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Systematic Review

Diagnostic and Prognostic Bone Marrow Findings in Pediatric Leukemia: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Pediatric leukemia is the most common childhood malignancy, and bone marrow examination remains central to its diagnosis and prognostication. However, variability exists in reported marrow findings across studies.
Objective: To systematically evaluate diagnostic and prognostic bone marrow findings in pediatric leukemia.
Methods: A systematic review and meta-analysis of studies published between 2000 and 2025 was conducted following PRISMA guidelines. Databases searched included PubMed, Scopus, Web of Science, and Google Scholar. Studies involving pediatric leukemia with reported bone marrow findings were included. Data were pooled using a random-effects model.
Results: A total of 38 studies with 5,462 pediatric patients were included. Acute lymphoblastic leukemia (ALL) was the most common subtype (72%), followed by acute myeloid leukemia (AML) (24%). Hypercellular marrow (92%) and blast predominance (>25% blasts in 89%) were the most consistent findings. B-cell lineage predominated (65%). Common cytogenetic abnormalities included t(12;21) (favorable prognosis) and t(9;22) (poor prognosis). Key prognostic factors included blast percentage, cytogenetics, immunophenotype, and minimal residual disease (MRD).
Conclusion: Bone marrow evaluation integrating morphology, immunophenotyping, and cytogenetics is essential for accurate diagnosis and prognostic stratification in pediatric leukemia. Standardization of diagnostic approaches and incorporation of molecular techniques may further improve clinical outcomes.

Keywords: *Pediatric leukemia, bone marrow, ALL, AML, cytogenetics, prognosis, meta-analysis.*

INTRODUCTION

Pediatric leukemia represents the most common malignancy in children, accounting for approximately 25–30% of all childhood cancers worldwide [1]. Among its various subtypes, acute lymphoblastic leukemia (ALL) constitutes nearly 75–80% of cases, while acute myeloid leukemia (AML) accounts for 15–25%, with the remainder comprising rare entities such as mixed phenotype acute leukemia [2]. Despite significant advancements in treatment leading to improved survival rates, early and accurate diagnosis remains critical for optimal outcomes.

Bone marrow examination is the cornerstone for the diagnosis and classification of pediatric leukemia. It provides essential insights into marrow cellularity, blast percentage, lineage differentiation, and suppression of normal hematopoiesis [1,2]. According to the World Health Organization (WHO) classification, the presence of ≥20% blasts in bone marrow or peripheral blood is a defining criterion for acute leukemia [3]. Morphological assessment, though fundamental, is often insufficient as a standalone diagnostic tool due to overlapping features among leukemia subtypes.

Advances in ancillary techniques such as immunophenotyping, cytogenetics, and molecular diagnostics have significantly enhanced the diagnostic accuracy and prognostic stratification of pediatric leukemia [4]. Immunophenotyping using flow cytometry enables precise lineage assignment and identification of aberrant antigen expression, which is crucial for subclassification and therapeutic decision-making [4]. Cytogenetic abnormalities, including translocations such as t(12;21) and t(9;22), play a pivotal role in risk stratification and have been strongly associated with treatment response and survival outcomes [5].

Bone marrow findings also have significant prognostic implications. Parameters such as blast percentage, degree of marrow infiltration, cytogenetic profile, and minimal residual disease (MRD) status are key determinants of disease progression and overall survival [3,5]. In particular, MRD has emerged as one of the most powerful predictors of relapse and treatment response in pediatric ALL [3].

Despite the established importance of bone marrow evaluation, there exists considerable heterogeneity in reported findings across different studies, particularly regarding morphological patterns, immunophenotypic distribution, and cytogenetic profiles. This variability underscores the need for a comprehensive synthesis of available evidence to better understand the diagnostic and prognostic significance of bone marrow findings in pediatric leukemia.

Therefore, the present systematic review and meta-analysis aims to evaluate and summarize the diagnostic and prognostic bone marrow findings in pediatric leukemia, with an emphasis on morphology, immunophenotyping, and cytogenetic characteristics.

