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Outcome of Adult Patients with Acute Lymphoblastic Leukemia Receiving MRC UK-ALL XII Protocol: A Single Centre Study

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Abstract

Objective: This study aims to evaluate treatment outcomes, complications, and survival factors that influence the overall survival.
Methodology: A retrospective cohort study was conducted at Aga Khan University, Karachi between January 2011 and December 2022. Data was collected on patients' demographics, laboratory parameters, disease phenotype, cytogenetics, remission rates, minimal residual disease (MRD), and survival outcomes. Kaplan-Meier and Cox regression analyses were used to assess disease-free survival (DFS) and overall survival (OS), along with prognostic factors of treatment response.
Results: The study consisted of 200 adult ALL patients, who received MRC UKALL XII regimen. Complete morphological remission was achieved in 66.5% of patients. MRD-negative patients had better long-term survival (40%) than MRD-positive (20%). At the end of follow-up period, 150 patients had died (75%) while only 50 were alive, with the most common cause of death being relapse-related mortality (65.3%). The median overall survival (OS) and median disease-free survival (DFS) were 15.35 months and 12.1 months respectively. Relapse rate was 50%, which varied by age.
Conclusion: Our findings offer meaningful analysis for the treatment outcome of UKALL XII protocol in adult ALL patients in Pakistan. Age, gender, MRD status, initial WBC count, and cytogenetics are some key prognostic indicators that need further investigation to improve outcomes in our region.
Keywords: Adults, Acute Lymphoblastic Leukemia, MRC UK-ALL XII, Outcome, MRD.

Introduction

Acute lymphoblastic leukemia (ALL) is a malignant hematologic condition due to abnormal and uncontrolled proliferation of lymphoid precursor cells in the marrow and other organs.[1] Globally, the number of new leukemia cases increased from 354,500 to 518,500 cases from 1990 to 2017, with the subtype of ALL increasing to 64,200 cases worldwide and 8,030 cases in Southeast Asia, highlighting the significant burden of the disease.[2]

With considerable variation by age, the incidence of ALL is found to be the highest in children (1–4 years) followed by a sharp decrease through childhood (5–14 years), adolescence, young adulthood (15–39 years) and the lowest incidence observed between 25 years and 45 years.[3] Despite a high incidence, it has presented with a favorable prognosis in children in terms of survival owing to the well tolerated treatment currently available for the pediatric age group.[4] However, the results remain suboptimal in adults and elderly patients with the 5-year overall survival at only 30-40% despite the improvements brought by the conventional chemotherapy.[5]

More recently with the introduction of new diagnostic and therapeutic procedures, the prognosis of adult acute leukemia has shown better outcomes over the years.[6] In the last decade, treatment strategies with monoclonal antibodies, bispecific antibody constructs, and chimeric antigen receptor T cellular therapies have revolutionized the treatment of ALL and they may have the potential to raise the cure rates in adults to levels achieved in pediatric ALL.[7] One such regimen is the Medical Research Council United Kingdom (MRC UKALL) XII protocol, which is based on pediatric treatment approach but has shown efficacy in adult patients.[8] This protocol includes risk-adapted therapy and central nervous system (CNS) prophylaxis, leading to complete remission (CR) rates exceeding 80% and improved outcome in selected populations.[9]

In spite of these advancements, adult patients have varying outcomes, particularly in low- and middle-income countries likely due to limited access to supportive healthcare, diagnostic resources, and novel treatments. Factors such as age, gender, initial white blood cell (WBC) count, immunophenotypic subtype (B-ALL vs T-ALL), Philadelphia chromosome status (Ph), cytogenetic

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abnormalities, and early treatment response are well established predictors of overall outcomes.[10–12] Disease monitoring with minimal residual disease (MRD) testing and conducting allogeneic hematopoietic stem cell transplantation (HSCT) in high-risk patients have additionally enhanced risk stratification, which seems pertinent to personalizing treatment strategies.[13]

While significant research has been focused on the outcomes of adults diagnosed with ALL globally, there remains a gap of data from our region even though leukemia (5.3%) is ranked amongst the top five prevalent cancers in all age groups in Pakistan.[14] Thus, regional studies will play an important role in understanding the impact of standardized treatment protocols such as MRC UKALL XII in clinical settings with varying patient demographics and resource availability. This study aims to describe the clinical outcomes of adult patients (aged ≥18 years) diagnosed with ALL and treated with the UKALL XII protocol at a single tertiary care center in Pakistan. By analyzing survival outcomes, remission rates, and associated prognostic factors, this research provides valuable insights into the efficacy of this protocol in a local context, contributing to the broader understanding of adult ALL treatment outcomes.[10]

Methodology

This retrospective cohort study examined data over a 12-year period, from January 2011 to December 2022at a tertiary care center in Pakistan. The study included adult patients (aged ≥18 years) who were newly diagnosed with ALL and began treatment with the UKALL XII protocol at our institution. Unique medical record identifiers were used to retrieve data from the hospital's electronic medical records (EMR)and follow-up data was censored until December 2024. The study approval was given by the institutional review board of Aga Khan University Hospital, Pakistan.

