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Predictors of Survival and Relapse among Children Diagnosed with Acute Leukemia in Northen Tanzania

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Abstract

Background: Acute Leukemia is the most common childhood cancer, with two main types: ALL and AML. In Tanzania, recent improvements in treatment and survival have been noted, but the latest data is from 2013. This study will update survival and relapse information from 2013 to 2020 to help enhance future treatment strategies. **Methodology:** This study was conducted at two tertiary hospitals in Tanzania. The study analyzed data from children diagnosed with Acute Leukemia between January 2015 to December 2020. Patient data were collected via questionnaires and analyzed using STATA software. **Results:** This study included a total of 95 participants 64 had age less than 10 years and majority were males 56.8%, 55 had duration of symptoms for more than 1 month 66 had ALL, 49 had attained remission, the overall three years survival was 44.2% with those children with no health insurance having high risk of dying, rate of relapse was 18.4%, with those diagnosed with B-ALL having low risk of relapse. **Conclusion:** This study provides insights into survival and relapse predictors for childhood leukemia in northern Tanzania. It found an overall survival rate of 44.2%, with health insurance and minimal residual disease after induction being key predictors of survival. The relapse rate was 18.4%, with health insurance linked to a lower relapse risk. Health insurance emerged as a strong predictor of better survival, leading to the recommendation that all children should have health insurance. Additionally, the study suggests that policymakers should support the expansion of global health coverage in Tanzania.

Keywords

Acute Leukemia, Relapse, Survival

1. Background

Leukemia is the most common cancer in children. It is a malignancy that arises from proliferation of hematopoietic cells leading to disruption of normal marrow function and marrow failure. The clinical manifestations of leukemia are result of the unregulated proliferation of the malignant clone and bone marrow failure. There are two main subtypes of acute leukemias in children: the commoner acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Acute leukemia constitutes about 40% of all childhood cancers [1]. Leukemia accounted for approximately 2.5% of all new cancer incidence and 3.1% of cancer-related mortality. ALL is the most common type of childhood cancers. Approximately 75% of people under age 20 diagnosed with leukemia are diagnosed with ALL. Most cases occur between age 2 and 5. AML is the second most common form of leukemia in children second to ALL. However, most cases of AML occur in adults. Childhood AML is more common during the first 2 years of life and during the teenage years. [2] [3].

It is a life-threatening condition that requires immediate and intensive medical intervention. While significant advancements have been made in the treatment of acute leukemia in developed countries, the situation in low-resource settings, such as Northern Tanzania, remains challenging [4]. The treatment of leukemia involves systemic chemotherapy, intrathecal chemotherapy, radiation for patients with persistent CNS involvement with definitive treatment being bone marrow transplant. However due to limited resources lower- and middle-income countries such as Tanzania are limited to the first three modes of treatment and for patients with which require bone marrow transplants will have to travel to countries such as India which is more often not the case due to financial issues. Both subtypes have their own treatment protocol and, in both hospitals, (BMC and KCMC) the same protocols were used in treatment, the ALL treatment has 5 phases remission induction phase, consolidation phase, escalating Capizzi, delayed intensification and maintenance phase duration of treatment can take 2 to three years to complete.

AML treatment has two main phases which are induction phase consolidation phase. Leukemia accounts for a significant proportion of childhood cancers in various countries. In the United States, it constitutes 27% of childhood cancer cases [5]. In Ireland and France, leukemia represents approximately 30% of childhood cancers. In Shanghai, China, it accounts for 35% of childhood cancer cases. Similarly, in Iraq, leukemia comprises approximately 29.65% of childhood cancers [6] [7].

Leukemia incidences are generally higher in developed countries compared to developing countries. This is often due to better diagnostic facilities, which are

closely associated with the economic status of a country. Developed countries have more advanced healthcare infrastructure and access to sophisticated diagnostic technologies, leading to more accurate and timely leukemia diagnoses. In contrast, developing countries may have limited resources and face challenges in accurate detection and reporting of leukemia cases. Improving diagnostic capabilities in developing countries is essential for better detection and management of leukemia [8]. According to a study by Okello and colleagues [9], leukemias account for an estimated 10% of all cancers in Sub Saharan Africa. However, determining the precise incidences and treatment outcomes of leukemias in the region is challenging due to the underdevelopment of population-based cancer registries. In sub-Saharan Africa, a study conducted in Mali focused on the epidemiological, clinical, and therapeutic aspects of acute lymphoblastic leukemia (ALL). The study findings indicated a poor prognosis for ALL patients in their center. One contributing factor identified was late diagnosis. The study suggested that early diagnosis, along with tailored treatment protocols for high-risk patients, could potentially reduce early deaths and improve survival rates for patients in remission [10].