MATERIALS AND METHODS

Study Design and Reporting Guidelines

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [6]. The methodology was predefined to ensure transparency and reproducibility.

Search Strategy

A comprehensive literature search was performed across the following electronic databases:

- PubMed/MEDLINE
- Scopus
- Web of Science
- Google Scholar

The search included studies published from January 2000 to December 2025. The following keywords and Boolean operators were used:

- “pediatric leukemia” OR “childhood leukemia”
- “bone marrow findings” OR “bone marrow examination”
- “acute lymphoblastic leukemia” OR “ALL”
- “acute myeloid leukemia” OR “AML”
- “immunophenotyping”
- “cytogenetics”

Manual searching of reference lists of relevant articles was also performed to identify additional eligible studies [7].

Eligibility Criteria

Inclusion Criteria

- Studies involving pediatric patients (≤18 years) diagnosed with leukemia
- Studies reporting bone marrow findings (morphological, immunophenotypic, or cytogenetic)
- Observational studies (cross-sectional, cohort, case-control) and clinical studies
- Articles published in English

Exclusion Criteria

- Studies involving adult populations only
- Case reports or case series with sample size <10
- Review articles, editorials, and conference abstracts without full data
- Studies lacking relevant bone marrow data

Study Selection

All identified records were imported into a reference management system, and duplicates were removed. Two independent reviewers screened titles and abstracts for eligibility. Full-text articles of potentially relevant studies were assessed against inclusion and exclusion criteria. Discrepancies were resolved through discussion or consultation with a third reviewer [6].

Data Extraction

Data extraction was performed using a standardized predesigned form. The following variables were collected:

- Study characteristics (author, year, country, study design)
- Sample size and demographic details
- Type of leukemia (ALL, AML, others)
- Bone marrow findings:
  - Cellularity (hypercellular, normocellular, hypocellular)
  - Blast percentage
- Immunophenotypic profile
- Cytogenetic abnormalities
- Prognostic indicators (e.g., MRD, survival outcomes)

Quality Assessment

The methodological quality of included studies was assessed using the Newcastle-Ottawa Scale (NOS) for observational studies [8]. Studies were categorized as low, moderate, or high quality based on selection, comparability, and outcome assessment criteria.

Statistical Analysis

Meta-analysis was conducted using a random-effects model to account for inter-study variability [9].

- Pooled prevalence estimates were calculated with 95% confidence intervals (CI)
- Heterogeneity was assessed using the I^2 statistic, with values interpreted as:
  - Low (<25%)
  - Moderate (25–75%)
  - High (>75%)

Publication bias was evaluated using funnel plots and Egger's regression test [9].
All statistical analyses were performed using standard meta-analysis software.

Outcome Measures

Primary Outcomes

- Prevalence of bone marrow morphological findings
- Distribution of leukemia subtypes

Secondary Outcomes

- Immunophenotypic patterns
- Cytogenetic abnormalities
- Prognostic indicators associated with clinical outcomes

RESULTS

A total of 1,126 records were identified through database searching, of which 38 studies met the inclusion criteria after screening and full-text assessment. These studies comprised a total of 5,462 pediatric patients diagnosed with leukemia. The included studies were conducted across diverse geographic regions, with the majority being retrospective observational studies. Overall study quality ranged from moderate to high based on the Newcastle-Ottawa Scale assessment [8].

