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TREATMENT RESPONSE EVALUATION OF THE INDUCTION CHEMOTHERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

Zubair Ali Memon[1], Jawad Ali Memon[2*], Mohammad Sibtain Shah[3], Mohammad Saleh Chandio[4], Ameeran Baloch[5]

[1]Assistant Consultant Adult Oncology King Faisal Specialist Hospital & Research Centre Jeddah, Saudi Arabia
[2*]Associate Professor Diagnostic Radiology Peoples University of Medical & Health Sciences for Women PUMHSW.SBA
[3]Assistant Professor Oncology Peoples University of Medical & Health Sciences for Women PUMHSW.SBA
[4]Senior Registrar Oncology Gambat Institute of Medical Sciences (GIMS) Gambat
[5]Consultant Clinical Oncologist Nuclear Institute of Medicine & Radiotherapy (NIMRA) Jamshoro

***Corresponding Author:** Jawad Ali Memon
*Associate Professor Diagnostic Radiology Peoples University of Medical & Health Sciences for Women PUMHSW.SBA, Email: jawad_nimra@yahoo.com

ABSTRACT

Background: Acute lymphoblastic leukemia (ALL) is the most common malignancy in children and represents 75–80% of acute leukemia in this age group. The likelihood of long-term cure in ALL depends on the clinical and laboratory features and the treatment received. The initial response to the induction chemotherapy is one of the most important prognostic marker & future guide to the management options.

Aims & Objectives: To assess response of the induction chemotherapy in children with acute lymphoblastic leukemia.

Patients & Methods: We have retrospectively evaluated the 101 diagnosed cases of acute lymphoblastic leukemia treated in our hospital from 2013 to 2016 and analyzed the response of standard induction chemotherapy (MRCALL97) after 28 day by bone marrow biopsy**.**

Results: Out of 101, 16 (15.85%) patients died due to infective and hemorrhagic complications and could not complete the induction therapy. Out of 85, there were 52 (61.2%) male & 33 (32.8%) female patients. Mean age of the patients was 10.16. ± 4.87 years and the age ranges between 01-18 years. Mean white blood cell (WBC) counts & the mean blast cell percent at diagnoses was 39.2 ± 60.88/microlitre and 71.7 ± 21.2% respectively. 63 (74.1%) patients have blast cells above 50% & 22 (25.9%) patients with blast cells below 50% noted. 9 (10.6%) patient's shows CNS involvement at initial workup. Post chemotherapy bone marrow biopsy on day 28 shows complete remission (CR) in 65 (76.47%) patients including 42(64.6%) male and 23 (35.4%) female. induction failure occurred in 20 (23.5%) patients including 10 (50%) male and 10 (50%) female. All 9 patients with CNS involvement at presentation could not achieve complete remission.

Conclusions: This study contributes to a better understanding of the factors influencing induction chemotherapy outcomes and highlights areas for future research and clinical practice improvements.

Key words:

INTRODUCTION

Acute lymphoblastic leukemia (ALL) is a malignant hematologic disease characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood and other organs [1]. ALL is the most common type of leukemia in paediatric age group in the United States & represents 75 to 85% of all acute leukemias and incidence rate is also rapidly rising in Pakistan as well [2]

Leukemia treatment is primarily based on chemotherapy. Traditionally, four components of ALL treatment are induction, consolidation, maintenance, and central nervous system (CNS) prophylaxis. The likelihood of long-term cure in ALL depends on the clinical and laboratory features and the treatment received. The initial response to the induction chemotherapy is one of the most important prognostic marker & future guide to the management options. [3,4,5]Children who responds completely in induction chemotherapy have a better outlook than those who does not. Among patients with initial induction failure, some never have a complete remission and those who respond have early relapse. Study shows both the overall survival rate and the EFS for the patients who fail induction therapy compared to those who responded to therapy were markedly lower .[6]

The current study is planned with the aim to assess & document the response of conventional induction chemotherapy in children with acute lymphoblastic leukemia (ALL) treated in public sector tertiary care hospital of a developing country Pakistan.