Eligibility for inclusion required patients to be treatment-naïve at the time of presentation and those who had received the UKALL XII protocol as initial therapy. Exclusion criteria included patients with previous treatment at an outside facility, those who were treated with alternative protocols such as Hyper-CVAD, BFM, or only supportively, and those with chronic myeloid leukemia (CML) transformed into ALL.

Baseline variables for our study included demographics (age, gender), hematologic and biochemical parameters at diagnosis (hemoglobin, white blood cells (WBC) count, platelet count, serum lactate dehydrogenase (LDH), uric acid, calcium), disease phenotype (B-ALL vs. T-ALL), cytogenetic findings, and Philadelphia chromosome (Ph) status. Additionally, conventional karyotyping and BCR-ABL PCR were performed as diagnostic tests for the majority of patients.

According to the latest NCCN guidelines, patients were risk stratified into standard and high-risk groups.[15] The treatment response variables included achievement of complete morphological remission and minimal residual disease (MRD) status after induction phase I assessed by flow cytometry. The target outcome of the study was to inspect the overall survival (OS) and disease-free survival (DFS). OS was defined as the time from diagnosis to death or the last follow-up, while DFS was defined as the time from diagnosis to either relapse, death, or the time of data censoring, whichever occurred first. For patients who underwent allogeneic transplantation, the duration of DFS also included the post-transplant period. Initially, MRD assessment was unavailable due to limited institutional facilities. However, starting in 2016, MRD testing became a routine part of clinical practice and was conducted in most patients using flow cytometry.

Data were compiled into a computerized database and analyzed using Power BI and Cursor AI. Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages. Kaplan–Meier survival analysis was used to estimate OS and DFS, and comparisons between groups were made using the log-rank test. Multivariate analysis was performed using Cox proportional hazards regression to identify variables independently associated with treatment outcomes, including CR and MRD negativity.

MRC UKALL XII protocol was the standard treatment used in all patients in this study. The induction regimen was standardized across the cohort and included CNS prophylaxis, along with specific management for patients with CNS involvement at presentation.

Induction was divided in two sequential phases, with phase 1 of induction therapy lasting from weeks 1 to 4 and phase 2 lasting from weeks 5 to 8. All patients received phase 1 which included daunorubicin 60 mg/m² intravenously (IV) on Days 1, 8, 15, and 22; vincristine 1.4 mg/m² IV on Days 1, 8, 15, and 22; L-asparaginase 10,000 IU intramuscularly (IM) or IV from Days 17 to 28;

prednisone 60 mg/m² orally in divided doses from Days 1 to 28; and methotrexate 12.5 mg intrathecally (IT) on Day 15. Irrespective of the presence of residual leukemia in the bone marrow at the end of Phase 1, all patients proceeded to receive Phase 2 of induction. Phase 2 consisted of cyclophosphamide 650 mg/m² IV on Days 1, 15, and 29; cytarabine 75 mg/m² IV on Days 1–4, 8–11, 15–18, and 22–25; oral 6-mercaptopurine 60 mg/m² daily from Days 1 to 28; and IT methotrexate 12.5 mg on Days 1, 8, 15, and 22.

At the end of phase 1 induction, patients were assessed for both morphological and molecular response and those who failed to achieve complete remission (CR) were reassessed for CR after Phase 2 induction. Diagnostic lumbar puncture was performed on all patients at baseline. In patients with CNS involvement at the time of diagnosis, IT methotrexate was weekly administered until the clearance of blast cells from cerebrospinal fluid (CSF). Additionally, cranial irradiation 2,400 cGy along with spinal cord irradiation 1,200 cGy were administered during phase 2 of induction therapy. Notably, patients with CNS leukemia at diagnosis skipped IT methotrexate during Phase 2.

After phase 2 induction, patients who achieved were divided into two groups. Allogeneic hematopoietic stem cell transplantation (HSCT) was considered for individuals under the age of 50 who were classified as high risk. The high-risk group included those with Philadelphia chromosome positivity, complex cytogenetic abnormalities, persistent MRD after induction, or those who relapsed after achieving CR post-Phase 2 provided they had an HLA-matched sibling donor. Despite being eligible for undergoing transplant, only a small subset proceeded with it primarily due to financial constraints and logistical barriers. Patients who did not fall under the high-risk criteria advanced toward intensification and consolidation therapy as per protocol.