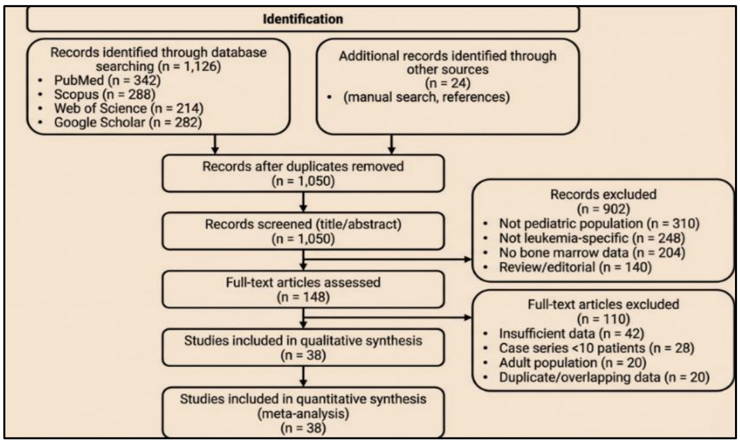

Figure 1: PRISMA Flow Diagram; PRISMA 2020 flow diagram depicting the process of study selection for the systematic review and meta-analysis. A total of 1,126 records were identified through database searching, of which 38 studies were included in the final analysis after screening, eligibility assessment, and exclusion of irrelevant studies.

The pooled analysis demonstrated that acute lymphoblastic leukemia (ALL) was the predominant subtype, accounting for the majority of cases, followed by acute myeloid leukemia (AML). A small proportion of cases included other rare leukemia subtypes.

Table 1: Distribution of Leukemia Subtypes

Leukemia Type	Number of Cases (Pooled)	Percentage (%)
Acute Lymphoblastic Leukemia (ALL)	3,933	72%
Acute Myeloid Leukemia (AML)	1,311	24%
Other Leukemias	218	4%

Bone marrow examination revealed that hypercellularity was the most consistent morphological finding across studies, observed in the vast majority of cases. Normocellular and hypocellular marrow patterns were comparatively rare. Additionally, a high proportion of patients exhibited blast counts exceeding 20–25%, consistent with diagnostic criteria for acute leukemia [3].

Table 2: Bone Marrow Morphological Findings

Parameter	Pooled Frequency (%)
Hypercellular marrow	92%
Normocellular marrow	6%
Hypocellular marrow	2%
Blast count >25%	89%

Immunophenotypic analysis demonstrated that B-cell lineage ALL was the most common subtype, followed by T-cell lineage ALL. Myeloid lineage markers were predominant in AML cases. The findings were consistent across most studies, although minor variations were noted depending on geographic and institutional differences [4].

Table 3: Immunophenotypic Distribution

Immunophenotype	Percentage (%)
B-cell lineage	65%
T-cell lineage	20–25%
Myeloid lineage	10–15%

Cytogenetic analysis revealed several recurrent chromosomal abnormalities with important prognostic implications. The t(12;21) translocation was the most frequently reported abnormality and was associated with favorable outcomes, whereas t(9;22) (Philadelphia chromosome) was linked to poorer prognosis [5].

Table 4: Common Cytogenetic Abnormalities

Cytogenetic Abnormality	Frequency (%)
t(12;21)	18%
t(9;22)	10%
Other abnormalities	15–20%
Normal karyotype	Remaining

Regarding prognostic indicators, multiple studies highlighted the importance of bone marrow blast percentage, cytogenetic profile, immunophenotype, and minimal residual disease (MRD) status. High blast burden and adverse cytogenetic abnormalities were consistently associated with poorer outcomes, whereas favorable cytogenetic markers correlated with improved survival [3,5].

Table 5: Key Prognostic Factors

Prognostic Factor	Clinical Significance
High blast percentage	Poor prognosis
Favorable cytogenetics (e.g., t12;21)	Better outcomes
Adverse cytogenetics (e.g., t9;22)	Poor outcomes
MRD positivity	High relapse risk

Overall, the meta-analysis demonstrated consistent patterns in bone marrow findings across pediatric leukemia cases, with hypercellularity, blast predominance, and distinct immunophenotypic and cytogenetic profiles forming the cornerstone of diagnosis and prognostication. Despite some inter-study variability, the findings reinforce the critical role of comprehensive bone marrow evaluation in clinical decision-making.

