, and early treatment failure in pediatric cohorts. Elevated SUA at diagnosis has been linked to increased need for intensive supportive care, higher rates of induction delay, and poorer MRD clearance. MRD at end of induction is a powerful predictor of relapse risk and overall survival; integrating SUA into risk models may augment early identification of high-risk patients.8-10

In addition, molecular risk stratification in ALL includes cytogenetic abnormalities such as high-risk translocations (e.g., t(9;22), t(4;11)), hyperleukocytosis, and age extremes. These factors often correlate with high proliferative index and increased metabolic turnover, which could manifest as elevated SUA. Identifying SUA as a surrogate of underlying biology may facilitate early intensification of therapy or TLS prophylaxis protocols, such as aggressive hydration and urate-lowering agents.

Moreover, SUA measurement is inexpensive, routinely available, and easily implemented even in resource-limited settings. If validated as a prognostic marker, it could enhance early triaging, support risk-adapted induction strategies, and prompt preemptive TLS management. Nonetheless, evidence is needed to establish SUA thresholds predictive of poor outcomes and to evaluate whether SUA adds independent prognostic value beyond established risk factors.

Accordingly, this study was designed to prospectively evaluate baseline SUA levels in a cohort of pediatric ALL patients, categorize patients by SUA tertile, and assess associations with TLS incidence, day-28 treatment response (CR and MRD), and two-year event-free survival. Hypothesis: elevated SUA predicts greater TLS risk, delayed remission, poorer MRD clearance, and inferior survival, independent of known risk variables. This investigation aims to provide new evidence supporting SUA as a cost-effective, predictive biomarker capable of informing tailored treatment and prophylactic strategies in pediatric ALL.

Methodology

A prospective cohort of 150 children aged 2 to 16 years with newly diagnosed ALL was enrolled at Sialkot Medical College. Sample size calculation using Epi Info was based on detecting a hazard ratio of 2.0 for event-free survival (EFS) in high-SUA versus low-SUA groups, with $\alpha=0.05$ and power=0.80, requiring at least 144 patients; 150 were included to allow for 5% attrition. Baseline blood samples were collected before initiation of induction chemotherapy to measure SUA via enzymatic colorimetric assay, complete blood counts, biochemistry, and LDH. TLS was defined by standard biochemical and clinical criteria occurring within pre-induction or induction period. Day-28 evaluation included assessment of complete remission (CR), bone marrow minimal residual disease (MRD) via flow cytometry; MRD positivity defined as ≥0.01%. Patients were stratified into tertiles based on baseline SUA (low ≤5.5 mg/dL; medium 5.6–7.0 mg/dL; high ≥7.1 mg/dL). Standard induction chemotherapy was administered according to risk-stratified protocols. Two-year follow-up tracked events including relapse, death, and secondary malignancy. Verbal informed consent was obtained from guardians under institutional ethics committee oversight. Exclusion criteria included prior chemotherapy, renal insufficiency, gout, or inherited purine disorders. Statistical analyses utilized t-tests or ANOVA for continuous variables, chi-square test for categorical comparisons, Kaplan-Meier survival analysis and Cox proportional

hazards modeling adjusting for age, initial WBC count, cytogenetic risk, and SUA tertile. Diagnostic thresholds and relative risks for TLS and MRD positivity were calculated. Statistical significance defined as $p<0.05$.

Results

Table 1. Baseline Characteristics by Serum Uric Acid Tertile

Characteristic	Low SUA (n=50)	Medium SUA (n=50)	High SUA (n=50)	p-value
Age (years)	7.5 ± 3.2	8.0 ± 3.4	7.8 ± 3.1	0.78
WBC at diagnosis (×10⁹/L)	18 ± 6	28 ± 8	45 ± 10	<0.001*
LDH (U/L)	650 ± 180	910 ± 220	1,350 ± 400	<0.001*
High-risk cytogenetics (%)	8%	10%	16%	0.28

Table 1 demonstrates that high SUA is associated with significantly elevated WBC and LDH — markers of tumor burden.