Intensification therapy consisted of three cycles of high-dose methotrexate 3 g/m² administered IV on Days 1, 8, and 22 with each dose followed by L-asparaginase 10,000 IU on Days 2, 9, and 23 along with standard leucovorin rescue to mitigate the toxicity. For consolidation therapy, patients were given CNS prophylaxis with cranial irradiation at a total dose of 2,400 cGy and IT cytarabine 50 mgweekly forfour weeks. This was followed by maintenance CNS-directed therapy, during which IT cytarabine 50 mg was administered every three months for a total of four doses.Maintenance therapy was continued for a period of 2.5 years from the start of intensification therapy. It consisted of vincristine 1.4 mg/m² IV every three months, prednisone 60 mg/m² orallyfor five consecutive days every three months, daily 6-mercaptopurine 75 mg/m² orally, and oral or IT methotrexate 20 mg/m² administered weekly.

Results

A total of 200 adult patients diagnosed with acute lymphoblastic leukemia (ALL) and treated with the UKALL XII protocol between January 2011 and December 2022 were included in the study. The median age at diagnosis was 30 years (range: 19–65), with a mean age of 33.75 years. The age distribution showed single peak that is in young adults (20-30yr age). The majority of patients were male (72%), and the predominant immunophenotypic subtype was B-cell ALL (68.5%), followed by T-cell ALL (31.5%). Only 6 patients had CNS disease at the time of presentation. Baseline hematological and biochemical parameters were also documented (Table I).

Table I: Baseline Laboratory Parameters.

Baseline Parameters	Mean	Median	SD	Range
Hemoglobin (g/dl)	9.35	9.10	2.48	2.8-16.7
WBC count (×10⁹/L)	41.39	11.80	81.66	0.3-486.0
Blast percentage	43.31	40.00	34.90	0-95.0
Platelet count (×10⁹/L)	83.75	45.00	89.94	2.0-601.0
LDH (IU/L)	2035.00	1011.50	3495.80	164.0-38932.0
Uric acid (mg/dl)	7.27	6.15	5.17	0.5-45.3
Calcium (mg/dl)	8.54	8.60	0.75	5.9-11.0

Cytogenetic evaluation revealed normal karyotype in 46% of patients, while 7.5% exhibited complex karyotypes (table II). Philadelphia chromosome positivity was identified in 17.5% of cases (table III). Of these, only 1 patient had double Philadelphia positivity. CNS involvement at diagnosis was rare, occurring in only 2.5% of patients. Risk stratification classified 59% of patients as high-risk and 41% as standard risk according to NCCN guidelines.

Following induction therapy, complete morphological remission (CR) was achieved in 133 patients (66.5%). An additional 15.5% (n=31) failed to achieve remission, while remission assessment could not be completed in 6% (n=12) due to early mortality (figure 1).[1]

Table II. Cytogenetics Status.		
Cytogenetic Status	Number	Percentage
Normal	92	46%
Unknown	47	23.5%
Complex karyotype	15	7.5%
Hypodipoidy	1	0.5%
Hyperdiploidy	9	4.5%
Monosomy 7	3	1.5 %
Trisomy 21	2	1%
Others	31	15.5%

Table II. Philadelphia Chromosome Status.		
Philadelphia Status	(n)	Percentage
Negative	123	61.5%
Unknown	42	21%
Positive	35	17.5%

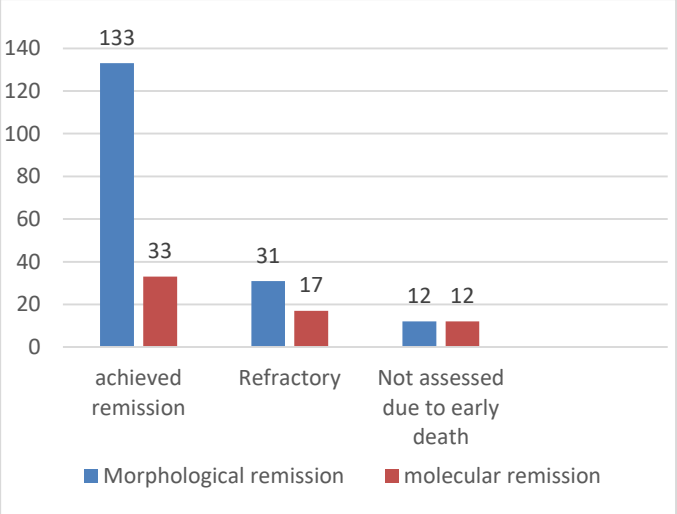

Figure 1. Response Assessment Post Induction Phase I.

On multivariate analysis, higher platelet counts were significantly associated with increased likelihood of achieving morphological remission (OR: 1.02; 95% CI: 1.01–1.03; p = 0.002). In contrast, elevated LDH levels (OR: 0.999; p = 0.003), higher WBC counts (OR: 0.994; p = 0.031), and high-risk disease status (OR: 0.38; 95% CI: 0.17–0.86; p = 0.020) were linked to reduced odds of remission.

