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Treatment outcomes and prognostic factors in children diagnosed with acute myeloid leukaemia in Uganda

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Abstract

Background Treatment of paediatric acute myeloid leukaemia (AML) is challenging in low- and middle-income countries (LMICs) due to resource constraints with subsequent poorer outcome. This study evaluated treatment outcomes and the determinants of survival in paediatric AML patients in Uganda.

Methods This retrospective cohort study reviewed data from children with AML treated at three centres in Uganda between January 2016 and December 2022. Treatment comprised induction with daunorubicin and cytarabine and consolidation with high-dose cytarabine. Patients with acute promyelocytic leukaemia were treated on protocols adapted from Children's Oncology Group AAML 1331. All patients received supportive care. The data were analysed using SPSS Version 20.

Results One-hundred and fifty-nine children with AML were included with a median age at diagnosis of 9.0 years (IQR: 3.0–12.0). Of the 149 patients who initiated therapy, 69 (46.3%) achieved complete remission after the first induction therapy (CR1), and 81 (54.4%) achieved complete remission (CR) overall. Treatment-related mortality occurred in 50 (31.4%) of the patients, with an early death rate of 27.7% (n = 44). Among the 81 patients who achieved CR, 37 (45.7%) relapsed, of whom 27 (73.0%) subsequently died. The one-, three-, and five-year OS were 39.0%, 25.1%, and 16.7%, respectively. The corresponding EFS were 37.0%, 22.9%, and 15.2%, respectively. Median OS and EFS were 7.4 months (95% CI: 4.3–10.6) and 6.9 months (95% CI: 4.4–9.6), respectively. Factors significantly associated with poor OS included poor nutritional status ($p=0.026$), delayed neutrophil recovery following induction ($p=0.030$), failure to achieve CR1 ($p=0.031$), and failure to complete treatment ($p<0.001$).

Conclusions Survival rates among children with AML in this study were low. Several clinical and biological prognostic factors influenced survival outcomes in this resource-limited setting. Improving outcomes will require improving supportive care or adopting resource-adapted treatment protocols that address the supportive care challenges in such a resource-limited setting.

Keywords Acute myeloid leukaemia, Paediatric, Treatment outcomes, Prognostic factors, Resource-limited setting, Africa, Uganda

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Introduction

Paediatric acute myeloid leukaemia (AML) treatment remains a significant challenge in many low- and middle-income countries (LMICs), including across Africa, and is a major cause of morbidity and mortality in these settings [1–3]. Chemotherapy combined with multidisciplinary care continues to be the cornerstone of AML management [4, 5]. Despite substantial improvements over recent decades, driven by advances in understanding disease heterogeneity at clinical, cytogenetic, and molecular levels [6–8], AML remains a life-threatening malignancy in children, with great disparity in prognosis by geographic and socioeconomic contexts.

In high-income countries (HICs), treatment outcomes for paediatric AML have improved substantially over recent decades, achieving five-year overall survival (OS) rates as high as 74% ± 2% for AML overall [9, 10]. Excellent outcomes have particularly been observed in patients with acute promyelocytic leukaemia (APML), with two-year event-free survival (EFS) and OS rates of 98% and 99%, respectively, for standard-risk disease, based on data from the Children's Oncology Group (COG-AAML 1331) [11]. These improvements are largely attributed to the availability of advanced supportive care to alleviate the high toxicity of AML protocols [9, 12], in addition to refined risk stratification and risk-adapted regimens, and improved salvage therapies, including haematopoietic stem cell transplantation (HSCT) [9, 12, 13]. Advanced supportive care remains a vital component to improved and sustained good outcomes given the high intensity and toxicity of AML protocols [13].

Treatment of childhood AML remains exceptionally challenging in low-income countries (LICs) despite the fact that over 80% of childhood cancer cases worldwide occur in these settings [14, 15]. Survival rates in children with AML in LICs, including across Africa, remain low, with five-year overall survival (OS) rates below 40% [2, 16]. This poor prognosis is largely attributed to late presentation, lack of standardised risk-adapted treatment protocols, a high prevalence of comorbidities such as malnutrition, infectious complications, and lack of blood product support. These factors exacerbate the toxicity of intensive chemotherapy regimens amid suboptimal supportive care leading to increased treatment-related morbidity and mortality, most notably early deaths [3, 17, 18]. In many LMICs, mortality associated with both the disease and the related treatment can reach up to 50% [19], compounded by high rates of treatment abandonment and relapse [2, 3]. For example, in Kenya, Van Weelderen et al. reported two-year OS and EFS probabilities of 7% and 4%, respectively [14], and in Egypt, relapse and mortality rates reached 21.7% and 69.6%, respectively [20] which are all substantially inferior to outcomes observed in HICs. Treatment approaches for paediatric AML vary

considerably across LICs; in many African centres, palliative care remains the primary option [1, 21].

The likelihood of cure for a given patient with paediatric AML depends on multiple prognostic factors [22], most importantly genetic abnormalities and the achievement of minimal residual disease (MRD) negativity, which denote superior survival outcomes [23, 24]. While these factors have become integral to routine AML management, particularly in HICs, they remain largely unavailable in most LMICs. However, several clinical and morphological factors also influence treatment response and outcomes in AML [25]. Age, sex, ethnicity, and geographic variation have been identified in multiple studies as important prognostic determinants [26, 27]. Additionally, French-American-British (FAB) subtypes correlate with prognosis; subtypes M5, M6, and M7 are generally associated with poorer outcomes compared to M1–M4, with M0 carrying the worst prognosis overall [25]. However, context-specific data from many LMICs on how these clinical parameters affect paediatric AML outcomes remain limited.

Uganda, a LIC in East Africa, has relatively new paediatric-focused oncology services with limited treatment facilities for childhood cancers and lacks harmonised treatment protocols. A preliminary single-centre report of adult and paediatric AML patients diagnosed and treated from 2016 to 2020 revealed a 30-day induction mortality rate of 32% and a 12-month mortality rate of 70% [28]. Additionally, 39% of patients were undernourished, which is associated with increased risk of death from toxicity and reduced EFS in LMICs [28, 29]. Despite this, there remains a paucity of contextual data on prognostic factors, treatment approaches and outcomes for paediatric AML in Uganda, as well as in the broader African and LMIC contexts. This study aimed to evaluate treatment outcomes and the factors that inform prognosis of paediatric AML at a national level.

Methods

This was a multicentre, retrospective cohort study investigating the records of children and adolescents under 18 years of age, diagnosed with and treated for AML at three cancer treatment centres in Uganda from January 2016 to December 2022. Two of the facilities were from the central region, including the national referral cancer centre, and one was in the western region. Collectively, the three centres manage approximately 700 new childhood cancer diagnoses per year. All children diagnosed with AML between January 2016 and December 2022 under the age of 18 years were included. Patients were excluded if management data were not available.

Diagnosis was established based on the morphological evaluation of bone marrow aspirates and/or peripheral blood smears by experienced haematologists. Flow

cytometry was performed in a limited subset of cases where the service was available. Cytogenetic and molecular analyses were not routinely accessible within the country and were conducted only for a few patients through referral to external laboratories. Central nervous system (CNS) involvement was evaluated through the analysis of cerebrospinal fluid (CSF) and was defined as the presence of more than 5 white blood cells (WBCs)/mm³ of CSF with blasts in a non-bloody sample, which was classified as CNS3 [30]. Additional investigations—such as chest radiography, abdominal ultrasonography, and brain computed tomography (CT)—were undertaken when clinically indicated.