In Cote d'Ivoire, a study reported that acute leukemia accounted for approximately 4% of all childhood malignancies [11]. Similarly, a study conducted in Nigeria found that acute leukemia constituted 16.9% of all childhood malignancies in their population [12]. Moreover, a study conducted in Kenya in 2012 provided insights into the prevalence of acute leukemia among childhood malignancies in the region. The findings indicated that acute lymphoblastic leukemia (ALL) accounted for approximately 15% of all childhood malignancies, while acute myeloid leukemia (AML) accounted for 5.1% [13].

Moreover, the entity discusses on the progress made in improving survival rates for acute leukemia, especially in higher-income countries. However, there is a significant disparity globally, with lower survival rates in low- and middle-income countries compared to high-income countries. A study by Ssenyonga [14], covering 258 cancer registries in 61 countries from 2000 to 2014, found that the 5-year survival rate for children with leukemia in low- and middle-income countries is about 20%, whereas it is around 80% in high-income countries. Reducing these disparities and improving global access to effective treatments is crucial.

A study done in 2013 compared the treatment outcomes of childhood acute leukemia in Tanzania to those of high-income countries. The results revealed a stark contrast in survival rates. The estimated 2-year event-free survival for patients with acute lymphoblastic leukemia (ALL) was 33%, while for acute myeloid leukemia (AML), the survival rate was 0%. This is in stark contrast to higher-income countries, where survival rates for childhood acute leukemia could reach up to 85% [13].

Globally, the early relapse rate for standard-risk leukemia patients is 35%, compared to 50% for high-risk patients, while late relapse rates are 5% and 1%, respectively. However, among those who survive for three years or more, the risk of late relapse is similar for both groups (8% for high-risk and 11% for standard-risk). A

20-year retrospective study in Thailand involving 472 patients found that 32.8% experienced relapses, primarily in the bone marrow [15]. In Tanzania, about 60% of patients with acute leukemia experienced a relapse within two years of therapy, reflecting challenges such as late diagnoses, limited access to specialized treatments, and barriers to optimal follow-up care [16].

The study found that AML had a particularly poor prognosis in Tanzania due to the intensity of therapy and drug toxicity. The 2-year survival rate for AML was reported as 0%, indicating significant challenges in effectively treating and managing this subtype of leukemia in the Tanzanian context. Our study aims at highlighting the predictors of survival and relapses among children diagnosed with leukemia in Tanzania.

2. Materials and Methods

This retrospective analytical cohort study examined pediatric acute leukemia (AL) cases at Kilimanjaro Christian Medical Centre (KCMC) and Bugando Medical Centre (BMC) in Tanzania. The study reviewed medical records of children aged 0 - 18 years diagnosed with AL, including acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML), between January 1, 2015, and December 31, 2020. Conducted from October 2022 to July 2023, the study focused on outcomes such as overall survival, relapse rates, and predictors of these outcomes. Both KCMC and BMC are tertiary hospitals serving large populations, with KCMC covering northern Tanzania and parts of Kenya and BMC serving the Lake Zone and neighboring countries. The study utilized convenient sampling to include all eligible patients who met the inclusion criteria.

Key variables analyzed included demographic factors (age, gender), clinical indicators (white cell count, CNS involvement, hepatosplenomegaly, LDH levels), treatment-related factors (regimen, minimal residual disease status), and socioeconomic aspects (insurance status, distance from the hospital). By identifying predictors of survival and relapse, the study aims to provide insights into improving care and outcomes for pediatric AL patients in the region, addressing gaps in oncology services in resource-limited settings.

Data collection and analysis methods: The study utilized a structured data extraction sheet for collecting information in three main areas: sociodemographic details (age, sex, and address), clinical characteristics (age at diagnosis, leukemia subtype), and outcomes (3-year survival, relapse rates, and their predictors). Ethical clearance was obtained from Kilimanjaro Christian Medical University College (KCMUCo) and permissions from relevant hospital departments. Data were collected by identifying children aged 0 - 18 years diagnosed with acute leukemia between January 2015 and December 2020 using the Oncology Registry and EHMS system to access electronic medical records.