Minimal Residual Disease (MRD) Analysis:MRD status was available for a subset of patients (n = 50). Among them, 33 (16.5%) were MRD-negative and 17 (8.5%) were MRD-positive. The majority, 138 patients (69%), had unknown MRD status, while 12 patients (6%) could not be assessed due to early mortality.

In univariate analysis, MRD negativity was higher in standard-risk patients (78.9%) compared to high-risk patients (58.1%). MRD response rates were similar between B-ALL (66.7%) and T-ALL (64.7%), with no significant difference. Philadelphia-negative patients showed a trend toward better MRD clearance, though not statistically significant.

Multivariate logistic regression analysis identified four independent predictors significantly associated with achieving MRD negativity. Standard-risk status, lower WBC and platelet counts, and B-cell immunophenotype were independently associated with higher odds of achieving MRD negativity. These factors may reflect a lower disease burden and better early treatment response.

Various complications associated with the UKALL XII protocol were observed, with febrile neutropenia and mucositis accounting for the majority (figure2). Regarding specific chemotherapeutic agents, methotrexate (MTX) toxicity was observed in six patients, vincristine-induced neuropathy in three, paralytic ileus in four, and infusion-related reactions to asparaginase in four patients. One patient developed pancreatitis, likely secondary to asparaginase. Additionally, two patients experienced carpopedal spasms and one developed iatrogenic obstructive hydrocephalus.

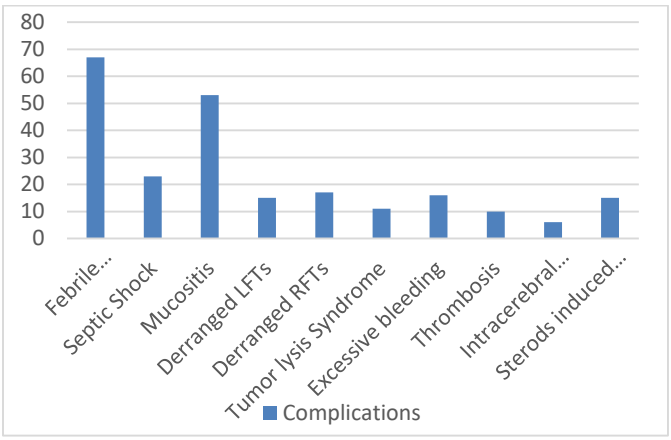

Figure 2. Complications

Several unrelated complications were also noted, including reactivation of tuberculosis, pneumothorax, anterior wall myocardial infarction (MI), cardiomyopathy, non-ST elevation myocardial infarction (NSTEMI), and one case of Bell's palsy.

[1] Data was missing for a group of patients with morphological remission (n=24) and molecular remission (n=138).

At the end of follow-up period, 150 patients had died (75%) while only 50 were alive. The most common cause of death was relapse-related mortality (65.3%), followed by induction mortality (15.6%) and chemotherapy-related toxicity (8.8%). Among the 13 patients who underwent allogeneic stem cell transplantation, outcomes were not analyzed separately due to the small sample size. Of these, only four were alive at the end of the follow-up period. Interestingly, two patients had transformed to JAK2 negative polycythemia vera (PV) by the end of follow-up.

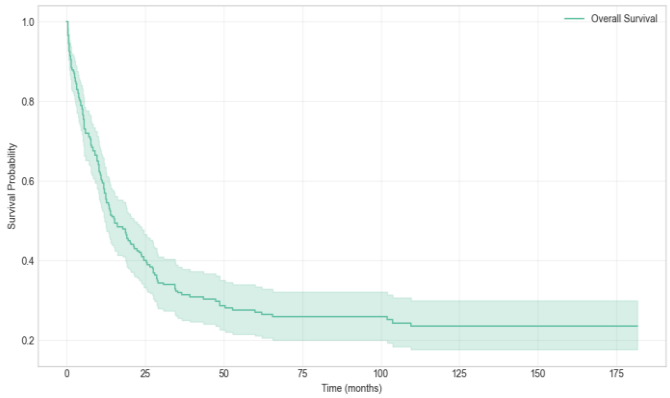

Figure 3. Overall Survival.