Patients diagnosed with AML were treated with two courses of anthracycline-based induction chemotherapy. Each induction course comprised intravenous infusion of daunorubicin at 50 mg/m²/day on days 1, 3, and 5, in combination with cytarabine 100 mg/m²/day given as a 12-hourly infusion on days 1–10. The second induction course was identical to the first, except that cytarabine was administered for eight days, in accordance with the 10+3 protocol (Supplementary Tables 1 and 2). A few patients received induction treatment based on the 7+3 schedule, where cytarabine, at the same dose as above, was administered from days 1–7 for both induction courses. Induction therapy was followed by two courses of consolidation therapy with high-dose cytarabine (HiDAC) at 3,000 mg/m² given every 12 h on days 1, 3, and 5 (Supplementary Tables 3 and 4). Patients with APML received all-trans retinoic acid (ATRA)-based protocols adapted from the Children's Oncology Group AAML1331 study (Supplementary Tables 5 and 6). All patients routinely received prophylactic triple intrathecal therapy (TIT)—comprising hydrocortisone, methotrexate, and cytarabine—during each cycle of treatment. For patients with CNS involvement, TIT was administered twice weekly until CSF clearance was achieved, followed by two additional doses thereafter and monthly TIT until completion of chemotherapy. In cases of relapse, for some patients, salvage therapy was provided using the fludarabine, cytarabine (Ara-C), and granulocyte colony-stimulating factor (FLAG) regimen (Supplementary Table 7). All patients received supportive therapy, including intravenous fluid administration, transfusion of blood and blood products, and antibiotic prophylaxis and treatment, as well as antifungal and antiviral prophylaxis. However, the availability of blood and blood product (e.g., platelet) transfusions remained inconsistent, posing a significant challenge in this setting. Similarly, paediatric intensive care services, including mechanical ventilation and vasopressor support, were largely unavailable.

Data collected included socio-demographic characteristics (age and sex); disease features (baseline laboratory values, central nervous system [CNS] status, FAB

classification, and nutritional status); treatment (chemotherapy regimens); and outcomes (current status, dates of relapse, death, disease progression, and last follow-up). Nutritional status was assessed on the basis of weight-for-height, body mass index (BMI)-for-age, and mid-upper arm circumference (MUAC) z-scores, and categorized as normal (z-score > -2 SD), moderately (z-score < -2 and > -3SD), or severely (z-score < -3 SD) malnourished as per the World Health Organization criteria [31]. For comparison, age was grouped as < 10 years and ≥ 10 years based on the median age (9.0 years) as a cut point, which is also consistent with other studies. [1, 32], while WBC was categorized as < 50,000/L and ≥ 50,000/L [21, 32], platelets (< 20,000 and ≥ 20,000/L) and haemoglobin (< 7 and ≥ 7 g/dL) [21], and LDH as < 500 U/L and ≥ 500 U/L [33].

Response to chemotherapy was assessed based on bone marrow (BM) morphology on day 28 of induction therapy after haematologic recovery. Complete Remission (CR): was defined as less than 5% bone marrow blasts on BM morphology and absence of extramedullary disease. Partial remission (PR) was defined as failure to achieve CR after the first course of induction chemotherapy, with residual blasts > 5% but < 15%, followed by achievement of CR after two courses of induction therapy. Refractory disease (RD) was defined as failure to achieve CR after one course of induction chemotherapy – characterised by less than a 50% reduction in blasts and > 15% residual blasts – with failure to achieve CR after two courses of induction chemotherapy [21, 34]. Relapse was defined by detection of ≥ 5% blasts in the BM, identification of circulating blasts, or emergence of extramedullary disease after initial CR [35]. Treatment-Related Mortality (TRM) was defined as death occurring within 35 days of any chemotherapy cycle without evidence of disease relapse [17]. Early Death (ED) was defined as death occurring during induction before CR assessment or achievement, or within 42 days of diagnosis. Treatment abandonment was defined as the failure to initiate or complete curative treatment or an unplanned hiatus of four weeks or longer in the scheduled treatment, excluding cases in which palliative care was chosen or treatment was discontinued due to toxicity, as determined by the primary oncologist [36]. Overall Survival (OS) was defined as time from diagnosis to death from any cause. Event-Free Survival (EFS) was defined as time from diagnosis to the first event, defined as disease progression, relapse, treatment abandonment or death from any cause, whichever occurred first.

Data were analysed using Statistical Package for Social Sciences software (SPSS for Windows, Version 27.0. Chicago, SPSS Inc.). Categorical variables were summarised as proportions, while continuous variables were reported as means (± standard deviation) for normally

distributed data or medians (interquartile range) for non-normally distributed data. Survival probabilities were estimated using the Kaplan–Meier method, with differences compared by the log-rank test [37]. Patients alive at the end of follow-up or last contact were censored. The impact of covariates on survival was assessed using Cox proportional hazards regression [38]. Variables significant in bivariable analysis were included in the multivariable model. Adjusted hazard ratios (aHR) with 95% confidence intervals (CI) were reported. A two-sided p -value < 0.05 was considered statistically significant.

Results

Data from 159 children diagnosed with AML were analysed – 135 (84.9%) were non-APML/ML-DS AML, 13 (8.2%) were APML, and 11 (6.9%) were myeloid leukaemia of Down syndrome (ML-DS). Overall, 57 (35.8%) of the cases had flow cytometry confirmation, including nine of the 13 (69.2%) APML subtype. The median age at diagnosis was 9.0 years (interquartile range [IQR]: 3.0–12.0 years). Median age was higher among children with APML at 12.0 years (IQR: 10.5–14.0) and notably lower in those with ML-DS at 1.6 years (IQR: 0.7–2.0). Males constituted 87 patients (54.7%) with a male-to-female ratio of 1.2:1. Thirty-nine percent ($n=62$) of children were malnourished (Table 1).

Haematological and biochemical characteristics of paediatric AML

The most common FAB classifications observed were M7 (24.4%), M5 (22.2%), and M4 (17.8%). Cytogenetic testing was performed in only 10 (6.3%) patients, of whom six (60.0%) had t(8;21) translocation. The median baseline WBC count for the whole cohort was $32.0 \times 10^9/L$ (IQR: 10.3–81.6), with 18.2% ($n=29$) of patients presenting with $WBC \geq 50.0 \times 10^9/L$. Of the 96 patients with

documented CNS status, 14.6% (14/96) had CNS involvement (Table 2).

Age and baseline WBC distribution among children with AML

The age distribution did not significantly differ by sex (Fig. 1A) but showed a statistically significant variation across FAB subtypes and AML categories. Patients with FAB M3 AML were older (median age 12.0 years; range 6.0–15.0 years), whereas those with the FAB M7 subtype were notably younger (median age 1.7 years; range 11 months–10.0 years) ($p < 0.001$) (Fig. 1B). Children with ML-DS were significantly younger (median age 1.7 years; range 11 months–2.6 years) than the other AML patients (median age 9.0 years; range 11 months–17.0 years) and the AML M3 (APML) subtype (median age 12.0 years; range 6.0–15.0 years) ($p < 0.001$) (Fig. 1C). WBC counts at diagnosis did not significantly vary between AML subtypes (Fig. 1D).

Management and outcomes of children with AML

Chemotherapy was initiated in 149 (93.7%) of the patients. The most common reasons for not initiating treatment were early death before initiation ($n=4$; 40.0%) and parental refusal of treatment ($n=4$; 40.0%). The 10 + 3 AD (cytarabine-arabinoside plus daunorubicin) protocol was the predominant chemotherapy regimen, used in 92 (61.7%) of cases. More than half of the patients who initiated therapy ($n=78$; 52.3%) completed treatment, defined as receiving all required chemotherapy cycles: two induction and two consolidation cycles for AML, and all the cycles for APML. The primary reasons for non-completion were death in 56 patients (78.9%) and treatment abandonment in 12 patients (16.9%). Complete remission after the first induction (CR1) was achieved in 69 (46.3%) patients. Overall, 81 (54.4%) achieved CR after two

Table 1 Sociodemographic characteristics of children with AML ($n=159$)

Variable	Whole cohort		AML (non-APML/ML-DS)		M3 subtype (APML)		ML-DS	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Number of patients	159	100	135	84.9	13	8.2	11	6.9
Age (years)								
Median (IQR)	9.0	3.0–12.0	9.0	4.0–12.0	12.0	10.5–14.0	1.6	0.7–2.0
< 1	9	5.7	7	5.2	0	0.0	2	18.2
1–9.9	80	50.3	69	51.1	2	15.4	9	81.8
≥ 10	70	44.0	59	43.7	11	84.6	0	0.0
Sex								
Male	87	54.7	76	56.3	4	30.8	7	63.6
Female	72	45.3	59	43.7	9	69.2	4	36.4
Nutritional status								
Normal	97	61.0	80	59.3	9	59.3	8	72.7
Moderately malnourished	30	18.9	28	20.7	1	20.7	1	9.1
Severely malnourished	32	20.1	27	20.0	3	20.0	2	18.2