Data analysis was performed using STATA version 18. Descriptive statistics summarized categorical variables as frequencies and percentages and continuous variables using measures of central tendency and dispersion. Kaplan-Meier

models estimated survival probabilities across subgroups, while bivariate and multivariate Cox regression identified predictors of survival and relapse. Variables with a P-value < 0.05 were considered statistically significant. The primary outcomes focused on 3-year survival status (Yes/No) and relapse rates (Yes/No).

3. Results

This study included a total of 95 study participants. The mean (SD) age of the study participants was 7.5 (4.9) years. However; 64 (67.4%) had age <10 years, 54 (56.8%) were males, median (IQR) distance from home to hospital was 90.0 (30.0 - 219.0) kilometers, 28 (29.5%) had insurance (Table 1).

Table 1. Socio demographic characteristics of the study participants (N = 95).

Characteristics	Hospital		Total n (%)
	KCMC	BMC	
	n (%)	n (%)	
	64	31	
Age (years)			
<10	44 (68.7)	20 (64.5)	64 (67.4)
≥10	20 (31.3)	11 (35.5)	31 (32.6)
Mean ± (SD)			7.5 (4.9)
Sex			
Male	38 (59.4)	16 (51.6)	54 (56.8)
Female	26 (40.6)	15 (48.4)	41 (43.2)
Distance from the hospital			
<50	28 (43.7)	7 (22.6)	35 (36.8)
≥50	36 (56.3)	24 (77.4)	60 (63.2)
Median (IQR)			90.0 (30.0 - 219)
Insurance			
No	39 (60.9)	28 (90.3)	67 (70.5)
Yes	25 (39.1)	3 (9.7)	28 (29.5)

3.1. Clinical Characteristics of Study Participants

55 (57.9%) had symptoms for more than a month, 49 (51.6%) had normal body temperature, 76 (80.0%) had hepatomegaly, 78 (82.1%) had splenomegaly, 28 (29.5%) had mediastinal mass, 6 (6.3%) had pleural effusion, 90 (94.7%) had lymphadenopathy, 12 (12.6%) had chloroma, 34 (35.8%) (Table 2).

Table 2. Clinical characteristics of the study participants.

Characteristics	Hospital		Total n (%)
	KCMC	BMC	
	n (%)	n (%)	
	64	31	
Duration of symptoms (months)			
≤1	28 (43.7)	12 (38.7)	40 (42.1)
>1	36 (56.3)	19 (61.3)	55 (57.9)

Continued

Temperature			
<36.5	8 (12.5)	1 (3.2)	9 (9.5)
36.5 - 37.5	35 (54.7)	19 (61.3)	54 (56.8)
>37.5	21 (32.8)	11 (35.5)	32 (33.7)
Hepatomegaly			
No	14 (21.9)	5 (16.1)	19 (20.0)
Yes	50 (78.1)	26 (83.9)	76 (80.0)
Splenomegaly			
No	12 (18.7)	5 (16.1)	17 (17.9)
Yes	52 (81.3)	26 (83.9)	78 (82.1)
Mediastinal mass			
No	43 (67.2)	24 (77.4)	67 (70.5)
Yes	21 (32.8)	7 (22.6)	28 (29.5)
Pleural effusion			
No	60 (93.8)	29 (93.6)	89 (93.7)
Yes	4 (6.2)	2 (6.4)	6 (6.3)
Lymphadenopathy			
No	4 (6.3)	1 (3.2)	5 (5.3)
Yes	60 (93.7)	30 (96.8)	90 (94.7)
Chloroma			
No	57 (89.1)	26 (83.9)	83 (87.4)
Yes	7 (10.9)	5 (16.1)	12 (12.6)

A fraction of the patients; 49 (51.6%) had white cell count <50, 48 (50.5%) had platelet ≤20, 5 (5.3%) had hemoglobin ≥11 g/dl, 79 (83.2%) had uric acid <500, 49 (51.6%) had LDH <1000, 94 (98.6%) had creatinine <100, 76 (80.0%), 11 (11.6%) had CNS involvement, 66 (69.5%) had ALL (Table 3).

Table 3. Laboratory characteristics of the study participants (N = 95).