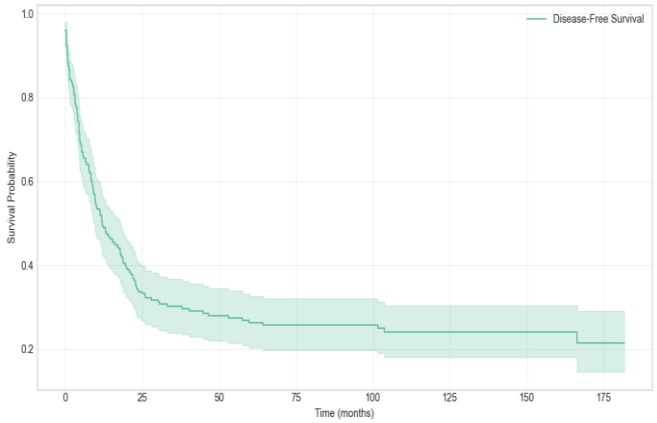

Figure 4. Disease Free Survival.

Survival analysis showed a median overall survival (OS) of 15.35 months and a median disease-free survival (DFS) of 12.1 months(figure 3,4). The 1-year, 2-year, and 3-year OS rates were 57.0%, 41.0%, and 31.9% respectively, while DFS rates at the same intervals were 52.0%, 35.2%, and 31.4%. At final follow-up, 25% of patients were alive. MRD-negative patients demonstrated superior long-term survival compared to MRD-positive patients (40% vs. 20% at 5 years), although this difference was not statistically significant (p = 0.2817 for OS, p = 0.4382 for PFS).

Pediatric patients (0–20 years) showed a trend toward better survival, though not statistically significant (p = 0.0679). No significant survival differences were observed by gender (p = 0.6706) or ALL subtype (B-ALL vs. T-ALL; p = 0.5418).

While Philadelphia-negative and standard-risk patients showed better survival trends, these differences were not statistically significant (p = 0.5268 and p = 0.1501, respectively). In contrast, MRD status was a strong prognostic factor (p < 0.0001), with MRD-negative patients showing significantly better 5-year survival (40%) than MRD-positive patients (20%) (figure 5).

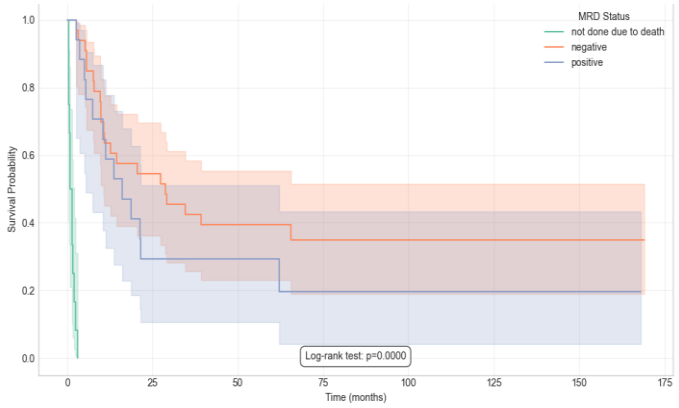

Figure 5. Survival by MRD.

Cytogenetic abnormalities significantly affected survival (p = 0.0001) (figure 6). Patients with complex karyotypes had the highest 5-year survival (40%), followed by those with normal karyotype (25%), while Monosomy 7 was linked to poor prognosis and early mortality.

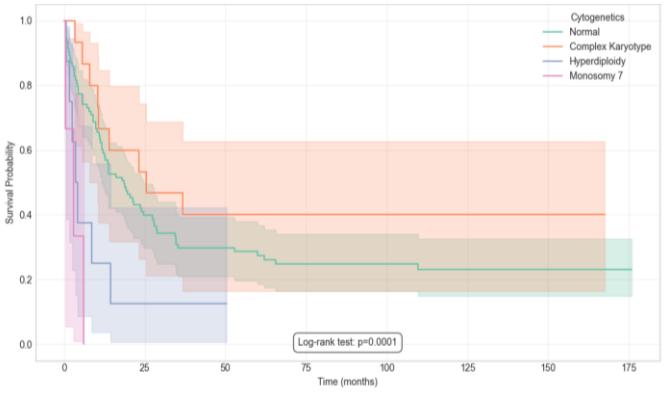

Figure 6. Survival by Cytogenetics

The cox proportional hazards model demonstrated (C-index = 0.787) that higher platelet counts were protective (HR: 0.996; p = 0.0006), while elevated uric acid predicted worse outcomes (HR: 1.044; p = 0.043). Morphological remission significantly reduced mortality

risk (HR: 0.304; p < 0.0001). Risk group and WBC count showed non-significant trends.

Kaplan-Meier analysis showed significantly better overall survival in patients who achieved remission (n=133), with 35% surviving long-term. In contrast, none of the non-responders (n=31) survived beyond 1,500 days, and early deaths (n=12) occurred within 100 days. Progression-free survival followed a similar pattern, favoring those who attained remission (figure 7).