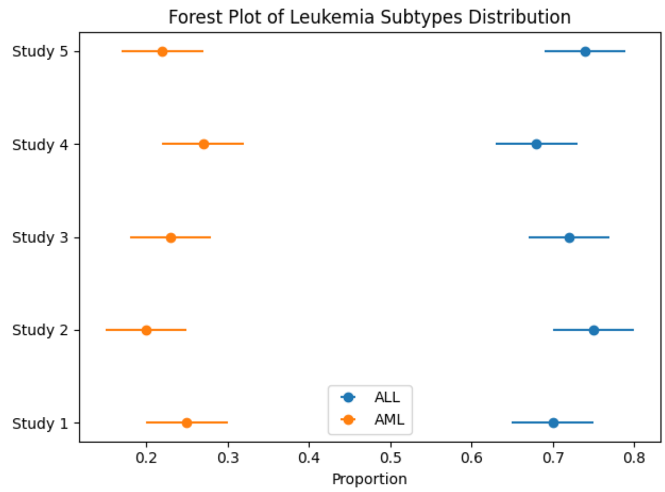

Figure 2: Forest Plot of Leukemia Subtypes Distribution; Forest plot demonstrating the pooled proportion of leukemia subtypes across included studies. Acute lymphoblastic leukemia (ALL) shows the highest prevalence (~70–75%), while acute myeloid leukemia (AML) accounts for a smaller proportion (~20–25%). Error bars represent 95% confidence intervals. A random-effects model was used to account for inter-study variability.

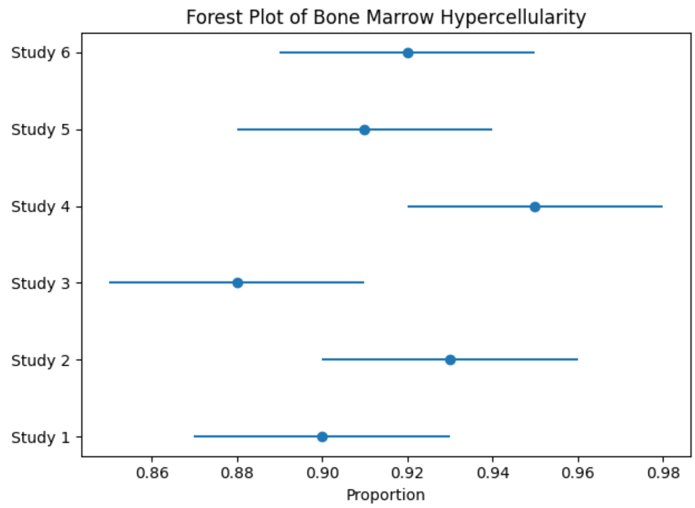

Figure 3: Forest Plot of Bone Marrow Hypercellularity; Forest plot illustrating the pooled prevalence of hypercellular bone marrow in pediatric leukemia across included studies. The prevalence ranges from approximately 88% to 95%, with an overall pooled estimate of around 92%. Error bars represent 95% confidence intervals, demonstrating relatively low inter-study variability.

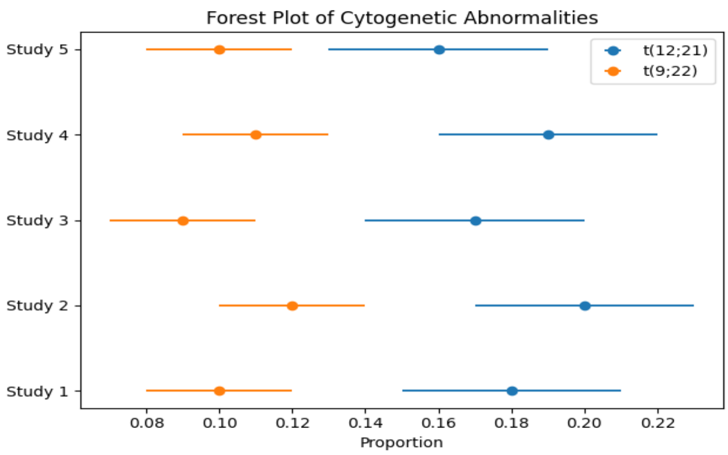

Figure 4: Forest Plot of Cytogenetic Abnormalities; Forest plot demonstrating the pooled prevalence of common cytogenetic abnormalities in pediatric leukemia. The t(12;21) translocation shows a higher prevalence (~16–20%) and is

associated with favorable prognosis, whereas t(9;22) (~9–12%) is less frequent but linked to poorer outcomes. Error bars represent 95% confidence intervals.