Characteristics	Hospital		Total n (%)
	KCMC	BMC	
	n (%)	n (%)	
	64	31	
White cell count			
<50	35 (54.7)	14 (45.2)	49 (51.6)
≥50	29 (45.3)	17 (54.8)	46 (48.4)
Platelet cell count			
≤20	33 (51.6)	15 (48.4)	48 (50.5)
>20	31 (48.4)	16 (51.6)	47 (49.5)
Hemoglobin level			
≥11.0	4 (6.3)	1 (3.2)	5 (5.3)
7.0 - 10.9	20 (31.2)	10 (32.3)	30 (31.6)
<7.0	40 (62.5)	20 (64.5)	60 (63.1)
Uric acid level			
<500	52 (81.3)	27 (87.1)	79 (83.2)
≥500	12 (18.7)	4 (12.9)	16 (16.8)
LDH			
<1000	28 (43.7)	21 (67.7)	49 (51.6)

Continued

≥1000	36 (56.3)	10 (32.3)	46 (48.4)
Creatinine			
<100	63 (98.4)	31 (100)	94 (98.9)
≥100	1 (1.6)	-	1 (1.1)
CNS involvement			
No	56 (87.5)	29 (93.6)	85 (89.5)
Yes	8 (12.5)	2 (6.4)	10 (10.5)
Cancer subtypes			
B-ALL	25 (39.1)	9 (29.0)	34 (35.8)
T-ALL	21 (32.8)	11 (35.5)	32 (33.7)
AML	18 (28.1)	11 (35.5)	29 (30.5)

3.2. Treatment Characteristics of the Study Participants

67 (70.5%) were started on treatment, 29 (43.3%) treated with regimen C, 60 (89.5%) completed induction, 49 (81.7%) had MRD negative after induction 5 (6.1%) had a change in treatment regimen (Table 4).

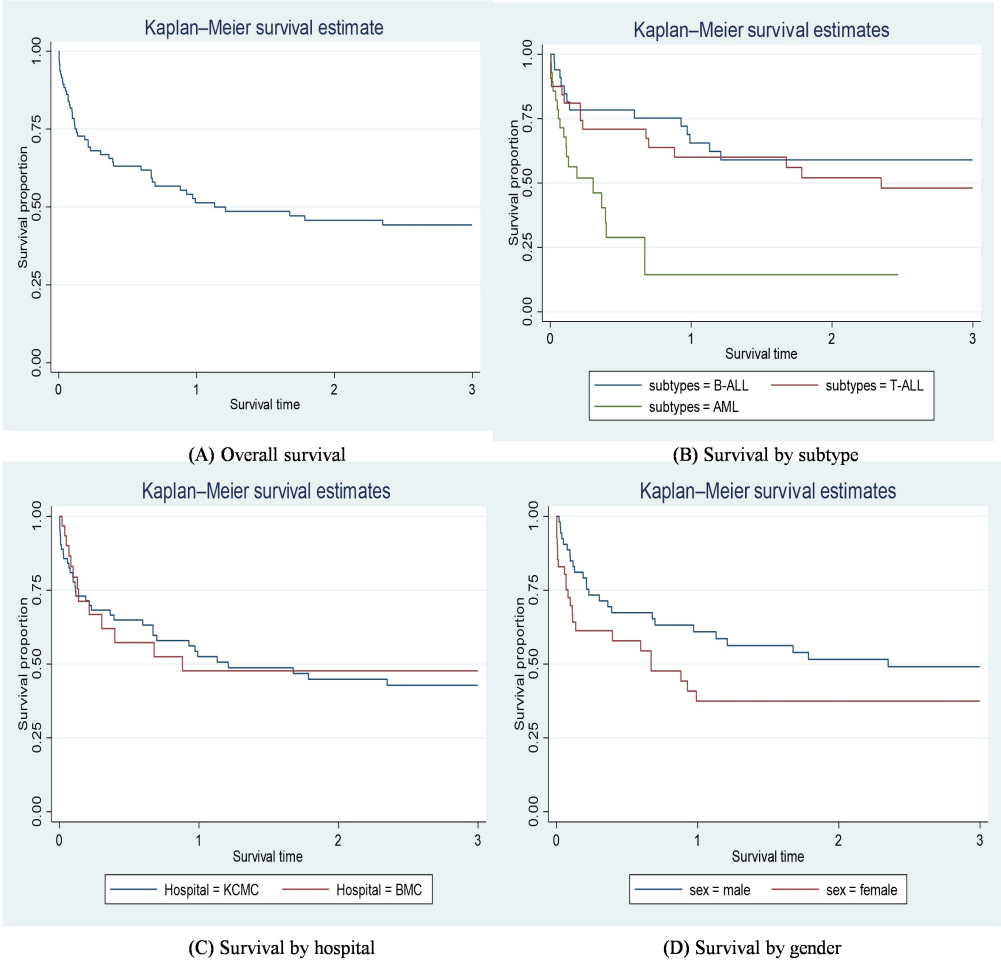
Table 4. Treatment characteristics of the study participants (N = 95).