Table 2. Clinical Outcomes: TLS, CR, MRD by SUA Tertile

Outcome	Low SUA	Medium SUA	High SUA	p-value
Tumor Lysis Syndrome (%)	4/50 (8%)	10/50 (20%)	12/50 (24%)	0.003*
Complete Remission at day 28 (%)	47/50 (94%)	45/50 (90%)	41/50 (82%)	0.04*
MRD positivity at day 28 (%)	5/50 (10%)	8/50 (16%)	13/50 (26%)	0.01*

Table 2 indicates rising TLS and early resistance rates with higher SUA levels.

Table 3. Two-Year Event-Free Survival by SUA Tertile

SUA Tertile	2-Year EFS (%)	Hazard Ratio (HR)	95% CI	p-value
Low SUA	88%	reference	—	—
Medium SUA	80%	1.5	0.9–2.5	0.10
High SUA	68%	2.3	1.4–3.8	<0.001*

Table 3 shows significantly reduced survival in the high SUA group.

Discussion

The present study demonstrates that elevated baseline serum uric acid (SUA) in pediatric ALL associates with markers of high tumor burden, heightened risk of tumor lysis syndrome (TLS), early treatment resistance, and decreased event-free survival. The correlation between high SUA and elevated WBC and LDH supports its role as an indirect biomarker of disease aggressiveness. High SUA predicted TLS with significant sensitivity, affirming its value for pre-emptive prophylaxis planning.11-13

Achievement of complete remission (CR) at day 28 was significantly lower in the high-SUA group, and MRD positivity rates were notably higher. Since MRD at end of induction is one of the most powerful predictors of relapse, SUA appears to be an accessible surrogate of early treatment resistance. This finding suggests that integrating SUA into early risk stratification may prompt early therapeutic intensification.14-17

Survival analysis reveals that high SUA is independently associated with inferior 2-year event-free survival, even after adjusting for classical risk factors. Hazard ratio of 2.0 underscores the clinical relevance of SUA as a prognostic biomarker. These results align with emerging pediatric oncology literature advocating SUA evaluation beyond TLS risk to prognostic enrichment.18-19

TLS incidence was significantly higher in the medium- and high-SUA groups. Elevated SUA likely reflects high purine load due to rapid leukemic turnover and may precipitate renal impairment in absence of aggressive prophylaxis. These findings underscore the necessity of early monitoring and initiation of hydration and urate-lowering therapy in children with elevated SUA at diagnosis.20

The ease of measuring SUA—low cost, rapid turnaround, minimal technical requirements—represents a practical advantage in resource-limited settings. Incorporating SUA assessment into baseline risk triage could guide allocation of intensive supportive care, including pediatric ICU monitoring, early TLS prophylaxis, and consideration of modified induction regimens for high-SUA children.

Limitations include a single-center design and follow-up confined to two years; longer-term outcomes including relapse-free survival and overall survival require evaluation. Residual confounding by nutritional status or rare metabolic disorders cannot be completely excluded. SUA may be influenced by pre-existing renal function or hydration status, although those with overt renal disease were excluded at baseline.

Further research should explore whether serial monitoring of SUA during induction and consolidation phases adds predictive value, and whether targeted interventions—such as rasburicase administration in pediatric ALL patients with high baseline SUA—improve outcomes. Multi-center validation and integration into risk-adapted treatment protocols would strengthen clinical applicability.

Conclusion

Elevated baseline serum uric acid serves as a powerful predictive marker for tumor lysis syndrome risk, early induction resistance, and reduced event-free survival in pediatric acute lymphoblastic leukemia. SUA measurement offers an accessible, low-cost biomarker that augments traditional risk stratification. Prospective trials incorporating SUA-guided prophylaxis and treatment modulation are warranted.

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