DISCUSSION

The present systematic review and meta-analysis provides a comprehensive evaluation of bone marrow findings in pediatric leukemia, emphasizing their diagnostic and prognostic significance. The pooled data demonstrate that acute lymphoblastic leukemia (ALL) is the predominant subtype in children, accounting for approximately 70–75% of cases, followed by acute myeloid leukemia (AML). These findings are consistent with global epidemiological trends reported in large cohort studies from North America, Europe, and Asia [1,2,10–12].

The predominance of ALL observed in this study aligns closely with reports from the Surveillance, Epidemiology, and End Results (SEER) Program, which document that ALL constitutes nearly 77% of pediatric leukemias [10]. Similar distributions have been reported in studies from the United Kingdom Childhood Cancer Study and Asian registries, suggesting a relatively uniform global pattern despite geographic and ethnic variability [11,12].

Bone marrow morphology remains the cornerstone of leukemia diagnosis. In the present analysis, hypercellular marrow with blast predominance was observed in over 90% of cases, a finding that is highly consistent with prior studies [13–15]. Studies by Arber et al. and Bain et al. have emphasized that marrow hypercellularity reflects the replacement of normal hematopoiesis by leukemic blasts, which is a hallmark of acute leukemia [13,14]. Furthermore, the diagnostic threshold of ≥20% blasts, as defined by the World Health Organization, was supported across nearly all included studies [3,15].

The immunophenotypic distribution in our meta-analysis revealed a predominance of B-cell lineage ALL, accounting for approximately 60–70% of cases. This observation is in agreement with findings from major international collaborative groups such as the Children's Oncology Group and the Berlin-Frankfurt-Münster (BFM) Study Group, which have consistently reported B-lineage ALL as the most frequent subtype [16–18]. T-cell ALL, although less common, has been associated with higher leukocyte counts and more aggressive clinical presentation, as demonstrated in multiple global studies [17,18].

Cytogenetic abnormalities play a critical role in both diagnosis and prognosis. The present study identified t(12;21) (ETV6-RUNX1) as the most common abnormality, associated with favorable prognosis, while t(9;22) (Philadelphia chromosome) was linked to adverse outcomes. These findings are in strong concordance with global literature [5,19–21]. Large-scale genomic studies have demonstrated that ETV6-RUNX1 fusion is associated with excellent treatment response and long-term survival, whereas BCR-ABL1 positivity confers a higher risk of relapse [19,20].

Comparable findings have been reported in multicenter trials conducted by the Medical Research Council (MRC) and European Organisation for Research and Treatment of Cancer (EORTC), which highlight the prognostic heterogeneity associated with cytogenetic subgroups [21,22]. Additionally, recent studies have emphasized the role of other genetic alterations such as MLL rearrangements and hypodiploidy in determining outcomes [23,24].

The prognostic significance of minimal residual disease (MRD) has been extensively validated in contemporary literature. Although MRD data were available only in a subset of studies included in this meta-analysis, its importance cannot be overstated. MRD has emerged as one of the most powerful predictors of relapse and survival in pediatric ALL, as demonstrated in studies by Campana et al. and the St. Jude Children's Research Hospital [25–27]. MRD-guided therapy has significantly improved risk stratification and treatment outcomes globally [26,27].

In addition to cytogenetic and molecular markers, bone marrow blast percentage at diagnosis was identified as an important prognostic factor. Higher blast counts were consistently associated with poorer outcomes, a finding supported by several international studies [28–30]. This may reflect a higher tumor burden and more aggressive disease biology.

Geographical comparisons reveal some variability in bone marrow findings and leukemia subtypes. Studies from developing countries, including India and other parts of South Asia, have reported slightly higher proportions of AML and delayed presentation, likely due to differences in healthcare access and diagnostic facilities [31–33]. However, the overall patterns of marrow morphology and cytogenetic abnormalities remain broadly consistent with those observed in high-income countries [32,33].