Characteristics	Hospital		Total n (%)
	KCMC	BMC	
	n (%)	n (%)	
	64	31	
Patient started treatment			
No	15 (23.4)	13 (41.9)	28 (29.5)
Yes	49 (76.6)	18 (58.1)	67 (70.5)
Treatment regimen (n = 67)			
Regimen B	17 (34.7)	7 (38.9)	24 (35.8)
Regimen C	22 (44.9)	7 (38.9)	29 (43.3)
AD protocol	10 (20.4)	4 (22.2)	14 (20.9)
Patient complete induction (n = 67)			
No	4 (8.2)	3 (16.7)	7 (10.5)
Yes	45 (91.8)	15 (83.3)	60 (89.5)
MRD after induction (n = 60)			
Negative	35 (77.8)	14 (93.3)	49 (81.7)
Positive	10 (22.2)	1 (6.7)	11 (18.3)
Change treatment regimen (n = 67)			
No	44 (91.7)	18 (94.7)	62 (93.9)
Yes	4 (8.3)	1 (5.3)	5 (6.1)

3.3. Three Years Survival for Children Diagnosed with Acute Leukemia in Northern Tanzania

The overall survival rates for acute leukemia (AL) were 78.4% at one year, 51.4% at two years, and 44.2% at three years. Specifically, patients with B-ALL had survival rates of 78.4% at one year, 65.6% at two years, and 59.0% at three years. For those with T-ALL, the survival rates were 70.8% at one year, 60.1% at two years, and 48.4% at three years. Patients with AML had a survival rate of 78.6% at one

year, but only 14.3% at two years, with no data for three years as all AML patients had died by then. Overall survival rates were 42.8% at KCMC and 47.7% at BMC (Figures 1(A)-(D)).



(A) Overall survival

(B) Survival by subtype

(C) Survival by hospital

(D) Survival by gender

Figure 1. Kaplan Meier three years' survival estimation children with leukemia.

3.4. Predictors of Survival among Children Diagnosed with Leukemia in Northern Tanzania

In three years of survival in bivariate the predictors of survival were, children with AL with no health insurance had significant 5.2 times higher risk of dying as compared to those with health insurance (HR: 5.2; 95% CI: 2.19, 12.34). Children with B-ALL 0.26 times better survival compared to those with AML (HR: 0.26; 95% CI: 0.13, 0.56), children with negative MRD had 0.21 times better survival outcomes compared to those with positive MRD (HR: 0.21; 95% CI: 0.08, 0.56) (Table 5). In multivariable, after adjusting for other factors the predictors of survival were, children with AL with no health insurance had 58.43 times higher risk of dying compared to those with health insurance (HR: 58.43; 95% CI: 5.86, 582.56). Children with MRD negative after induction had 1564.36 times better survival than those with positive MRD (HR: 1564.36; 95% CI: 41.1, 59537.14) (Table 5).

Table 5. Predictors of survival among children diagnosed with acute leukemia in Northern Tanzania.