APML Acute promyelocytic leukaemia, ML-DS Myeloid leukaemia of Down syndrome, IQR Interquartile range

Table 2 Haematological and Biochemical characteristics of paediatric AML ($n = 159$)

Variable	<i>n</i>	%
FAB classification ($n = 90$)		
M0/M1	0	0.0
M2	10	11.1
M3	13	14.5
M4	16	17.8
M5	20	22.2
M6	9	10.0
M7	22	24.4
Specific cytogenetics ($n = 10$)		
t(8;21)	6	60.0
t(2;7)	1	10.0
Monosomy 7	1	10.0
Normal karyotype	2	20.0
CNS involvement ($n = 96$)*		
Yes	14	14.6
No	82	85.4
Haematological parameters		
	Median	Ranges
WBC counts ($\times 10^9/L$) (median + IQR)	32.0	10.3–81.6
< 50	130	81.8
≥ 50	29	18.2
ANC counts ($\times 10^9/L$)	3.5	1.4–13.0
Monocytes ($\times 10^9/L$)	7.0	1.7–25.6
Baseline Hb level (g/dL)	5.8	4.3–7.6
PLT counts ($\times 10^9/L$)	24.5	10.8–56.0
Biochemical parameters		
LDH (U/L)	750.5	444.5–1699.3
Serum albumin (g/L)	33.1	30.0–38.0

WBC White blood cell, ANC Absolute neutrophil count, Hb Haemoglobin, PLT Platelets, PBF Peripheral blood film, BM Bone marrow, LDH Lactate dehydrogenase

*CNS Central nervous system – five of whom had clinical signs of CNS disease

induction courses. By the end of the follow-up period, most patients ($n = 97$; 61.0%) had died. Treatment-related mortality (TRM) occurred in close to one-third (31.4%; $n = 50$) of the patient cohort (Table 3).

Relapse and outcome

Thirty-seven (45.7%) patients who achieved CR experienced relapse, including two with APML. Among the relapses, 30 (81.1%) were confined to the bone marrow (BM), four (10.8%) involved both BM and CNS, and one (2.7%) each had isolated CNS relapse, combined BM and testicular relapse, and combined BM and cutaneous myeloid sarcoma relapse. The median time from diagnosis to relapse was 9.1 months (range: 1.4–33.9 months). Two (5.4%) relapsed patients were treated with curative intent post-relapse and received haematopoietic stem cell transplantation (HSCT) abroad; both were alive at the time of this study. Among patients who experienced relapse, 28 (75.7%) received salvage chemotherapy, while seven (18.9%) received supportive care only. The most

commonly administered salvage regimen was FLAG (fludarabine, cytarabine, and granulocyte-colony stimulating factor) (Supplementary Table 7). Of the 35 patients who received palliative care, 27 (77.1%) died, five (14.3%) had an unknown outcome, and three (8.6%) remained alive.

Survival outcomes of children with AML

The median follow-up time from diagnosis was 49.6 months (95% CI 35.5–63.8). The median OS was 7.4 months (95% CI: 4.3–10.6). The one-, three-, and five-year OS rates were 39.0% (95% CI 31.4–46.6), 25.1% (95% CI 17.8–32.4), and 16.7% (95% CI 8.5–24.9), respectively (Fig. 2A). The median event-free survival (EFS) was 6.9 months (95% CI: 4.4–9.6), with one-, three-, and five-year EFS rates of 37.0% (95% CI 29.4–44.6), 22.9% (95% CI 16.0–29.8), and 15.2% (95% CI 7.6–22.8), respectively (Fig. 2B).

OS and EFS were significantly better in children with diagnostic white blood cell (WBC) counts less than $50 \times 10^9/L$, normal nutritional status, no central nervous system (CNS) involvement, post-induction absolute neutrophil count (ANC) recovery time of less than 21 days, achievement of complete remission after induction, and those who completed treatment. Specifically, the three-year OS was 30.0% in children with baseline WBC less than $50 \times 10^9/L$, compared to 16.9% in those with WBC greater and equal to $50 \times 10^9/L$ ($p = 0.021$). Corresponding EFS rates were 28.1% and 14.3% for the low and high WBC groups, respectively ($p = 0.012$). OS was 30.8% among well-nourished children, decreasing to 23.3% and 6.7% in moderately and severely malnourished children, respectively ($p < 0.001$). EFS followed a similar pattern, with rates of 27.1% in well-nourished children and 6.7% in severely malnourished children ($p < 0.001$). Children without CNS involvement had a three-year OS of 31.5%, compared to 26.8% in those with CNS involvement ($p = 0.035$). The EFS rates were 31.5% for children without CNS involvement and 21.4% for those with CNS involvement ($p = 0.005$) (Table 4; Figs. 3A–D).

The three-year OS was 44.6% in children with a post-induction one ANC recovery time of less than 21 days, decreasing sharply to 8.4% in those with a recovery time of 21 days or more ($p = 0.003$). Corresponding EFS rates were 41.5% and 6.8% for the less than 21 days and 21 days or more groups, respectively ($p = 0.001$). Children who achieved complete remission after the first induction (CR1) had a three-year OS of 43.6%, compared to 9.9% in those who did not achieve CR1 ($p < 0.001$). EFS was 40.4% in the CR1 group versus 19.8% in those who did not achieve CR1 ($p < 0.001$). Patients who completed treatment had a significantly better three-year OS of 46.3%, while treatment non-completion resulted in a significant drop in OS to 2.2% ($p < 0.001$). Likewise, EFS was 43.6%

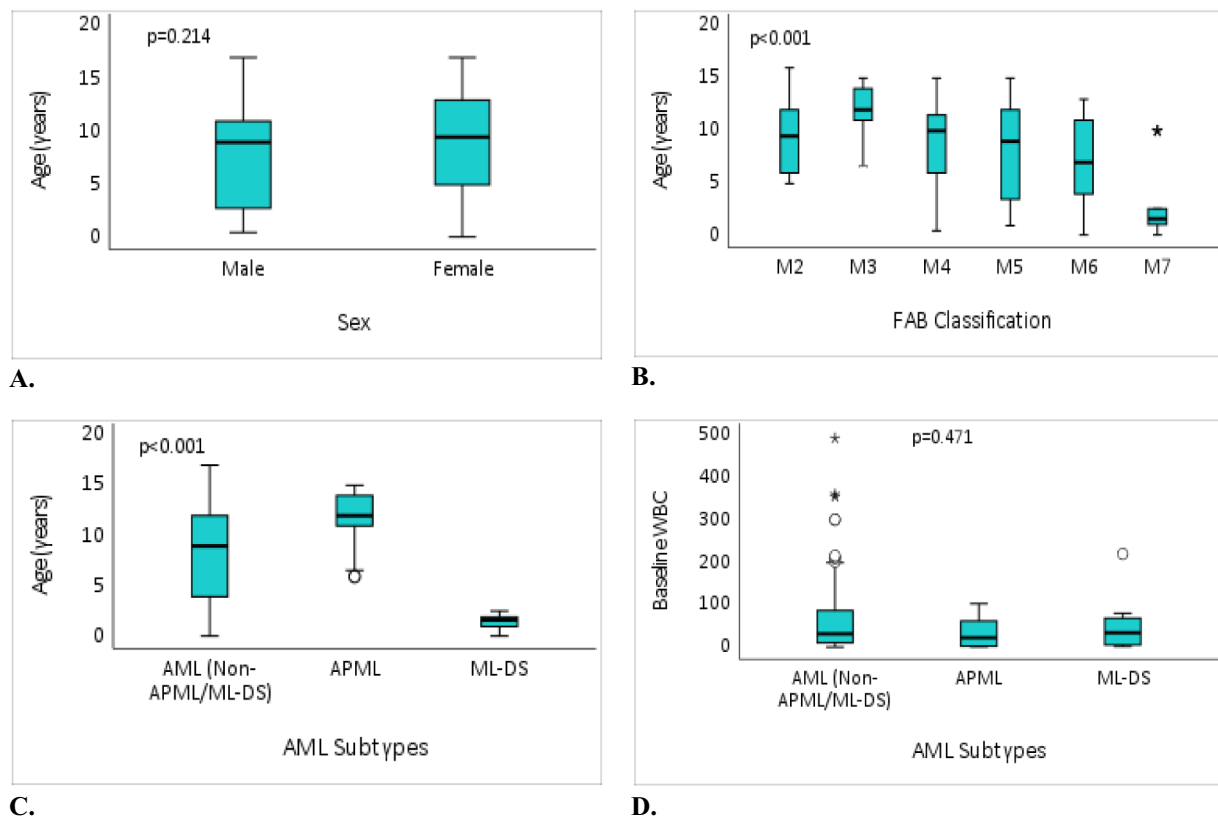


Fig. 1 Box plot of Sex, FAB classification and AML subtype with Age and baseline WBC count. **A** Age distribution by sex. **B** Age distribution by FAB classification. **C** Age distribution by AML subtype. **D** Baseline WBC by AML subtype