Materials & methods:

After approval from the ethical committee, this retrospective descriptive case study was conducted in department of oncology GIMS Gambat , Pakistan. We have retrospectively analyzed the response of induction chemotherapy in 101 children with acute lymphoblastic leukemia treated in our hospital from 2021 to 2024. The inclusion criteria were bone marrow biopsy proven cases of acute lymphoblastic leukemia of age between 1 to 18 years. The patients of higher age, taken any prior treatment, transferred acute lymphoblastic leukemia and cannot complete chemotherapy due to associated diseases, were excluded. Detailed clinical history, clinical examination and base line investigations were evaluated. All patients' base line total blood parameters especially total leucocyte count (TLC) and blast cell percent in bone marrow biopsy and in peripheral blood smear were noted. All patients received the standard four drug regimen four-drug regimen (vincristine, prednisone, donorubicinn, and *L*-asparaginase,).

The response to induction therapy was evaluated on 28 days after treatment initiation by bone marrow biopsy. Complete remission is defined as less than 5 percent blasts in a recovering bone marrow aspirate, the absence of leukemic blasts in blood and no evidence of localized disease after the completion of induction chemotherapy. Induction failure definition used was the persistence of leukemic blasts in the bone marrow >5%.

Results

16 (15.85%) patients died due to infective and hemorrhagic complications and could not complete the induction therapy. Out of 85, there were 52 (61.2%) male & 33 (32.8%) female patients (figure 1). Mean age of the patients was 10.16. ± 4.87 years and the age ranges between 01-18 years (figure 2). Mean white blood cells (WBC) counts & the mean blast cell percent at diagnoses was 39.2 $\pm$ 60.88 /mm^3 and 71.7 $\pm$ 21.2% respectively. 63 (74.1%) patients have blast cells above 50% & 22 (25.9%) patients with blast cells below 50% noted (table 1).

Post chemotherapy bone marrow biopsy on day 28 shows complete remission (CR) in 65 (76.4%) patients including 42(64.6%) male and 23 (35.4%) female. Induction failure occurred in 20 (23.5%) patients including 10 (50%) male and 10 (50%) female. All 9 patients with CNS involvement at presentation, could not achieve complete remission.

There were 46 (54.1%) patients who were above 10 years and 39 (45.8%) patients were below 10 years. Patients who were above 10 years, 33 (50.7%) patients achieved complete remission. Patients who were below 10 years 32 (49.2%) patients achieved complete remission (table 2).

Patients with WBC count above 50,000, 49 (75.4%) patients achieved complete remission where as 16 (24.6) patients who presented with WBC counts less 50,000, achieved complete remission (figure 3).
47 (72..3%) patients with blast cells above 50% achieved complete remission and 18 (27.7%) patients with blast cells below 50% achieved complete remission (Table 3).

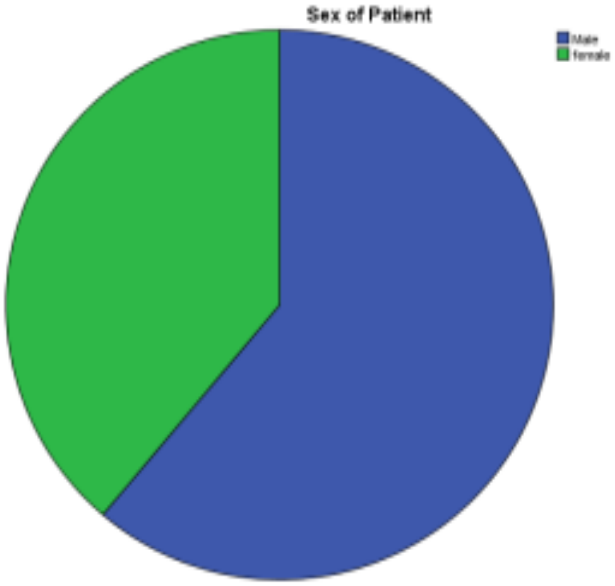

Figure 1: patient gender distribution.

