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A Comprehensive Mini Review of Clinical Biochemical Parameters in the Diagnosis of Acute Lymphoblastic Leukemia in Children

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ABSTRACT

Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy, accounting for up to 30% of all childhood cancers and approximately 80% of childhood leukemias. Despite advances in therapy, ALL remains a significant cause of pediatric cancer mortality, especially in low- and middle-income countries. This review synthesizes data from over fifty peer-reviewed studies to elucidate the role of clinical biochemical parameters—including liver enzymes, lactate dehydrogenase (LDH), uric acid, renal function tests, and proteomic biomarkers—in the diagnosis, prognosis, and monitoring of pediatric ALL. The review also discusses the impact of various treatment modalities on these parameters and highlights the integration of molecular genetics and minimal residual disease (MRD) detection in risk stratification and personalized therapy.

Keywords*: Acute lymphoblastic leukemia, Pediatric oncology, Biochemical markers.*

Article Information

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1. INTRODUCTION

Acute lymphoblastic leukemia (ALL) is the leading cancer in children, representing 25–30% of all pediatric malignancies and about 80% of childhood leukemias (1). While survival rates have improved (2), ALL remains a major cause of cancer-related mortality in children, particularly in resource-limited settings (3). The disease is characterized by the malignant proliferation of lymphoid progenitor cells in the bone marrow, resulting in hematopoietic failure and systemic complications. Clinical biochemical parameters are essential for diagnosis, risk assessment, monitoring therapy, and predicting prognosis (4,5).

2. Epidemiology and Pathogenesis

ALL predominantly affects children aged 2–5 years, with a slight male predominance. Etiology is multifactorial, involving genetic predispositions (e.g., Down syndrome) (6), environmental exposures (e.g., ionizing radiation), and acquired somatic mutations. Chromosomal abnormalities, such as t(12;21), hyperdiploidy (7), and the Philadelphia chromosome (BCR-ABL1), are key drivers of leukemogenesis and influence prognosis (8) .

3. Clinical Presentation

Symptoms of ALL reflect both marrow failure and extramedullary infiltration (9,10,11,12,13,14):

- Fatigue and pallor (anemia, 40–50%)
- Fever (60–70%)
- Bleeding and bruising (thrombocytopenia, 75%)
- Bone pain (23%)

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- Lymphadenopathy, hepatomegaly, splenomegaly
- CNS involvement: headaches, vomiting, cranial nerve palsies
- Mediastinal masses (more common in T-cell ALL)

4. Hematological and Biochemical Profiles

4.1 Hematological Parameters (15-21)

- **Hemoglobin:** Most children present with significant anemia (mean Hb <8 g/dL) .
- **Platelets:** Thrombocytopenia (<100,000/mm³) in ~75% .
- **White Blood Cell Count:** Variable; >50,000/mm³ in 20% (worse prognosis) .
- **Neutropenia:** Absolute neutrophil count <500/mm³ increases infection risk .

4.2 Biochemical Markers

Biochemical parameters are vital for assessing organ function, tumor burden, and therapy-related complications (22–24).

Table 1. Common Biochemical Markers in Pediatric ALL

ALT / AST	< 40 U/L	Elevated	Hepatic infiltration or drug toxicity
LDH	< 250 U/L	Markedly elevated	Tumor burden, poor prognosis
Uric Acid	< 7 mg/dL	Elevated	Risk of tumor lysis syndrome
Creatinine	0.5-1.2 mg/dL	Normal/Elevated	Renal function, therapy complications
Total Protein	6-8 g/dL	Decreased	Nutritional status, disease severity

- **Liver Enzymes (ALT, AST):** Elevated at diagnosis and during therapy, reflecting leukemic infiltration or drug toxicity (25).
- **LDH:** Markedly increased due to high cell turnover; correlates with tumor burden and prognosis.
- **Uric Acid:** Hyperuricemia is frequent, especially during induction therapy, and is a risk factor for tumor lysis syndrome (26).
- **Renal Function (Creatinine, Urea):** May be altered due to uric acid nephropathy or nephrotoxic drugs (27).
- **Electrolytes (Potassium, Phosphate, Calcium):** Imbalances signal tumor lysis syndrome and require urgent intervention (28).
- **Serum Proteins:** Hypoproteinemia is common, reflecting nutritional status and disease severity (29,30).
- **Malondialdehyde (MDA):** Marker of oxidative stress, significantly elevated in ALL patients (31).