in patients who completed treatment and dropped drastically to 1.5% in those who did not complete treatment ($p < 0.001$) (Table 4; Figs. 3E–3H).

Multivariable analysis identified malnutrition (OS: $p = 0.026$; EFS: $p = 0.035$), delayed ANC recovery following the first induction chemotherapy (OS: $p = 0.030$; EFS: $p = 0.039$), failure to achieve complete remission after the first induction course (OS: $p = 0.031$; EFS: $p = 0.035$), and treatment non-completion ($p < 0.001$ for both OS and EFS) as the most statistically significant predictors of inferior OS and EFS among children with AML in the current study setting (Table 5).

Discussion

Acute myeloid leukaemia represents a challenging disease to treat, particularly in low-resource settings [3, 39]. This study was conducted in Uganda, a low-income country that currently lacks comprehensive data on the treatment outcomes of paediatric AML and offers a unique opportunity to explore contextual factors that influence the disease treatment outcomes. Our study demonstrates low OS and EFS rates, alongside high treatment-related mortality, among children with AML in the study setting. Independent poor prognostic factors identified included

poor nutritional status, delayed ANC recovery following first induction chemotherapy, failure to achieve remission after the first induction, and treatment non-completion.

The 10+3 chemotherapy protocol is the predominant treatment regimen for childhood AML in the current study setting, with nearly one-fifth of patients receiving upfront palliative care. This contrasts with many other settings, where the 7+3 protocol is more commonly used [1, 14], highlighting variability in AML treatment approaches. The absence of in-country cytogenetic testing capacity means that patients with adverse cytogenetics cannot be identified. This limitation, common to many LICs, is particularly significant given the well-established prognostic value of cytogenetic abnormalities, which are important for optimal risk stratification and treatment planning and have become the standard of care in high-resource settings [21, 40]. This finding is of clinical significance, as AML patients from different geographic regions or ethnic backgrounds may exhibit distinct genetic abnormalities [33]. The lack of African based data further underscores the need for cytogenetic profiling to inform tailored treatment strategies in African settings [41].

Table 3 Management and outcomes of children with AML

Variable	n	%
Management characteristics		
Chemotherapy initiation		
Yes	149	93.7
No	10	6.3
Reason for not initiating treatment (n = 10)		
Died before initiation	4	40.0
Declined	4	40.0
Too sick	1	10.0
Referred abroad	1	10.0
Therapeutic intent (n = 149)		
Curative	110	73.8
Palliative	28	18.8
Curative followed by palliative	11	7.4
Treatment protocol (n = 149)		
10 + 3 protocol	92	61.7
7 + 3 protocol	5	3.4
APML protocol	13	8.7
ML-DS protocol	11	7.4
Palliative protocol	28	18.8
Treatment outcomes		
Completed treatment‡ (n = 149)		
Yes	78	52.3
No	71	47.7
Reasons for not completing treatment (n = 71)		
Died	56	78.9
Abandoned treatment	12	16.9
Discharged on total palliation	3	4.2
Post-induction one outcome* (n = 149)		
CR1	69	46.3
No CR1	21	14.1
Not assessed	59	39.6
Overall post-induction CR* (n = 149)		
CR	81	54.4
No CR/not assessed	68	45.6
Final outcome at end of follow-up (n = 159)		
Alive	32	20.2
Died	97	61.0
Abandoned treatment	12	7.5
Lost to follow-up	12	7.5
Discharged on total palliation	6	3.8
Treatment-related Mortality (n = 159)		
Yes	50	31.4
No	109	68.6

APML Acute promyelocytic leukaemia, ML-DS Myeloid leukaemia of Down Syndrome, CR Complete remission

‡That is, received all the required cycles of chemotherapy – 2 induction and 2 consolidation for AML, and all the course of chemotherapy for APML

*Denotes CR rates among patients who were alive at the end of induction and were therefore assessed

In this cohort, 54.4% of paediatric AML patients achieved CR following induction chemotherapy, with 46.3% achieving CR after the first cycle (CR1) and an additional 8.1% after the second (CR2). The remission

rate in our cohort is considerably lower than the 80% reported by Ghafoor et al. in Pakistan [42], the 85.7% reported by Jastaniah et al. in Saudi Arabia [43] and the 82%–95% range reported by cooperative study groups in HICs [7, 44]. The observed disparity in CR rates may reflect multifactorial challenges in LMIC settings, including treatment abandonment, upfront palliative intent, uncharacterised high-risk disease biology, and TRM. Achieving CR1 was independently associated with improved survival and reduced mortality, aligning with findings from cooperative oncology groups in HICs, where achieving CR was also associated with longer relapse-free survival [45]. This may be explained by the fact that patients with poor prognostic features, such as delayed response, are more likely to achieve only partial remission rather than CR [46], underscoring the need for early response monitoring (e.g., morphological and MRD assessments).

TRM remains a major challenge in the management of AML in LMICs, including resource-limited settings in Africa [2, 3], a pattern also observed in our patient cohort. In this study, the TRM was occurred in 31.4% (n = 50) of the whole cohort, with an early death (ED) rate of 27.7% (n = 44), including eight patients who died before initiation of chemotherapy. The TRM rate in our cohort is slightly higher than the 23.3% and 20.8% reported by Gupta et al. [17] in Central America and Jastaniah et al. [40] in Saudi Arabia, respectively. The ED rate observed here contrasts sharply with the 4.1%–5.9% rates reported by cooperative groups in HICs [43, 47]. Notably, the Japanese Childhood AML Cooperative Study Group recently reported induction death rates as low as 0.9% and 1.7% [48, 49]. The substantially higher TRM and ED rates observed in our cohort highlight the significant challenges encountered in LICs, including limited supportive care infrastructure amidst dose-intensive chemotherapy protocols, inadequate antimicrobial and microbiological support, treatment interruptions, as well as unexplored pharmacogenomics. Evidence suggests that differences in the incidence and severity of chemotherapy-related toxicities across patient populations can often be linked to ethnicity, primarily through pharmacogenomic variation [50–52]. As a result, expert opinion increasingly supports genotype-guided dosing over broad, ethnicity-based modifications [50].