Predictor	Hospital		Total	P value	AHR (95% CI)	P value
	KCMC	BMC	CHR (95% CI)			
Age						
0 - 9	44 (68.8)	20 (64.5)	1		1	
10 above	20 (31.3)	11 (35.5)	1.71 (0.96 - 3.06)	0.069	2.81 (0.45 - 17.550)	0.269
Gender						
Male	38 (59.4)	16 (51.6)	0.63 (0.35 - 1.11)	0.111	0.99 (0.16 - 5.980)	0.989
Female	26 (40.6)	15 (48.4)	1		1	
Distance from hospital						
<50 KM	28 (43.8)	7 (22.6)	1		1	
≥50	36 (56.3)	24 (77.4)	1.41 (0.77 - 2.58)	0.267	0.35 (0.58 - 2.180)	0.262
Health insurance status						
No	39 (60.9)	28 (90.3)	5.21 (2.19 - 12.34)	**<0.001**	58.43 (5.86 - 582.56)	**0.001**
Yes	25 (39.1)	3 (9.7)	1		1	
Cancer subtype						
B-ALL	25 (39.1)	9 (29)	0.26 (0.13 - 0.560)	**<0.001**	15.84 (0.81 - 307.97)	0.068
T-ALL	21 (32.8)	11 (35.5)	0.36 (0.18 - 0.740)	**0.005**	0.93 (0.11 - 7.85)	0.945
AML	18 (28.1)	11 (35.5)	1		1	
Duration of symptoms						
≤1 month	28 (43.8)	12 (38.7)	1		1	
>1 month	36 (56.3)	19 (61.3)	0.89 (0.49 - 1.50)	0.691	0.28 (0.04 - 1.92)	0.196
White cell count						
<50	35 (54.7)	14 (45.2)	1		1	
≥50	29 (45.3)	17 (54.8)	1.5 (0.86 - 2.73)	0.145	2.88 (0.30 - 27.54)	0.359
Hepatomegaly						
No	14 (21.9)	5 (16.1)	1		1	
Yes	50 (78.1)	26 (83.9)	0.86 (0.43 - 1.690)	0.666	3.60 (0.23 - 57.52)	0.365
Splenomegaly						
No	12 (18.8)	5 (16.1)	1		1	
Yes	52 (81.3)	26 (83.9)	0.87 (0.42 - 1.79)	0.699	0.31 (0.01 - 9.19)	0.496
MRD						
Negative	34 (75.6)	14 (93.3)	0.21 (0.08 - 0.56)	**0.002**	15.36 (41.10 - 59.14)	**<0.001**
Positive	11 (24.4)	1 (6.7)	1		1	
CNS involvement						
No	55 (85.9)	29 (93.5)	1		1	
Yes	9 (14.1)	2 (6.5)	0.50 (0.18 - 1.40)	0.190	0.77 (0.82 - 7.44)	0.828

Among 95 children with leukemia, 49 (51.2%) attained complete remission and among these 9 had relapse, bone marrow was the commonest site in 8 patients and 1 had both CNS and bone marrow relapse, the rate of relapse was 18.4%. Of the 9 patients who had relapsed after attaining remission, all of the succumbed after 2 years of follow-up.

3.5. Predictors of Relapse

In three years of follow up, in bivariate analysis the predictors of relapse were children with AL B-ALL subtype had 0.14 times lower risk of relapse compared to those with AML (HR: 0.14; 95% CI: 0.02, 1.03). Children with hepatomegaly on admission had significant 0.24 times higher risk of relapse compared to those who

had no hepatomegaly (HR: 0.24; 95% CI: 0.06, 0.89). In multivariable analysis after adjusting to other factors the predictors of relapse were children with AL with no health insurance had 58.43 times higher risk of relapse compared to those with health insurance (HR: 58.43; 95% CI: 5.86, 582.56) (Table 6).

Table 6. Predictors of relapse among children diagnosed with acute leukemia.

Predictor	Hospital		Total	CHR (95% CI)	P value	AHR (95% CI)	P value
	KCMC	BMC					
Age							
0 - 9	44 (68.8)	20 (64.5)	64 (67.4)	1		1	
10 above	20 (31.3)	11 (35.5)	31 (32.6)	3.46 (0.92 - 12.90)	0.064	2.81 (0.451 - 7.550)	0.269
Gender							
Male	38 (59.4)	16 (51.6)	54 (56.8)	0.58 (0.16 - 2.17)	0.421	0.99 (0.16 - 5.980)	0.989
Female	26 (40.6)	15 (48.4)	41 (43.2)	1		1	
Distance to hospital							
<50 KM	28 (43.8)	7 (22.6)	35 (36.8)	1		1	
≥50	36 (56.3)	24 (77.4)	60 (63.2)	0.37 (0.01 - 1.47)	0.158	0.35 (0.58 - 2.180)	0.262
Health insurance							
No	39 (60.9)	28 (90.3)	67 (70.5)	1.82 (0.46 - 7.29)	0.395	58.43 (5.86 - 582.56)	**0.001**
Yes	25 (39.1)	3 (9.7)	28 (29.5)	1		1	
Cancer subtype							
B-ALL	25 (39.1)	9 (29)	34 (35.8)	0.14 (0.02 - 1.03)	**0.054**	15.84 (0.813 - 7.97)	0.068
T-ALL	21 (32.8)	11 (35.5)	32 (33.7)	0.51 (0.09 - 2.64)	0.421	0.93 (0.11 - 7.85)	0.945
AML	18 (28.1)	11 (35.5)	29 (30.5)	1		1	
White cell count							
<50	35 (54.7)	14 (45.2)	49 (51.6)	1		1	
≥50	29 (45.3)	17 (54.8)	46 (48.4)	1.22 (0.47 - 6.46)	0.412	2.88 (0.30 - 27.54)	0.359
Hepatomegaly							
No	14 (21.9)	5 (16.1)	19 (20.0)	1		1	
Yes	50 (78.1)	26 (83.9)	76 (80.0)	0.24 (0.06 - 0.89)	**0.033**	3.60 (0.23 - 57.52)	0.365
Splenomegaly							
No	12 (18.8)	5 (16.1)	17 (17.9)	1		1	
Yes	52 (81.3)	26 (83.9)	78 (82.1)	0.46 (0.12 - 1.84)	0.274	0.31 (0.01 - 9.19)	0.496
CNS involvement							
No	55 (85.9)	29 (93.5)	84 (88.4)	1		1	
Yes	9 (14.1)	2 (6.5)	11 (11.6)	0.53 (0.07 - 4.26)	0.552	0.77 (0.82 - 7.44)	0.828