5. Proteomic and Molecular Biomarkers

Recent advances have identified several proteins and genetic alterations as potential biomarkers for diagnosis, risk stratification, and targeted therapy (32–35).

Table 2. Selected Molecular and Proteomic Biomarkers in Pediatric ALL

Clusterin	Stress response protein	Risk stratification
ctDNA	Circulating tumor DNA	MRD/relapse monitoring
BCR-ABL1	Chromosomal translocation	Targeted therapy (TKI)
S100A9	Inflammation/progression	Prognosis, therapy response
Gelsolin	Cytoskeletal regulation	Disease progression

- **Clusterin, Ceruloplasmin, Apolipoproteins:** Differentially expressed in high- vs. low-risk ALL, may serve as prognostic markers (36-37).
- **Gene Fusions (e.g., KMT2A-TRIM29):** Define molecular subtypes and guide therapy (38).
- **ctDNA:** Non-invasive biomarker for monitoring MRD and relapse risk (39).

6. Prognostic Factors

Prognosis in pediatric ALL is determined by a combination of clinical, hematological, biochemical, and molecular features (40–42):

- **Age and WBC at Diagnosis:** 1–10 years and WBC <50,000/mm³ = better outcome.
- **Cytogenetics and Molecular Subtype:** Hyperdiploidy and t(12;21) are favorable; BCR-ABL1 and KMT2A rearrangements indicate higher risk.
- **Early Treatment Response:** Rapid clearance of blasts predicts remission and long-term survival.
- **Biochemical Markers:** Persistent elevation of LDH, uric acid, and liver enzymes may signal poor response or relapse.

7. Treatment and Monitoring

Standard therapy for pediatric ALL includes multi-agent chemotherapy, CNS prophylaxis, and, in selected cases, hematopoietic stem cell transplantation. Biochemical monitoring is essential throughout treatment to manage complications such as (43–51):

- **Tumor Lysis Syndrome:** Requires close monitoring of uric acid, electrolytes, and renal function.
- **Hepatotoxicity and Nephrotoxicity:** Regular assessment of liver and renal function to adjust therapy.
- **Minimal Residual Disease (MRD):** Molecular and proteomic markers, including ctDNA, are increasingly used for sensitive detection of residual leukemic cells and early relapse.

8. Long-Term Outcomes and Future Directions

Survival rates for pediatric ALL now exceed 85% in high-income countries, but outcomes remain suboptimal in resource-limited settings. Late effects of therapy, including cardiotoxicity, neurocognitive impairment, and secondary malignancies, are important considerations for survivorship care. Future research focuses on (51–60):

- **Personalized Therapy:** Integrating molecular and biochemical markers for individualized risk-adapted treatment.
- **Targeted Therapies:** Development of agents directed at specific genetic alterations (e.g., tyrosine kinase inhibitors for BCR-ABL1).
- **Non-Invasive Monitoring:** Use of ctDNA and proteomic profiles for early detection of relapse and therapy adjustment.

9. CONCLUSION

Acute lymphoblastic leukemia in children is a biologically and clinically heterogeneous disease. Integration of clinical, hematological, biochemical, proteomic, and molecular data is essential for optimal diagnosis, risk stratification, and management. Advances in biomarker discovery and molecular profiling promise to further improve outcomes and reduce treatment-related morbidity in pediatric ALL.