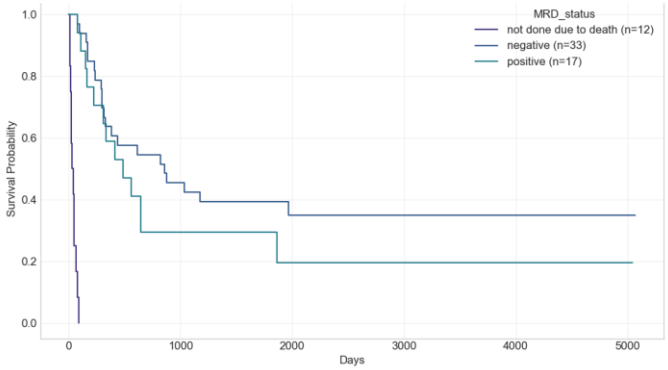

Figure 7. Morphological Remission

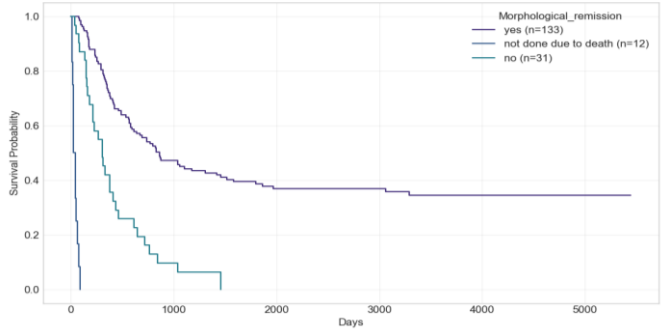

Figure 8. Overall Survival and MRD Status

Kaplan-Meier curves indicated that MRD-negative patients (n=33) had a higher long-term overall survival (35%) compared to MRD-positive patients (n=17), who showed a survival rate of 20%, despite the lack of statistical significance. A similar trend was seen inprogression-free survival(figure 8).

The Kaplan-Meier analysis revealed that patients with initial WBC counts of 0–10 × 10⁹/L (n=91) had the most favorable overall survival, with around 30% surviving long term. In contrast, those with WBC >100 × 10⁹/L (n=20) had the poorest outcomes, with no survivors beyond 3,200 days. A similar trend was observed in progression-free survival. Also, standard-risk patients (n=82) showed better long-term overall survival (≈30%) compared to high-risk patients (n=118), who had about 20% survival (figure 9).

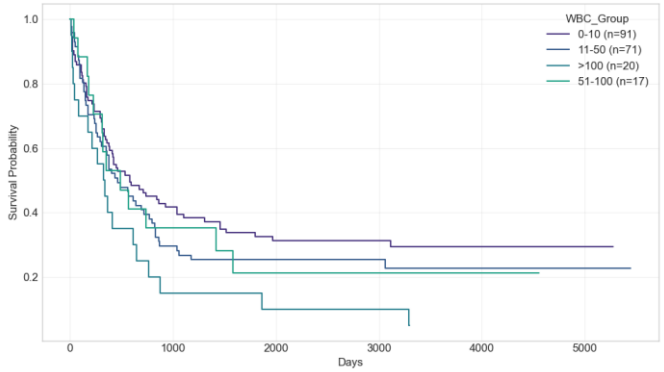

Figure 9. Overall Survival by WBC Group

The Kaplan-Meier curve for overall survival by age group shows that patients aged 0-20 years (n=36) had better early and mid-term survival compared to other age groups, with 30% long-term overall survival. Patients aged 61+ years (n=5) had the worst early outcomes, with survival dropping to 20% by 500 days. The 21-40 (n=106) and 41-60 (n=53) age groups had intermediateoutcomes. (figure 10).

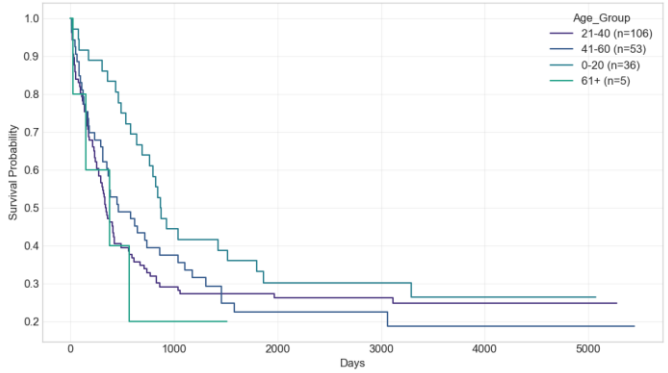

Figure 10. Overall Survival and Age Group

ALL type (p = 0.5443 for OS, p = 0.4658 for PFS), Philadelphia chromosome status (p = 0.5238 for OS, p = 0.5283 for PFS) and gender did not show a statistically significant impact on survival outcomes (p = 0.6678 for OS, p = 0.6349 for PFS).