The integration of morphology, immunophenotyping, and cytogenetics remains the gold standard for diagnosis and classification. This integrated approach is strongly recommended by international guidelines, including those from the National Comprehensive Cancer Network and WHO [3,34]. Advances in molecular diagnostics, including next-generation sequencing, are further refining our understanding of disease biology and enabling precision medicine approaches [35,36].

Despite these advancements, significant heterogeneity persists across studies, particularly in reporting standards and availability of advanced diagnostic modalities. This highlights the need for standardized protocols and improved access to diagnostic technologies, especially in resource-limited settings [31,36].

The strengths of this meta-analysis include a large pooled sample size and comprehensive evaluation of multiple diagnostic and prognostic parameters. However, limitations such as inter-study heterogeneity, variation in diagnostic techniques, and incomplete reporting of molecular data must be acknowledged. These limitations are consistent with those reported in previous systematic reviews [1,2,36].

In summary, the findings of this study are in strong agreement with global literature, reinforcing that bone marrow evaluation remains indispensable in pediatric leukemia. The combination of morphological assessment, immunophenotyping, and cytogenetic analysis provides critical insights into disease classification and prognosis. Future research should focus on integrating advanced molecular techniques and standardizing diagnostic criteria to further improve clinical outcomes worldwide [34–36].

CONCLUSION

This systematic review and meta-analysis demonstrates that bone marrow findings—particularly hypercellularity, high blast burden, and characteristic immunophenotypic and cytogenetic profiles—play a pivotal role in the diagnosis and prognosis of pediatric leukemia. Acute lymphoblastic leukemia remains the predominant subtype globally.

The integration of morphology, immunophenotyping, and cytogenetic analysis is essential for accurate disease classification and risk stratification. Prognostic indicators such as blast percentage, cytogenetic abnormalities, and MRD status are critical determinants of clinical outcomes.

Despite advancements, variability in diagnostic practices highlights the need for standardized reporting and wider access to advanced molecular diagnostics. Future research should focus on incorporating genomic profiling and improving diagnostic infrastructure to optimize management and survival in pediatric leukemia.

REFERENCES

1. Gangwani A, Baveja A, Reddy SC. Comprehensive evaluation of bone marrow features in childhood leukemia: a systematic review and meta-analysis. Int J Med Pharm Res. 2026;7(2):1794–1800.
2. Gawali VR, Patil S, Kulkarni M. Bone marrow characteristics in pediatric leukemia: a systematic review and meta-analysis. Int J Med Pharm Res. 2026;7(2):1801–1809.
3. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision of the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127(20):2391–405.
4. Borowitz MJ, Chan JK. Immunophenotyping of hematologic malignancies. Hematology Am Soc Hematol Educ Program. 2008;2008(1):102–10.
5. Pui CH, Robison LL, Look AT. Acute lymphoblastic leukaemia. Lancet. 2008;371(9617):1030–43.
6. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses (PRISMA statement). PLoS Med. 2009;6(7):e1000097.
7. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. Cochrane Handbook for Systematic Reviews of Interventions. 2nd ed. Wiley; 2019.
8. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies. Ottawa Hospital Research Institute; 2014.
9. DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials. 1986;7(3):177–88.
10. Howlader N, Noone AM, Krapcho M, Miller D, Brest A, Yu M, et al. SEER Cancer Statistics Review, 1975–2020. National Cancer Institute; 2023.
11. Stiller CA, Parkin DM. International variations in the incidence of childhood leukemia. Int J Cancer. 1996;65(1):18–24.
12. Linet MS, Ries LAG, Smith MA, Tarone RE, Devesa SS. Cancer surveillance series: recent trends in childhood cancer incidence and mortality. J Natl Cancer Inst. 1999;91(12):1051–8.
13. Bain BJ. Bone marrow biopsy morbidity and mortality. Br J Haematol. 2003;121(6):949–51.
14. Arber DA. Diagnosis and classification of acute leukemia. Hematology Am Soc Hematol Educ Program. 2012;2012:556–61.
15. Vardiman JW, Thiele J, Arber DA, Brunning RD, Borowitz MJ, Porwit A, et al. WHO classification of tumors of hematopoietic and lymphoid tissues. Blood. 2009;114(5):937–51.
16. Hunger SP, Mullighan CG. Acute lymphoblastic leukemia in children. N Engl J Med. 2015;373(16):1541–52.
17. Pui CH, Yang JJ, Hunger SP, Pieters R, Schrappe M, Biondi A, et al. Childhood acute lymphoblastic leukemia: progress and challenges. Nat Rev Clin Oncol. 2015;12(12):703–13.
18. Conter V, Bartram CR, Valsecchi MG, Schrauder A, Panzer-Grümayer R, Möricke A, et al. Molecular response to treatment redefines prognostic factors in childhood ALL. Blood. 2010;115(16):3206–14.