10. REFERENCES

1. Pui CH, Evans WE. Treatment of acute lymphoblastic leukemia. N Engl J Med. 2006;354(2):166-178.
2. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. N Engl J Med. 2015;373(16):1541-1552.
3. Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukaemia. Lancet. 2013;381(9881):1943-1955.
4. Pieters R, Carroll WL. Biology and treatment of acute lymphoblastic leukemia. Hematol Oncol Clin North Am. 2008;22(6):1197-1215.
5. Pui CH, Jeha S. New therapeutic strategies for the treatment of acute lymphoblastic leukaemia. Nat Rev Drug Discov. 2007;6(2):149-165.
6. Katz AJ, et al. Acute lymphoblastic leukemia: Incidence and survival in the

United States, 1975–2012. Cancer Causes Control. 2015;26(9):1389-1399.
7. Bhojwani D, Yang JJ, Pui CH. Biology of childhood acute lymphoblastic leukemia. Pediatr Clin North Am. 2015;62(1):47-60.
8. Moricke A, et al. Prognostic impact of age in children and adolescents with acute lymphoblastic leukemia: Data from the trial ALL-BFM 86. Blood. 2010;116(25):4679-4685.
9. Carroll WL, Raetz EA. Clinical and laboratory biology of childhood acute lymphoblastic leukemia. J Pediatr Hematol Oncol. 2005;27(3):123-126.
10. Silverman LB. Acute lymphoblastic leukemia in infancy. Pediatr Blood Cancer. 2014;61(1):4-7.
11. Borowitz MJ, et al. Prognostic significance of minimal residual disease in high risk B-ALL: A Children's Oncology Group Study. Blood. 2008;111(12):5477-5485.
12. Stanulla M, Schrappe M. Treatment of childhood acute lymphoblastic leukemia. Semin Hematol. 2008;46(1):52-63.
13. El-Baz HA, et al. Serum protein biomarkers in childhood acute lymphoblastic leukemia. Hematology. 2019;24(1):1-8.
14. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011;364(19):1844-1854.
15. Al-Hammami SA. Study of Some Biochemical Parameters in Iraqi Children with Acute Lymphoblastic Leukemia. Baghdad Sci J. 2015;12(2):173-183.
16. Wang X, et al. Molecular characterization and biomarker identification in pediatric B-cell acute lymphoblastic leukemia. J Clin Oncol. 2024;42(16_suppl):6524.
17. Mullighan CG, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. Nature. 2009;446(7137):758-764.
18. Roberts KG, et al. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. N Engl J Med. 2014;371(11):1005-1015.
19. Vrooman LM, Silverman LB. Childhood acute lymphoblastic leukemia: Update on prognostic factors. Curr Opin Pediatr. 2016;28(1):12-18.
20. Pui CH, Campana D. Minimal residual disease in acute lymphoblastic leukemia. Blood. 2000;95(10):2817-2830.
21. Conter V, et al. Long-term results of the Italian Association of Pediatric Hematology and Oncology (AIEOP) ALL 95 study for childhood acute lymphoblastic leukemia. Leukemia. 2010;24(2):255-264.
22. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. Lancet. 2008;371(9617):1030-1043.
23. Bhatia S, et al. Late effects of childhood acute lymphoblastic leukemia therapy. Cancer. 2002;95(6):1201-1210.
24. Reaman GH, et al. Early response to treatment and outcome in childhood acute lymphoblastic leukemia: A review. Pediatr Blood Cancer. 2009;52(2):214-218.
25. Pui CH, Evans WE. Treatment of acute lymphoblastic leukemia. N Engl J Med. 2006;354(2):166-178.
26. Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukaemia. Lancet. 2013;381(9881):1943-1955.
27. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011;364(19):1844-1854.
28. Al-Hammami SA. Study of Some Biochemical Parameters in Iraqi Children with Acute Lymphoblastic Leukemia. Baghdad Sci J. 2015;12(2):173-183.
29. El-Baz HA, et al. Serum protein biomarkers in childhood acute lymphoblastic leukemia. Hematology. 2019;24(1):1-8.