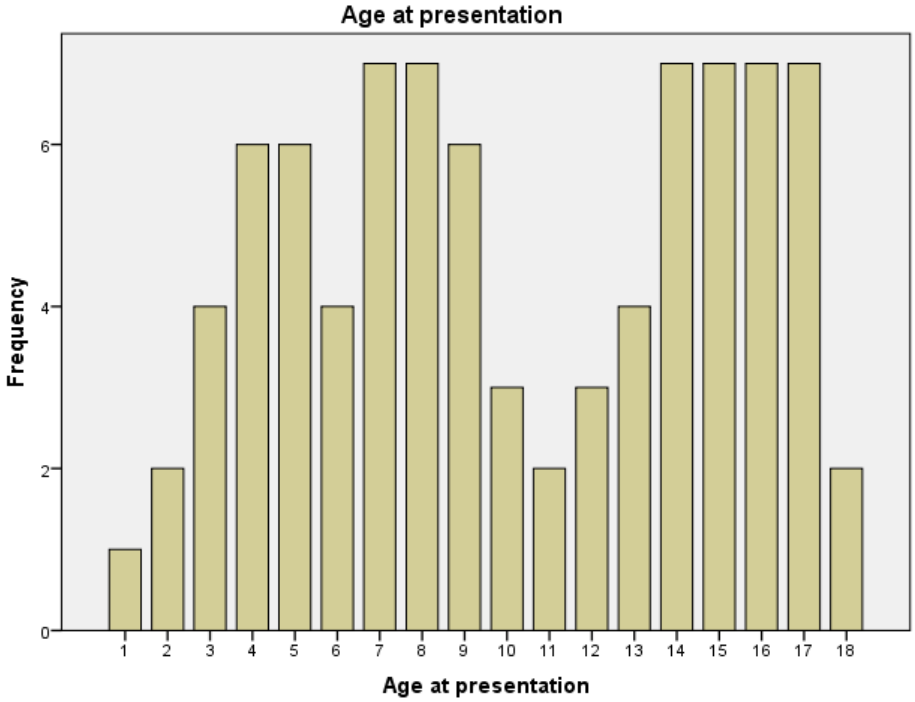

Figure 2: patient age distribution.

Mean WBC count at presentation	38.53 ± 60.90
Mean Hemoglobin level at presentation	8.74 ± 2.55
Mean platelets count at presentation	88.58 ± 87.7
Mean blast cell at presentation	71.7 ± 21.2

Table 1: Blood parameters at diagnoses.

		BM Biopsy 2		Total
		CR	No CR	
	age above 10	33 (50.7.%)	13 (65%)	46 (54.1%)
	age 10 or below	32 (49.2%)	7 (35%)	39 (45.9%)
Total		65	20	85

Table 2 : Complete remission according to age of patients

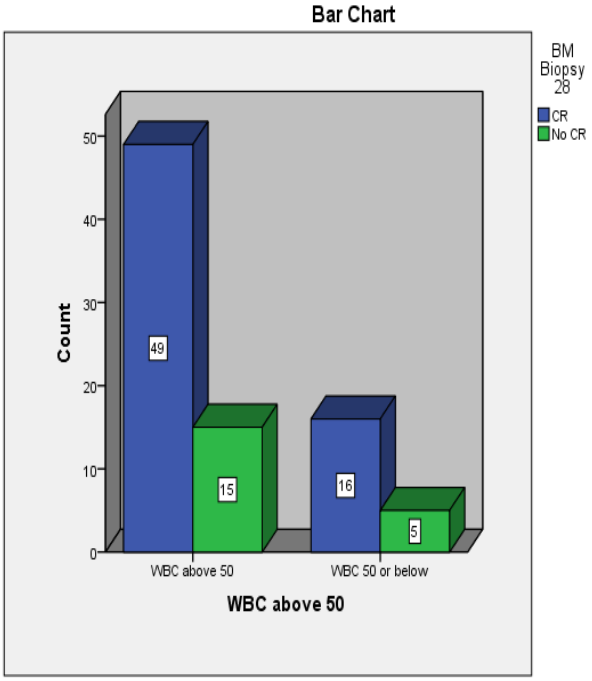

Figure 3 : Complete remission according toWhite cell count.