Kaplan-Meier analysis revealed significant survival differences by immunophenotype and WBC count. T-ALL patients with WBC ≥100 × 10⁹/L had the worst outcomes, with no 5-year survivors. B-ALL with WBC ≥30 × 10⁹/L showed intermediate survival, while B-ALL with WBC <30 × 10⁹/L and T-ALL with WBC <100 × 10⁹/L had 30% long-term survival. On Cox regression, T-ALL with WBC

≥100 × 10⁹/L was associated with a higher mortality risk (HR: 2.20; 95% CI: 1.19–4.09; p = 0.012) (figure 11).

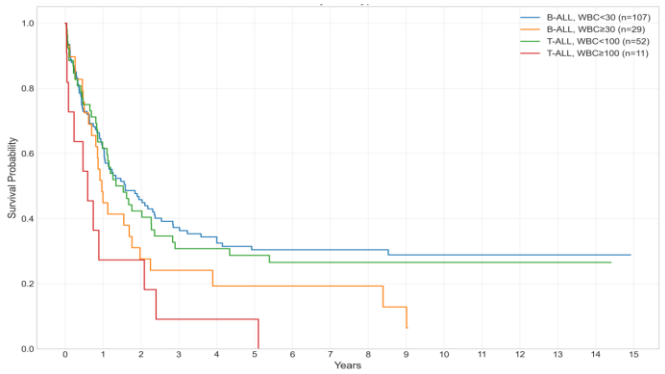

Figure 11. Overall Survival by WBC and ALL Phenotype.

Relapses occurred in 50% of patients, with rates varying by age. Highest percentage of relapse was observed in the 0–20 (58.3%) and 41–60 (54.7%) age groups, lower in 21–40 (45.3%), and lowest in those >60 years (40.0%) (figure 12).

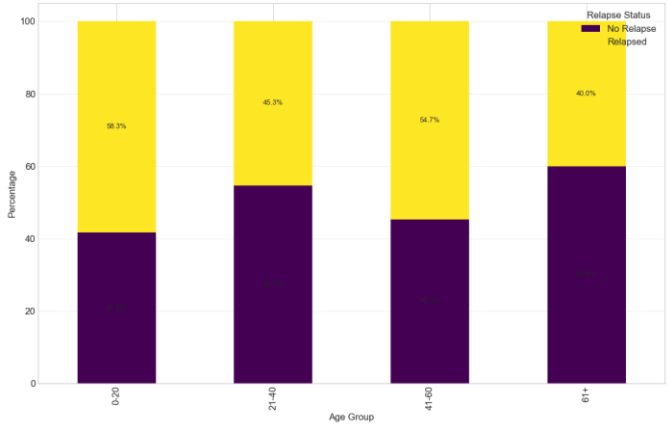

Figure 12. Relapse and Age.

MRD-positive patients had a higher relapse rate (70.6%) than MRD-negative patients (51.5%). Relapse risk was also linked to initial WBC count, highest in the 51–100 × 10⁹/L group (70.6%) and lowest in those with <10 × 10⁹/L (44.0%). No significant association was observed with gender, ALL subtype, Philadelphia chromosome status, or risk group.

Of all the relapsed patients, nine had combined systemic and CNS relapse.

Discussion

This retrospective study consisting of adult ALL patients treated with UKALL XII protocol in a South Asian population highlights the key factors that influence the treatment response and survival trends in this region. The median age of the participants was 30 years with a predominance of male gender (72%) which is consistent with global epidemiological patterns of the demography more commonly affected by ALL, suggesting a possible gender-based predisposition.(16,17) .Most patients presented with B-ALL (68.5%), while 31.5% had T-ALL, reflecting the previous distribution data from international studies.[18,19] The philadelphia positive status was observed in 17.5% of patients which is lower than that seen in the western studies (20–30%)(20), likely due to varying population genetics or methods of detection. More than half the participants were found to have high-risk disease (59%), demonstrating the aggressive nature of ALL in adult patients from low-resource settings. Only 2.5% of the population was found to have CNS involvement at presentation, suggesting potential underdiagnosis or limited imaging performed at the baseline. Even with these risk factors, favorable treatment responses were attained in our study, showcasing the growing potential of the UKALL XII protocol to overcome some adverse prognostic indicators.