4. Discussion

This retrospective cohort study aimed to identify factors influencing survival and relapse in children with acute leukemia in Northern Tanzania. Of the 95 participants, the overall three-year survival rate was 44.2%, an improvement from the 26.1% survival rate reported in a 2013 study. This increase is attributed to the growth in oncology centers, better-trained staff, and greater disease awareness. Despite still falling short compared to high-income countries, this progress brings Tanzania closer to achieving the WHO's goal of an overall survival rate greater than 60% by 2030 [17]. The study aimed to identify factors influencing survival and relapse in children with acute leukemia in Northern Tanzania. Of the 95

participants, the overall three-year survival rate was 44.2%, an improvement from the 26.1% survival rate reported in a 2013 study. This increase is attributed to the growth in oncology centers, better-trained staff, and greater disease awareness. Despite still falling short compared to high-income countries, this progress brings Tanzania closer to achieving the WHO's goal of an overall survival rate greater than 60% by 2030 [18]. Also these findings are similar to a study done in Kenya were by the 3 years overall survival in AML was 0% [19], although in their setting the main reason identified was due to early deaths secondary to treatment complications severe hemorrhage being leading cause of death. However, our study did not investigate the causes of death among participants. We did find that having health insurance was a predictor of survival. Approximately 70.5% of the children in our study lacked health insurance, which was associated with poorer survival outcomes. In Tanzania, a low-income country where many people cannot afford healthcare, patients often present with more advanced stages of the disease. This finding aligns with a study conducted in the United States, which also reported that patients with health insurance had better overall survival rates compared to those without, although in the U.S. study, access to healthcare was also influenced by the distance from health centers [20]. In contrast to this, a study done in Kenya did not find any significance in the survival in AML between those patients with health insurance and those with no health insurance this was due to most patients had early deaths due to treatment complications [19]. In our study, having a negative MRD after induction, was a predictor of survival [21] [22]. In our study the rate of relapse was found to be 18.4% which were 9 patients out of 49 who had attained complete remission, our findings are lower compared to a study done in Tanzania in 2013 were the rate of relapse was 23% [19] [21]. Another study done in Egypt showed the rate of relapse was 27% [23] which was higher compared to our study however in our case this can be bring bias to the outcome due to missing files in which most had died and cause of death was unknown. In our study at 2 years the 9 patients who had relapsed had succumbed, while in Egypt was 36.6% overall survival of relapsed patients in 5 years, in terms of site of relapse in both studies bone marrow was the commonest site of relapse in both studies [23]. The study also pinpointed health insurance status to be a crucial predictor of relapse this is due to the fact that those who had no health insurance came in late stages of the disease thus increasing the risk of relapse, similar finding was found in study done by [20].

5. Limitations of This Study

The lack of certain data and missing files led to their exclusion, which may affect the accuracy of the outcomes. Due to these missing files, survival rates could only be calculated for a three-year period. This limitation was necessary because obtaining retrospective follow-up data for all patients over longer durations was difficult. To maintain consistency and comparability in the results, we chose to assess outcomes within the same three-year timeframe for all patients.

6. Conclusion

This study offers valuable insights into the factors influencing survival and relapse in childhood leukemia in northern Tanzania. It found an overall survival rate of 44.2%, with health insurance and minimal residual disease after induction being significant predictors of survival. The relapse rate was 18.4%, and health insurance was associated with a reduced risk of relapse. Health insurance proved to be a strong predictor of better survival, highlighting the need for universal health insurance for all children. The study also recommends that policymakers work to expand global health coverage in Tanzania.