Gure

		BM Biopsy		Total
		CR	No CR	
	blast below 50%	18 (27.7%)	4 (20%)	22 (25.9%)
	blast above 50%	47 (72.3%)	16 (80%)	63 (74.1%)
Total		65	20	85

Table 3: Complete remission according to blast percent

Discussion:

Over the last three decades, survival for children with acute lymphoblastic leukemia has markedly improved due to risk stratified targeted intensive chemotherapy regimens and better supportive care. 5-year event-free survival rates of above 90% are reported in developed countries[7] The results are not promising in developing countries like Pakistan [8 & 9]. The inequality of available resources & needs between developed & developing countries is main reason of this great difference in cure & survival of children with acute lymphoblastic leukemia[10]. These includes scarcity of tertiary care hospitals, delayed diagnoses & referrals, poor hospital infrastructure, shortage of trained & experienced health personals & lack of access to supportive care & nutrition .

This study conducted in public sector tertiary care hospital of Pakistan with limited financial, technical & human resources. Most of the patients belongs to low socioeconomic family & travelled long distance to receive treatment.

The results of the study provide valuable insights into the response of induction chemotherapy in pediatric patients with acute lymphoblastic leukemia (ALL). The study evaluates multiple factors, including gender, age, initial white blood cell (WBC) counts, blast percentage, and central nervous system (CNS) involvement, highlighting their influence on treatment outcomes

In our study 16 (15.85%) patients died during induction chemotherapy mainly due to infective and hemorrhagic complications and could not complete the therapy. The mortality of 5% children is reported in developed countries due to toxic side effects of antileukemic treatment.[11, 12, 13] This underscores the vulnerability of pediatric ALL patients to treatment-related toxicities, particularly during the immunocompromised state induced by chemotherapy. Early recognition and management of complications, alongside infection prophylaxis and supportive care, are crucial to improve survival rates during induction therapy.

The complete remission induction (CR) was noted in 76.5% in our patients in contrast to above 90 % reported in large studies conducted in developed countries {14}. One of the reasons of this low rate of CR was due to occurrence of high risk factors in majority our patients. Most of our patients are male (61.2%), having age above 6 years (72%), TLC more than 50 /microlitre and CNS involvement (10.6%) at diagnoses. The male sex, older age, higher TLC and CNS involvement at presentation are well established causes of induction failure {15,16.17}

The complete remission (CR) rate was higher in males (**64.6%**) than in females (**35.4%**), but induction failure occurred equally in both genders (50% each).This suggests that while males may have better remission rates, factors such as baseline disease burden and biological differences in leukemia subtypes could influence outcomes. Further research is needed to elucidate gender-specific responses and tailor treatment protocols accordingly.

The mean age of patients was 10.16 years, with a broad range from 1 to 18 years. Patients above 10 years of age showed a CR rate of 50.7%, while those below 10 years had a comparable CR rate of 49.2%. Age is often a critical prognostic factor in ALL. While younger children typically have better outcomes, this study shows relatively similar responses across age groups. Patients older than 10 years might have experienced more aggressive disease subtypes, such as T-cell ALL, which could partially explain their outcomes despite aggressive therapy.

Elevated WBC counts are a well-known adverse prognostic factor. In our study, patients with WBC counts above 50,000/mm³ had a higher CR rate (75.4%) compared to those with counts below 50,000/mm³ (24.6%).This is counterintuitive to existing literature, which typically associates lower WBC counts with better outcomes.Possible explanations include differences in disease biology, supportive care, or small sample size. A significant proportion (74.1%) of patients presented with blast cells above 50%. Among these 72.3% achieved CR compared to 27.7% with blast cells below 50%.This finding aligns with studies suggesting that a higher percentage of blasts does not preclude a good response to chemotherapy but instead reflects the efficacy of the induction regimen.

All 9 patients with CNS involvement failed to achieve CR, highlighting its association with poor prognosis.CNS involvement indicates advanced disease and requires intensified treatment, including intrathecal chemotherapy and cranial irradiation. This highlights the importance of early CNS-directed therapy and enhanced supportive care.The overall CR rate of 76.4% is comparable to standard protocols for ALL in children.The induction failure rate of 23.5% warrants attention, particularly in identifying high-risk patients early to optimize treatment.The study demonstrates a reasonable response to induction therapy but highlights room for improvement, particularly in managing high-risk subgroups like those with CNS involvement or those experiencing complications during induction.

Conclusion

In conclusion, this study provides a robust assessment of factors influencing induction chemotherapy response in pediatric ALL. While the majority achieve remission, addressing the challenges in high-risk groups and treatment-related complications remains essential to improving survival and quality of life in these patients.

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