Relapse is a major cause of mortality in patients with AML, with relapse rates typically reported between 30 and 40% [17, 47]. In the present study, 45.7% of patients who achieved complete remission post-treatment experienced relapse, a rate comparable to that reported in other LMICs [14, 53]. This high relapse rate may be attributed to MRD positivity following induction therapy. Evidence indicates that residual MRD after induction is associated with a significantly worse prognosis compared to

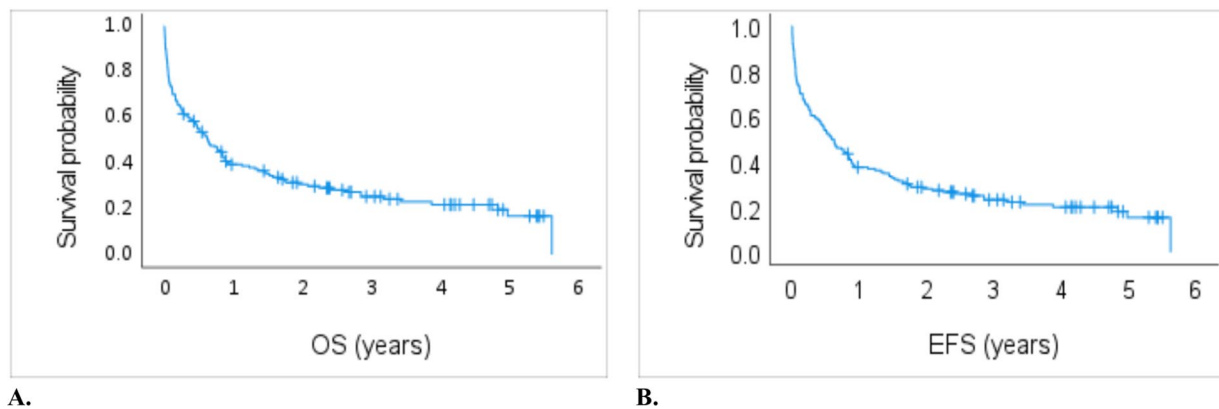


Fig. 2 Survival curves for children with AML. **A** Overall survival (OS). **B** Event-free survival (EFS)

MRD-negative status in paediatric AML [7, 54]. In this study, post-induction remission was defined morphologically by fewer than 5% blasts in bone marrow (haematological complete remission), with limited assessment of MRD. Nearly all patients with relapsed disease received only palliative care, with the majority succumbing to their illness. This outcome likely reflects the absence of salvage therapies, including haematopoietic stem cell transplantation (HSCT), which has been shown to improve survival in relapsed AML [42]. This benefit was also demonstrated by the two patients in this cohort who received HSCT abroad following relapse.

The current study demonstrated low OS and EFS probabilities, with median survival times of 7.4 and 6.9 months, respectively. The three-year OS and EFS rates in our cohort were 25.1% and 22.9%, respectively, which are considerably lower than those reported in high-income contexts, where 5-year OS for paediatric AML has reached up to 75% [9, 55], as well as some other LMICs [56]. However, these survival rates are consistent with reports from many LMICs [14, 17, 18, 39]. For example, in Tanzania, no patients survived beyond two years post-diagnosis, while in Kenya, the two-year OS and EFS probabilities were 7.0% and 4.0%, respectively [14, 18]. These survival disparities are likely attributable to inadequate supportive care, high treatment-related mortality, challenges in risk stratification, and lack of salvage therapies including HSCT [3], compounded by high rates of treatment abandonment and comorbidities such as malnutrition.

Malnutrition remains a significant factor associated with poor treatment outcomes in childhood cancers in LMICs [21], a finding confirmed in the present study. Survival was markedly worse among severely malnourished children, with three-year OS and EFS rates of $6.7\% \pm 4.6\%$. Malnutrition also emerged as an independent predictor of mortality. This is consistent with reports from Pakistan by Ghafoor et al. [21, 42] and is likely attributable to decreased chemotherapy tolerance,

increased toxicity, and a higher risk of TRM among malnourished patients [21, 57, 58]. Furthermore, malnutrition impairs immune function by reducing complement proteins, cytokines, and immunoglobulins, thereby increasing susceptibility to infections. This underscores the importance of correcting nutritional deficiencies and considering prophylactic antibiotics in undernourished children undergoing chemotherapy for AML [59]. Targeted nutritional interventions for high-risk groups have been shown to improve morbidity and mortality, as demonstrated in low-income country settings [58].

Time to neutrophil recovery following the first induction chemotherapy emerged as a significant clinical predictor of survival outcomes in this study. Both OS and EFS rates were significantly lower among patients with delayed neutrophil recovery beyond 21 days. In resource-limited settings, where supportive care infrastructure such as broad-spectrum antimicrobials and intensive care units is often inadequate, prolonged neutropenia substantially elevates the risk of treatment-related mortality [42, 56]. Overall and event-free survival rates were significantly higher in patients presenting with a lower WBC count ($< 50 \times 10^9/L$). This finding aligns with results from the Medical Research Council AML12 trial in paediatric AML [60], as well as several other studies [21, 42]. Hyperleukocytosis has been associated with an increased risk of TRM and lower CR rates [21, 42]. In the current study, 69.5% of children with diagnostic WBC equal to or more than $50 \times 10^9/L$ died, compared to 56.0% of those with WBC less than $50 \times 10^9/L$. This may be due to the heightened risk of metabolic complications such as tumour lysis syndrome and leukostasis, particularly in critical organs like the lungs and brain. Recognition and proactive management of hyperleukocytosis could thus improve outcomes.

Strengths and limitations of the study

This study was undertaken at more than one site in the country, including the national oncology referral

Table 4 Bivariable analysis of prognostic factors for OS and EFS among children with AML

Variable	n	3-year OS		3-year EFS	
		Value ± SE	p-value	Value ± SE	p-value
Sex					
Male	83	30.2 ± 5.4%	0.187	26.3 ± 5.0%	0.313
Female	71	19.9 ± 5.1%		19.3 ± 5.0%	
Age (years)					
< 10	85	27.2 ± 5.0%	0.836	25.1 ± 4.8%	0.801
≥ 10	69	23.5 ± 5.6%		21.2 ± 5.2%	
Nutrition status					
Normal	95	30.8 ± 5.2%	< 0.001*	27.1 ± 4.8%	< 0.001*
MAM	29	23.3 ± 8.0%		27.2 ± 8.3%	
SAM	30	6.7 ± 4.6%		6.7 ± 4.6%	
Baseline WBC					
< 50	99	30.0 ± 4.9%	0.021*	28.1 ± 4.8%	0.012*
≥ 50	55	16.9 ± 5.3%		14.3 ± 4.8%	
Platelets					
≥ 20	72	27.4 ± 5.7%	0.082	24.5 ± 5.3%	0.120
< 20	81	24.5 ± 4.9%		22.9 ± 4.7%	
Haemoglobin					
≥ 7	98	27.1 ± 4.8%	0.242	24.3 ± 4.5%	0.335
< 7	55	23.6 ± 6.0%		21.9 ± 5.8%	
FAB subtype					
M2	9	51.9 ± 17.6%	0.155	44.4 ± 16.6%	0.120
M3	12	10.4 ± 9.7%		10.4 ± 9.7%	
M4	16	18.8 ± 9.8%		18.8 ± 9.8%	
M5	19	23.0 ± 10.5%		15.8 ± 8.4%	
M6	9	44.4 ± 16.6%		44.4 ± 16.6%	
M7	22	36.4 ± 10.3%		36.4 ± 10.3%	
CNS involvement					
No	80	31.5 ± 5.3%	0.035*	31.5 ± 5.3%	0.005*
Yes	14	26.8 ± 12.3%		21.4 ± 11.0%	
Unknown	60	15.9 ± 5.5%		12.3 ± 4.5%	
LDH (U/L)‡					
< 500	20	34.8 ± 12.8%	0.052	28.5 ± 11.3%	0.073
≥ 500	44	18.1 ± 6.3%		15.2 ± 5.6%	
Time to ANC recovery (ID-1)					
< 21 days	75	44.6 ± 5.9%	0.003*	41.5 ± 5.8%	0.001*
≥ 21 days	22	8.4 ± 7.3%		6.8 ± 6.1%	
Time to ANC recovery (ID-2)					
< 21 days	65	41.1 ± 6.3%	0.150	38.6 ± 6.2%	0.220
≥ 21 days	12	65.6 ± 14.0%		58.3 ± 14.2%	
Remission after induction 1					
CR	69	43.6 ± 6.3%	< 0.001*	40.4 ± 6.1%	< 0.001*
No CR	21	9.9 ± 8.4%		19.8 ± 9.4%	
Not assessed	51	6.0 ± 3.9%		4.6 ± 3.1%	
Treatment completion					
Yes	78	46.3 ± 6.0%	< 0.001*	43.6 ± 5.9%	< 0.001*
No	68	2.2 ± 2.1%		1.5 ± 1.5%	

