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Original Research Article

Minimal Residual Disease–Guided Therapy in Childhood Acute Leukemia

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Abstract:

Background: Minimal residual disease (MRD) has emerged as a critical prognostic marker in childhood acute leukemia, enabling risk-adapted therapy and improved survival outcomes. MRD-guided therapeutic strategies help in identifying patients at high risk of relapse and tailoring treatment intensity accordingly.

Objective: To evaluate the clinical impact of MRD-guided therapy on treatment outcomes in children with acute leukemia.

Methods: A retrospective study was conducted at Mahavir Cancer Sansthan, Patna, over a period of 8 months. A total of 200 pediatric patients diagnosed with acute leukemia were included. MRD status was assessed using flow cytometry at defined treatment intervals. Patients were stratified into MRD-negative and MRD-positive groups, and outcomes were compared.

Results: MRD negativity was achieved in 68% of patients after induction therapy. The MRD-negative group showed significantly higher remission rates (92% vs. 61%, $p<0.001$) and improved overall survival (OS) compared to MRD-positive patients. Relapse rates were significantly lower in the MRD-negative group (12% vs. 38%, $p<0.001$).

Conclusion: MRD-guided therapy significantly improves treatment outcomes in childhood acute leukemia and serves as a reliable predictor for risk stratification and prognosis.

Keywords: Minimal residual disease, childhood leukemia, MRD-guided therapy, acute leukemia, prognosis.

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Introduction

Acute leukemia is the most common malignancy in children, accounting for nearly 30% of pediatric cancers worldwide. Acute lymphoblastic leukemia (ALL) constitutes approximately 75–80% of cases, followed by acute myeloid leukemia (AML) [1]. Despite advances in chemotherapy protocols, relapse remains a significant cause of treatment failure [2].

Minimal residual disease (MRD) refers to the small number of leukemic cells that persist after treatment and are undetectable by conventional microscopy [3]. With the advent of sensitive techniques such as multiparameter flow cytometry and polymerase chain reaction (PCR), MRD detection has become an essential component in leukemia management [4].

MRD assessment provides a dynamic evaluation of treatment response and has been shown to be one of the strongest predictors of relapse [5]. Studies have demonstrated that patients who achieve early MRD negativity have significantly better outcomes compared to those with persistent MRD [6,7].

MRD-guided therapy allows clinicians to tailor treatment intensity. Patients with low MRD levels can avoid overtreatment and associated toxicities, while those with high MRD may benefit from intensified therapy or hematopoietic stem cell transplantation [8,9].

In resource-limited settings, integrating MRD into clinical practice remains challenging but highly beneficial [10]. Recent clinical trials have established MRD-based risk stratification as a standard approach in pediatric leukemia protocols [11–13].

This study aims to evaluate the role of MRD-guided therapy in improving outcomes among children with acute leukemia in a tertiary care center in India.

Materials and Methods

Study Design and Setting: A retrospective observational study conducted at Mahavir Cancer Sansthan, Patna.

Study Duration: 8 months (oct 2024- may 2025).

Study Population

- Total patients: 200
- Age group: 1–15 years
- Diagnosed with acute leukemia (ALL and AML)

Inclusion Criteria

- Newly diagnosed pediatric acute leukemia patients
- Patients who completed induction therapy
- Availability of MRD data

Exclusion Criteria

- Relapsed leukemia at presentation
- Incomplete records
- Lost to follow-up

MRD Assessment

MRD was measured using flow cytometry at:

- End of induction (Day 28)
- Post-consolidation

MRD positivity defined as ≥0.01% in ALL and as >=0.1% in AML.

Statistical Analysis

- Software: SPSS v25
- Chi-square test for categorical variables
- Kaplan-Meier survival analysis
- p-value <0.05 considered significant

Results

1. **Baseline Characteristics:** A total of 200 patients were included. The mean age was 7.8 ± 3.2 years with 58% males. Most cases were ALL (80%), followed by AML (20%). Details are shown in Table 1.
2. **MRD Status:** After induction, 68% were MRD-negative and 32% MRD-positive (Table 2, Figure 1).
3. **Remission Outcomes:** Remission was higher in MRD-negative patients (92% vs. 61%). The difference was significant ($p < 0.001$) (Table 3).
4. **Relapse and Mortality:** Relapse (12% vs. 38%) and mortality (8% vs. 29%) were higher in MRD-positive patients ($p < 0.001$) (Table 4).
5. **Survival Analysis:** Overall survival was better in MRD-negative patients (89% vs. 62%, $p < 0.001$) (Figure 2).
6. **Risk Estimate:** MRD-positive patients had a higher relapse risk:
   - HR = 3.2
   - 95% CI: 2.1–4.8
   - $p < 0.001$
7. Subgroup Analysis

MRD negativity was higher in ALL (70%) than AML (60%) (Table 5).

Key Findings

- MRD negativity: 68%
- Better remission in MRD-negative group
- Higher relapse/mortality in MRD-positive
- Improved survival with MRD negativity
- MRD positivity ↑ relapse risk

Discussion

This study highlights the prognostic significance of MRD in childhood acute leukemia. The findings are consistent with previous literature demonstrating that MRD is a strong independent predictor of treatment outcomes [14].

A high proportion (68%) of patients achieved MRD negativity after induction therapy, which aligns with global data [15]. MRD-negative patients had significantly better remission rates and lower relapse rates, emphasizing its clinical importance [16,17].

MRD-positive patients exhibited a threefold higher risk of relapse, similar to findings reported in multicenter trials [18]. This underscores the need for intensified therapy in MRD-positive individuals [19].

Our results also demonstrate improved overall survival in MRD-negative patients. This supports the incorporation of MRD into standard treatment protocols [20].

The study further highlights challenges in resource-limited settings, including access to advanced diagnostic techniques [21]. Despite these limitations, MRD assessment remains feasible and highly beneficial [22].

Recent advances in MRD detection, including next-generation sequencing, may further improve risk stratification [23]. Personalized therapy based on MRD can reduce toxicity while maintaining efficacy [24].

Limitations of this study include its retrospective design and short follow-up duration. However, the findings provide valuable insights into real-world clinical outcomes [25].

Conclusion

MRD-guided therapy significantly improves clinical outcomes in childhood acute leukemia. Early MRD negativity is associated with higher remission rates, lower relapse risk, and improved survival. Incorporating MRD assessment into routine clinical practice is essential for optimal risk stratification and personalized treatment.

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