Following the induction therapy with the UKALL XII protocol, 66.5% of the cohort successfully reached complete morphological remission. This remission rate is expectedly lower in comparison to literature from high-income settings, where remission rates often exceed 80%.[21] The reduced response to the treatment could be because of various factors e.g., late diagnosis, other comorbidities, and poor management of complications due to resource constraints. Numerous important variables were found to be related to reduced remission rates and included: high white blood cell (WBC) count, high lactate dehydrogenase (LDH) levels, low platelet count and presence of high-risk disease which had been already identified as prognostic variables in response to treatment.[10,22] Its significance as a convenient prognostic tool in resource-limited environments is highlighted by the correlation existing between platelet count and remission rate. On the other hand, there was no statistically significant correlation between remission and sex, Philadelphia chromosome status, immunophenotype and hemoglobin concentrations. Recent publications recognize measurable residual disease (MRD) as a relevant prognostic marker in acute lymphoblastic leukemia (ALL), it is a better risk marker compared to traditional morphological examination of remission.[23] Even though the MRD data in this study were only on a subset of the cohort, the findings were encouraging.

Proportion of cases with MRD-negative was significantly greater in patients whose disease was of the standard-risk category, with low WBC, with low platelet count and B-cell immunophenotype. Moreover, the subgroup which tested MRD-negative had better survival results in which the five-year OS was 40 per cent as opposed to a five-year OS of 20 per cent in the MRD-positive patients. Although the small sample size did not allow drawing any statistical conclusions, the direction of the observation is related to a body of literature that believes that MRD is the strongest and best predictor of relapse and survival.[24,25]

All these findings reinforce the data from various studies confirming the correlation of MRD negative status with reduced disease burden and improved disease outcome.[26–28] In spite of having limited MRD testing in this cohort, its usefulness in assessing treatment response in patients and deciding to proceed with further therapies, such as allogeneic hematopoietic cell transplantation is critical. Integration of MRD monitoring as a routine clinical practice for ALL management, is essential for improving survival outcomes.

Toxicities observed in patients during treatment aligned with the adverse effects of the agents used in the UKALL XII protocol. Most frequently toxicities caused by these agents were febrile neutropenia and mucositis, which are consistent with the toxicity profile of intensive chemotherapy protocols.[29,30] Drug-related complications such as vincristine-induced neuropathy, methotrexate-related toxicity, paralytic ileus, and infusion-related reactions to asparaginase were also documented. These toxicities pose a strong barrier to achieving better quality of life and adherence to treatment as it can require dose adjustments which may compromise the treatment efficiency. Other complications included pancreatitis, carpopedal spasms and iatrogenic obstructive hydrocephalus. Several unrelated complications were also noted, including reactivation of tuberculosis, pneumothorax, anterior wall myocardial infarction (MI), cardiomyopathy, non-ST elevation myocardial infarction (NSTEMI), and one case of Bell's palsy. Among the causes of death, the most common cause was relapse-related mortality, followed by induction mortality and chemotherapy-related toxicity. The documentation of these complications in patients receiving the UKALL XII protocol warrants the need for regular monitoring, good supportive care, and early intervention to help reduce the morbidity and mortality rates. [31,32]

The median OS of 15.35 months and a median DFS of 12.1 months in this cohort is comparatively higher than a previous study conducted in a similar geographical population, likely due to improved supportive care, earlier detection and better prognostic factors.[10] The association of poor survival outcome with WBC ≥100 × 10^9/L, is consistent with existing literature that identifies hyperleukocytosis as a poor prognostic factor. [33,34]

It is worth noting that 50 percent of the total population experienced relapse a phenomenon that is also the leading cause of death in the study under review. MRD-positive patients had a higher relapse incidence (70.6%) than patients with MRD-negative did (51.5%); the difference is in agreement with similar findings in the literature.[35] The current report thus supports the prognostic role of MRD measurement and the importance of MRD in the treatment of acute lymphoblastic leukemia (ALL). Further, the higher the level of white blood cells present at the onset of the disease, the higher the rate of relapse and this reinforced the idea about the initial disease burden as a predictor of future outcomes. The fact that a smaller group of patients had combined systemic and central nervous system (CNS) relapses further underscores the need to have effective CNS-based therapy. Among the subpopulation of the patients, in which cytogenetic abnormalities were reported, Monosomy 7 was more likely to be associated with the worst survival rates. Such result corresponds to other studies that have already found Monosomy 7 as a high-risk factor which is often associated with ineffective reactions to induction chemotherapy and primary disease recurrence.[36] Risk stratification can be improved through the introduction of extensive cytogenetic and molecular profiling, and this may help the creation of personalized treatment plans.

Conclusion

Our study findings have given some insight into the factors that determined the outcome of the MRC UKALL12 protocol among adults having acute lymphoblastic leukemia. In particular, the overall positive response to the treatment measured by the high levels of remission and positive survival rates in patients with a measurable residual disease (MRD) negativity highlight the urgency of MRD determination. Although other ancillary parameters like the platelet counts and white blood cell differentials are of clinical interest, our findings reveal that there is need to add more diagnostic modalities that can further streamline the risk

stratification process. Lastly, future studies should consider the therapeutic usefulness of new agents to overcome current limitations in treatment, and to improve survival in the resource-limited environment.

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