MAM Moderate acute malnutrition, SAM Severe acute malnutrition, WBC White blood cell count, ANC absolute neutrophil count, ID-1 Induction 1, ID-2 Induction 2, FAB French-American-British classification, CNS Central nervous system, LDH Lactate dehydrogenase

‡Categorization was based on the prognostic level in childhood lymphoma documented by Song et al. [33]; **Normal karyotype, monosomy 7, t(2;7) and inv9; CR Complete remission

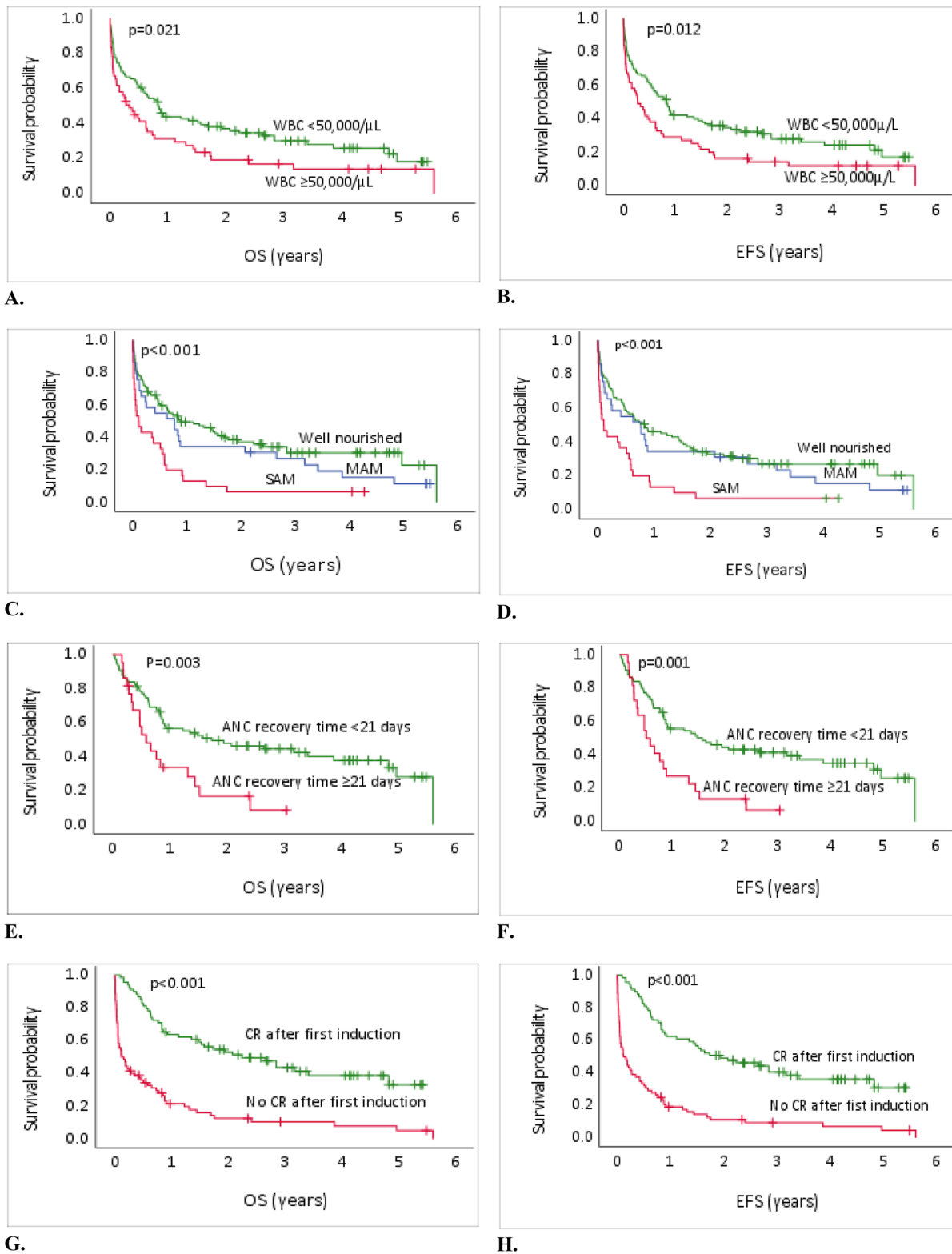


Fig. 3 Survival curves for children with AML. **A** OS by baseline WBC count. **B** EFS by baseline WBC count. **C** OS by nutrition status. **D** EFS by nutrition status. **E** OS by time to ANC recovery after first induction. **F** EFS by time to ANC recovery after first induction. **G** OS by Complete remission status after first induction. **H** EFS by Complete remission status after first induction

Table 5 Multivariable analysis of prognostic factors among children with AML

Model	Overall survival			Event-free survival		
	aHR	95% CI	p-value	aHR	95% CI	p-value
Malnutrition	2.02	1.09–3.75	0.026*	1.93	1.05–3.55	0.035*
Baseline WBC (≥ 50)	1.55	0.78–3.06	0.210	1.51	0.76–2.97	0.236
Delayed ANC recovery (ID-1)	2.31	1.09–4.91	0.030*	2.21	1.04–4.68	0.039*
CNS involvement (Yes)	1.60	0.53–4.79	0.402	1.94	0.72–5.26	0.191
Remission after induction 1 (No)	2.01	1.07–3.78	0.031*	1.96	1.05–3.68	0.035*
Treatment completion (No)	4.44	2.15–9.17	< 0.001*	4.44	2.15–9.16	< 0.001*

aHR Adjusted Hazard ratio, WBC White blood cell count, ANC Absolute neutrophil count, ID-1 Induction 1, CNS Central nervous system

centre. A notable limitation of the study is its retrospective design, with some incomplete or missing data that consequently restricted the sample size available for certain analyses. Likewise, cytogenetic and immunophenotypic profiling for disease characterisation were unavailable, and diagnoses were based solely on morphological features, rendering definitive diagnosis challenging and susceptible to diagnostic error. Nevertheless, the study offers valuable insights into treatment strategies and outcomes for paediatric acute myeloid leukaemia (AML) in real-world, resource-limited settings.

Conclusion

Survival outcomes among children with AML in this setting were low, with high rates of TRM and disease relapse. Several clinical and laboratory prognostic factors significantly influenced survival among children with AML in the study setting. Improvements of outcomes and quality of life of children with AML will require strategies to reduce TRM, including effective supportive care measures to manage the toxicity associated with the high intensity AML protocol and increase research into salvage strategies for AML in the African setting.

Abbreviations

AML	Acute myeloid leukaemia
ANC	Absolute neutrophil count
BM	Bone marrow
ML-DS	Myeloid leukaemia of Down Syndrome
FAB	French-American-British classification
HIC	High-income country
IQR	Interquartile range
LDH	Lactate dehydrogenase
LIC	Low-income countries
LMIC	Low-and middle-income countries
MDS	Myelodysplastic syndrome
PBF	Peripheral blood film
UCI	Uganda Cancer Institute
WBC	White blood cell

Supplementary Information

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Supplementary Material 1.

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Authors' contributions

RN conceptualized and initiated the study, and contributed to the study design, data collection, and interpretation of results. JvH, JBK, MK, NN, SS contributed to the design, supervised the study, and reviewed the draft manuscript, and critically revised the manuscript. BA and JZ supervised the study and critically revised the manuscript. All authors have read and approved the final manuscript.