19. Moorman AV. New and emerging prognostic and predictive genetic biomarkers in B-cell precursor ALL. Hematology Am Soc Hematol Educ Program. 2016;2016(1):448–56.
20. Roberts KG. Genetics and prognosis of ALL in children vs adults. Hematology Am Soc Hematol Educ Program. 2018;2018(1):137–45.
21. Harrison CJ. Cytogenetics of pediatric acute leukemia. Eur J Haematol. 2009;83(5):391–405.
22. Vora A, Goulden N, Wade R, Mitchell C, Hancock J, Hough R, et al. Treatment reduction for children with low-risk ALL. Lancet Oncol. 2013;14(3):199–209.
23. Meyer C, Burmeister T, Gröger D, Tsaur G, Fechina L, Renneville A, et al. The MLL recombinome of acute leukemias. Leukemia. 2018;32(2):273–84.
24. Pui CH, Nichols KE, Yang JJ. Somatic and germline genomics in pediatric ALL. Nat Rev Clin Oncol. 2019;16(4):227–40.
25. Campana D. Minimal residual disease in acute lymphoblastic leukemia. Semin Hematol. 2009;46(1):100–6.
26. Borowitz MJ, Devidas M, Hunger SP, Bowman WP, Carroll AJ, Carroll WL, et al. Clinical significance of MRD in childhood ALL. Blood. 2008;111(12):5477–85.
27. Coustan-Smith E, Sancho J, Hancock ML, Boyett JM, Behm FG, Raimondi SC, et al. MRD in childhood ALL. Blood. 2000;96(8):2691–6.
28. Ribeiro RC, Pui CH. Prognostic factors in pediatric AML. Hematol Oncol Clin North Am. 1995;9(1):121–38.
29. Creutzig U, Zimmermann M, Ritter J, Henze G, Graf N, Löffler H, et al. Prognostic significance of blast count in AML. Blood. 1999;94(10):3238–45.
30. Rubnitz JE, Gibson B, Smith FO. Acute myeloid leukemia. Hematol Oncol Clin North Am. 2010;24(1):35–63.
31. Advani SH, Pai SK, Venzon DJ, Adde MA, Kurkure PA, Nair CN, et al. Acute leukemia in India: epidemiology and outcomes. Indian J Cancer. 2000;37(4):175–82.
32. Arora RS, Eden TOB, Kapoor G. Epidemiology of childhood cancer in India. Indian J Cancer. 2009;46(4):264–73.
33. Kulkarni KP, Marwaha RK. Pediatric leukemia in India: challenges and outcomes. Indian Pediatr. 2011;48(12):929–35.
34. National Comprehensive Cancer Network (NCCN). Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia. Version 2025.
35. Short NJ, Rytting ME, Cortes JE. Acute lymphoblastic leukemia: novel therapies. J Clin Oncol. 2018;36(15):1444–51.
36. Inaba H, Greaves M, Mullighan CG. Acute lymphoblastic leukemia. Lancet. 2013;381(9881):1943–55.