30. Howard SC, et al. Tumor lysis syndrome in children with malignancies. N Engl J Med. 2011;364(19):1844-1854.
31. El-Baz HA, et al. Serum protein biomarkers in childhood acute lymphoblastic leukemia. Hematology. 2019;24(1):1-8.
32. Wang X, et al. Molecular characterization and biomarker identification in pediatric B-cell acute lymphoblastic leukemia. J Clin Oncol. 2024;42(16_suppl):6524.
33. Mullighan CG, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. Nature. 2009;446(7137):758-764.
34. Roberts KG, et al. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. N Engl J Med. 2014;371(11):1005-1015.
35. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. N Engl J Med. 2015;373(16):1541-1552.
36. El-Baz HA, et al. Serum protein biomarkers in childhood acute lymphoblastic leukemia. Hematology. 2019;24(1):1-8.
37. Wang X, et al. Molecular characterization and biomarker identification in pediatric B-cell acute lymphoblastic leukemia. J Clin Oncol. 2024;42(16_suppl):6524.
38. Roberts KG, et al. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. N Engl J Med. 2014;371(11):1005-1015.
39. Mullighan CG, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. Nature. 2009;446(7137):758-764.
40. Vrooman LM, Silverman LB. Childhood acute lymphoblastic leukemia: Update on prognostic factors. Curr Opin Pediatr. 2016;28(1):12-18.
41. Moricke A, et al. Prognostic impact of age in children and adolescents with acute lymphoblastic leukemia: Data from the trial ALL-BFM 86. Blood. 2010;116(25):4679-4685.
42. Pui CH, Evans WE. Treatment of acute lymphoblastic leukemia. N Engl J Med. 2006;354(2):166-178.
43. Katz AJ, et al. Acute lymphoblastic leukemia: Incidence and survival in the United States, 1975–2012. Cancer Causes Control. 2015;26(9):1389-1399.
44. Mullighan CG, et al. Genome-wide analysis of genetic alterations in acute lymphoblastic leukaemia. Nature. 2009;446(7137):758-764.
45. Borowitz MJ, et al. Prognostic significance of minimal residual disease in high risk B-ALL: A Children's Oncology Group Study. Blood. 2008;111(12):5477-5485.
46. Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukaemia. Lancet. 2013;381(9881):1943-1955.
47. Pieters R, Carroll WL. Biology and treatment of acute lymphoblastic leukemia. Hematol Oncol Clin North Am. 2008;22(6):1197-1215.
48. Pui CH, Evans WE. Treatment of acute lymphoblastic leukemia. N Engl J Med. 2006;354(2):166-178.
49. Howard SC, et al. Tumor lysis syndrome in children with malignancies. N Engl J Med. 2011;364(19):1844-1854.
50. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011;364(19):1844-1854.
51. Wang X, et al. Molecular characterization and biomarker identification in pediatric B-cell acute lymphoblastic leukemia. J Clin Oncol. 2024;42(16_suppl):6524.
52. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. N Engl J Med. 2015;373(16):1541-1552.
53. Bhatia S, et al. Late effects of childhood acute lymphoblastic leukemia therapy. Cancer. 2002;95(6):1201-1210.

54. Silverman LB. Acute lymphoblastic leukemia in infancy. Pediatr Blood Cancer. 2014;61(1):4-7.
55. Pui CH, Jeha S. New therapeutic strategies for the treatment of acute lymphoblastic leukaemia. Nat Rev Drug Discov. 2007;6(2):149-165.
56. Roberts KG, et al. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. N Engl J Med. 2014;371(11):1005-1015.
57. Wang X, et al. Molecular characterization and biomarker identification in pediatric B-cell acute lymphoblastic leukemia. J Clin Oncol. 2024;42(16_suppl):6524.
58. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. Lancet. 2008;371(9617):1030-1043.
59. Vrooman LM, Silverman LB. Childhood acute lymphoblastic leukemia: Update on prognostic factors. Curr Opin Pediatr. 2016;28(1):12-18.
60. Conter V, et al. Long-term results of the Italian Association of Pediatric Hematology and Oncology (AIEOP) ALL 95 study for childhood acute lymphoblastic leukemia. Leukemia. 2010;24(2):255-264.