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Data availability

All data relevant to the study are included in the article or uploaded as supplementary information. The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations, and the study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Uganda Cancer Institute Research and Ethics Committee (UCI-2024–97). The requirement for written informed consent and assent was waived by the ethics committee due to the retrospective data collection and no risk.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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References

- Mamo W, Moges A, Yesuf SA, Mohamedsaid A, Arega G. Treatment outcomes of pediatrics acute myeloid leukemia (AML) and associated factors in the country's tertiary referral hospital. Ethiopia. *BMC Cancer*. 2024;24(1):640.
- Nyeko R, Kruger M, Niyonzima N, Stijn V, van Heerden J. Paediatric acute myeloid leukaemia epidemiology, treatment approaches, and outcomes in Africa: a review of the literature. *BMC Cancer*. 2025;25(1):1140.
- Van Weelderden RE, Klein K, Natawidjaja MD, De Vries R, Kaspers GJ. Outcome of paediatric acute myeloid leukaemia (AML) in low- and middle-income countries: a systematic review of the literature. *Expert Rev Anticancer Ther*. 2021;21(7):765–80.
- Reinhardt D, Antoniou E, Waack K. Pediatric acute myeloid Leukemia—past, present, and future. *J Clin Med*. 2022;11(3):504. <https://doi.org/10.3390/jcm11030504>.
- Gupta S, Howard SC, Hunger SP, Antillon FG, Metzger ML, Israels T, et al.: Treating Childhood Cancer in Low- and Middle-Income Countries. In: Disease Control Priorities, Third Edition (Volume 3): Cancer. The World Bank 2015:121–146. https://doi.org/10.1596/1978-1591-4648-0349-1599_ch1597.
- Dohner H, Estey E, Amadori S, Appelbaum F, Buchner T, Burnett A, et al. Diagnosis and management of acute myeloid leukemia in adults: Recommendations from an international expert panel, on behalf of the European LeukemiaNet. *Blood*. 2009;115(3):453–74.
- Rubnitz JE, Inaba H. Childhood acute myeloid leukaemia. *Br J Haematol*. 2012;159(3):259–76. <https://doi.org/10.1111/bjh.12040>. (Epub 12012 Sep 12012).
- Kantarjian H, Kadia T, DiNardo C, Daver N, Borthakur G, Jabbour E, et al. Acute myeloid leukemia: current progress and future directions. *Blood Cancer J*. 2021;11(2):41.
- Reedijk AMJ, Klein K, Coebergh JWW, Kremer LC, Dinmohamed AG, de Haas V, et al. Improved survival for children and young adolescents with acute myeloid leukemia: a Dutch study on incidence, survival and mortality. *Leukemia*. 2019;33(6):1349–59.
- Creutzig U, Zimmermann M, Jean-Pierre B, Dworzak MN, Fleischhack G, Graf N, et al. Randomized trial comparing liposomal daunorubicin with idarubicin as induction for pediatric acute myeloid leukemia: results from Study AML-BFM 2004. *Blood*. 2013;122(1):37–43. <https://doi.org/10.1182/blood-2013-1102-484097>. (Epub 482013 May 484023).
- Kutny MA, Alonzo TA, Abba O, Rajpurkar M, Gerbing RB, Yi-Cheng W, et al. Assessment of Arsenic Trioxide and All-trans Retinoic Acid for the Treatment of Pediatric Acute Promyelocytic Leukemia - A Report From the Children's Oncology Group AAML1331 Trial. *JAMA Oncol*. 2021;8(1):1–9. <https://doi.org/10.1001/jamaoncol.2021.5206>.
- Zwaan CM, Kolb EA, Reinhardt D, et al. Collaborative efforts driving progress in paediatric acute myeloid leukaemia. *J Clin Oncol*. 2015;33(27):2949–62. <https://doi.org/10.1200/JCO.2015.2962.8289>.
- Klein K, de Haas V, Kaspers GJL. Clinical challenges in de novo paediatric acute myeloid leukaemia. *Expert Rev Anticancer Ther*. 2018;18(3):277–93.
- van Weelderden RE, Njuguna F, Klein K, et al. Outcomes of paediatric acute myeloid leukaemia treatment in Western Kenya. *Cancer Reports*. 2021;5(10):e1576. <https://doi.org/10.1002/cnr11572.1576>.
- Ward E, DeSantis C, Robbins A, et al. Childhood and adolescent cancer statistics, 2014. *CA Cancer J Clin*. 2014;64(2):83–103. <https://doi.org/10.3322/caac.12119>.
- Lins MM, Mello MJG, Ribeiro RC, De Camargo B, De Fatima Pessoa Militao de Albuquerque M, Thuler LCS: Survival and risk factors for mortality in pediatric patients with acute myeloid leukemia in a single reference center in low-middle-income country. *Ann Hematol*. 2019;98(6):1403–11.
- Gupta S, Bonilla M, Valverde P, et al. Treatment-related mortality in children with acute myeloid leukaemia in Central America: incidence, timing and predictors. *Eur J Cancer*. 2012;48(9):1363–9. <https://doi.org/10.1016/j.ejca.2011.1310.1009>.
- Kersten E, Scanlan P, Dubois SG, Matthay KK. Current treatment and outcome for childhood acute leukemia in Tanzania. *Pediatr Blood Cancer*. 2013;60(12):2047–53.
- Begum M, Islam A, Rahman AA, Akter M, Alam ST, Tasmeen R. Abandonment and outcome of childhood acute myeloid leukemia in a tertiary level hospital. *Mymensingh Med J*. 2018;27(1):95–102.
- Mourtada F, Assem M, El Leithy A, Hassan N, Hassan N. RUNX3 gene expression confers an independent overall survival advantage in non-M3 adult acute myeloid leukemia patients in Egypt. *Int J Cancer Biomed Res*. 2020;0(0):0–0. <https://doi.org/10.21608/jcbr.2020.27668.21027>.
- Ghafoor T, Khalil S, Farah T, Ahmed S, Sharif I. Prognostic factors in childhood acute myeloid leukemia; experience from a developing country. *Cancer Rep*. 2020;3:e1259. <https://doi.org/10.1002/cnr.1252.1259>.
- Estey E. Prognostic factors in acute myelogenous leukemia. *Leukemia*. 2001;15(4):670–2. <https://doi.org/10.1038/sj.leu.2402057>.
- Short NJ, Zhou S, Fu C, Berry DA, Walter RB, Freeman SD, et al. Association of measurable residual disease with survival outcomes in patients with acute myeloid leukemia: a systematic review and meta-analysis. *JAMA Oncol*. 2020;6(12):1890–9. <https://doi.org/10.1001/jamaoncol.2020.4600>.
- de Rooij J, Zwaan C, van den Heuvel-Eibrink M. Paediatric AML: from biology to clinical management. *J Clin Med*. 2015;4(1):127–49. <https://doi.org/10.3390/jcm4010127>.
- Asif N, Hassan K. Clinical manifestations of acute myeloid leukemia. *J Islamabad Med Dent Coll*. 2012;1211(1):6–9.
- Aplenc R, Alonzo TA, Gerbing RB, Smith FO, Meshinchi S, Ross JA, et al. Ethnicity and survival in childhood acute myeloid leukemia: a report from the Children's Oncology Group. *Blood*. 2006;108(1):74–80. <https://doi.org/10.1182/blood-2005-1110-4004>.
- Meshinchi S, Arceci RJ. Prognostic factors and risk-based therapy in pediatric acute myeloid leukemia. *Oncologist*. 2007;12(3):341–55. <https://doi.org/10.1634/theoncologist.1612-1633-1341>.
- Okello CD, Meshinchi S, Tarlock K, Warren P, Towleron AMH, Ddungu H, et al. Clinical Outcome and treatment-related mortality in patients with acute myeloid leukemia treated at the Uganda Cancer Institute. *Blood*. 2022;140(Suppl 1):8940–1. <https://doi.org/10.1182/Blood-2022-165982>.
- Minke H. W. Huibers, Geoffrey Manda, Allison Silverstein, Watipaso Wanda, Idah Mtete, Samuel Makuti, et al.: The Burden of Malnutrition in Childhood Cancer in Malawi – Risk Regardless of Age. *Nutrition and Cancer* 2022, 74(9):3322–3328, <https://doi.org/10.1080/01635581.01632022.02076888>.
- Creutzig U, van den Heuvel-Eibrink MM, Gibson B, et al. Diagnosis and management of acute myeloid leukaemia in children and adolescents: recommendations from an international expert panel. *Blood*. 2012;120(16):3187–205. <https://doi.org/10.1182/blood-2012-3103-362608>.
- WHO child growth standards and the identification of severe acute malnutrition in infants and children. Available at: <https://www.who.int/publications/i/item/9789241598163>.
- Razzouk BI, Estey E, Pounds S, Lensing S, Pierce S, Brandt m ea: impact of age on outcome of pediatric acute myeloid leukemia. *Cancer*. 2006;106(11):2495–502. <https://doi.org/10.1002/cncr.21892>.
- Song JS, Youn HS, Im HJ, Ghim T, Moon HN, Seo JJ. Treatment outcome and prognostic factors for children with advanced non-Hodgkin's lymphoma at a single institution. *Korean J Hematol*. 2006;41(3):157–66. <https://doi.org/10.5045/kjh.2006.5041.5043.5157>.
- Ferguson P, Hills RK, Grech A, Betteridge S, Kjeldsen L, Dennis M, et al. An operational definition of primary refractory acute myeloid leukemia allowing early identification of patients who may benefit from allogeneic stem cell transplantation. *Haematologica*. 2016;101(11):1351–8. <https://doi.org/10.3324/haematol.2016.148825>.
- DeWolf S, Tallman MS. How i treat relapsed or refractory AML. *Blood*. 2020;136(9):1023–32.
- Mostert SAR, Arreola M, et al. Abandonment of treatment for childhood cancer: position statement of a SIOP PODC Working Group. *Lancet Oncol*. 2011;12(8):719–20. [https://doi.org/10.1016/S1470-2045\(10\)170128-70120](https://doi.org/10.1016/S1470-2045(10)170128-70120).
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53:457–81.
- Cox DR. Regression models and life tables. *J R Stat Soc Series B Stat Methodol*. 1972;34:187–220.

39. Gallegos-Castorena S, Medina-Sanson A, Gonzalez-Ramella O, Sánchez-Zubieta F, Martínez-Avalos A. Improved treatment results in Mexican children with acute myeloid leukemia using a medical research council (MRC)-acute myeloid leukemia 10 modified protocol. *Leuk Lymphoma*. 2009;50(7):1132–7. <https://doi.org/10.1080/10428190902964768>.
40. Jastaniah W, Al Ghemlas I, Al Daama S, Ballourah W, Bayoumy M, Al-Anzi F, et al. Clinical characteristics and outcome of childhood de novo acute myeloid leukemia in Saudi Arabia: a multicenter SAPHOS leukemia group study. *Leuk Res*. 2016;49:66–72.
41. Koh Y, Kim I, Bae JY, Song EY, Kim HK, Yoon SS, et al. Prognosis of secondary acute myeloid leukemia is affected by the type of the preceding hematologic disorders and the presence of trisomy. *Jpn J Clin Oncol*. 2010;40(11):1037–45.
42. Ghafoor T, Sharif I, Bashir F, Ahmed S, Ashraf T, Khalil S, et al. Mortality in paediatric acute myeloid leukaemia. *J Pak Med Assoc*. 2020;70(12(B)):2316–22. <https://doi.org/10.5455/JPMA.2549>.
43. Creutzig U, Zimmermann M, Reinhardt D, et al. Early deaths and treatment-related mortality in children undergoing therapy for acute myeloid leukaemia: analysis of the multicentre clinical trials AML-BFM 93 and AML-BFM 98. *J Clin Oncol*. 2004;22(21):4384–93.
44. Rubnitz JE. How I treat pediatric acute myeloid leukemia. *Blood*. 2012;119(25):5980–8.
45. Walter RB, Kantarjian HM, Huang X, et al. Effect of complete remission and responses less than complete remission on survival in acute myeloid leukaemia: a combined Eastern Cooperative Oncology Group, Southwest Oncology Group, and M. D. Anderson Cancer Center Study. *J Clin Oncol*. 2010;28(10):1766–71.
46. Estey EH, Shen Y, Thall PF. Effect of time to complete remission on subsequent survival and disease-free survival time in AML, RAEB-t, and RAEB. *Blood*. 2000;95(1):72–7 (PMID: 10607687).
47. Molgaard-Hansen L, Mottonen M, Glosli H, et al. <article-title update="added">Early and treatment-related deaths in childhood acute myeloid leukaemia in the Nordic countries: 1984–2003. *Br J Haematol*. 2010;151(5):447–59. <https://doi.org/10.1111/j.1365-2141.2010.08389.x>.
48. Tsukimoto I, Tawa A, Horibe K, Tabuchi K, Kigasawa H, Tsuchida M, et al. Risk-stratified therapy and the intensive use of cytarabine improves the outcome in childhood acute myeloid leukemia: the AML99 trial from the Japanese Childhood AML Cooperative Study Group. *J Clin Oncol*. 2009;27(24):4007–13. <https://doi.org/10.1200/JCO.2008.4018.7948>.
49. Rubnitz JE, Inaba H, Dahl G, et al. Minimal residual disease-directed therapy for childhood acute myeloid leukaemia: results of the AML02 multicentre trial. *Lancet Oncol*. 2010;11(6):543–52. [https://doi.org/10.1016/S1470-2045\(10\)70090-70095](https://doi.org/10.1016/S1470-2045(10)70090-70095).
50. Glewis S, Alexander M, Khabib MNH, Brennan A, Lazarakis S, Martin J, et al. A systematic review and meta-analysis of toxicity and treatment outcomes with pharmacogenetic-guided dosing compared to standard of care BSA-based fluoropyrimidine dosing. *Br J Cancer*. 2022;127:126–36. <https://doi.org/10.1038/s41416-01022-01779-41416>.
51. Pathak S, Zajac KK, Annaji M, Govindarajulu M, Nadar RM, Bowen D, et al. Clinical outcomes of chemotherapy in cancer patients with different ethnicities. *Cancer Rep (Hoboken)*. 2023;6 Suppl 1(Suppl 1):e1830. <https://doi.org/10.1002/cnr.1832.1830>.
52. Hasegawa Y, Kawaguchi T, Kubo A, Sai-Hong IO, Nakagawa K, Takada M, et al. Ethnic difference in hematological toxicity in patients with non-small cell lung cancer treated with chemotherapy: a pooled analysis on Asian versus Non-Asian in Phase II and III clinical trials. *J Thorac Oncol*. 2011;6(11):1881–8.
53. Songthawee N, Sriporasawan P, Chavananon S, McNeil EB, Chotsampancharoen T. Relapsed childhood acute myeloid leukemia: experience from a single tertiary center in Thailand. *Asian Pac J Cancer Prev*. 2022;23(12):4079–84. <https://doi.org/10.31557/APJCP.2022.31523.31512.34079>.
54. Riley LC, Hann IM, Wheatley K, Stevens RF. Treatment-related deaths during induction and first remission of acute myeloid leukemia in children treated on the Tenth medical research council acute myeloid leukaemia trial (MRC AML10). *Br J Haematol*. 1999;106(2):436–44. <https://doi.org/10.1046/j.1365-2141.1999.01550.x>.
55. Tierens A, Arad-Cohen N, Cheuk D, De Moerloose B, Fernandez Navarro JM, Hasle H, et al. Mitoxantrone Versus Liposomal Daunorubicin in Induction of Pediatric AML With Risk Stratification Based on Flow Cytometry Measurement of Residual Disease. *J Clin Oncol*. 2014;42(18):2174–85. <https://doi.org/10.1200/JCO.2123.01841>.
56. de Morais RV, de Souza MV, de Souza Silva KA, Santiago P, Lorenzoni MC, Lorea CF, et al. Epidemiological evaluation and survival of children with acute myeloid leukemia. *Jornal de Pediatria*. 2021;97(2):204–10. <https://doi.org/10.1016/j.jpmed.2020.1002.1003>.
57. Ronit E, Arie L, Sophie L, Sergey P, Myriam WBA. Nutritional status of children with solid tumors. *Cancer*. 1999;86:119–25.
58. Israels T, Damen CWN, Cole M, et al. Malnourished Malawian patients presenting with large Wilms tumours have a decreased vincristine clearance rate. *Eur J Cancer*. 2010;46(10):1841–7.
59. Inaba H, Surprise HC, Pounds S, et al. Effect of body mass index on the outcome of children with acute myeloid leukemia. *Cancer*. 2012;118(23):5989–96. <https://doi.org/10.1002/cncr.27640>.
60. Gibson BE, Webb DK, Howman AJ, et al. Results of a randomized trial in children with Acute Myeloid Leukaemia: medical research council AML12 trial. *Br J Haematol*. 2011;155(3):366–76.

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