Availability of Data and Materials

On request, a copy of the data collected is available for review by the Editor-in-Chief of this journal.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Seth, R. and Singh, A. (2015) Leukemias in Children. *The Indian Journal of Pediatrics*, **82**, 817-824. https://doi.org/10.1007/s12098-015-1695-5

[2] Huang, J., Chan, S.C., Ngai, C.H., Lok, V., Zhang, L., Lucero-Prisno, D.E., *et al.* (2022) Disease Burden, Risk Factors, and Trends of Leukaemia: A Global Analysis. *Frontiers in Oncology*, **12**, Article 904292. https://doi.org/10.3389/fonc.2022.904292

[3] Kakaje, A., Alhalabi, M.M., Ghareeb, A., Karam, B., Mansour, B., Zahra, B., *et al.* (2020) Rates and Trends of Childhood Acute Lymphoblastic Leukaemia: An Epidemiology Study. *Scientific Reports*, **10**, Article No. 6756. https://doi.org/10.1038/s41598-020-63528-0

[4] Desandes, E., Clavel, J., Berger, C., Bernard, J., Blouin, P., de Lumley, L., *et al.* (2004) Cancer Incidence among Children in France, 1990-1999. *Pediatric Blood & Cancer*, **43**, 749-757. https://doi.org/10.1002/pbc.20148

[5] Linaberry, A.M. and Ross, J.A. (2007) Trends in Childhood Cancer Incidence in the U.S. (1994-2004). *Cancer*, **112**, 416-432. https://doi.org/10.1002/cncr.23169

[6] Bao, P., Zheng, Y., Wang, C., Gu, K., Jin, F. and Lu, W. (2009) Time Trends and

Characteristics of Childhood Cancer among Children Age 0 - 14 in Shanghai. *Pediatric Blood & Cancer*, **53**, 13-16. https://doi.org/10.1002/pbc.21939

[7] Al-Hashimi, M. (2021) Incidence of Childhood Leukemia in Iraq, 2000-2019. *Asian Pacific Journal of Cancer Prevention*, **22**, 3663-3670. https://doi.org/10.31557/apjcp.2021.22.11.3663

[8] Eden, T. (2010) Aetiology of Childhood Leukaemia. *Cancer Treatment Reviews*, **36**, 286-297. https://doi.org/10.1016/j.ctrv.2010.02.004

[9] Okello, C.D., Niyonzima, N., Ferraresso, M., Kadhumbula, S., Ddungu, H., Tarlock, K., *et al*. (2021) Haematological Malignancies in Sub-Saharan Africa: East Africa as an Example for Improving Care. *The Lancet Haematology*, **8**, e756-e769. https://doi.org/10.1016/s2352-3026(21)00198-8

[10] Togo, B., Traore, F., *et al*. (2018) Childhood Acute Lymphoblastic Leukemia in Sub Saharan Africa: 4 Years? Experience at the Pediatric Oncology Unit Bamako, Mali. *Journal of Child and Adolescent Health*, **2**, 24-26. https://doi.org/10.35841/child-health.2.2.24-25

[11] Yao, J.J.A., Couitchere, L., Atimere, Y., Koné, D., Azagoh-Kouadio, R., Oulai, M.S., *et al*. (2012) Childhood Cancer in Côte D'ivoire, 1995-2004—Challenges and Hopes. *South African Medical Journal*, **103**, Article 113. https://doi.org/10.7196/samj.6365

[12] Ochicha, O., Gwarzo, A.K. and Gwarzo, D. (2012) Pediatric Malignancies in Kano, Northern Nigeria. *World Journal of Pediatrics*, **8**, 235-239. https://doi.org/10.1007/s12519-012-0363-3

[13] Mostert, S., Njuguna, F., Kemps, L., Strother, M., Aluoch, L., Buziba, G., *et al*. (2012) Epidemiology of Diagnosed Childhood Cancer in Western Kenya. *Archives of Disease in Childhood*, **97**, 508-512. https://doi.org/10.1136/archdischild-2011-300829

[14] Ssenyonga, N., Stiller, C., Nakata, K., Shalkow, J., Redmond, S., Bulliard, J., *et al*. (2022) Worldwide Trends in Population-Based Survival for Children, Adolescents, and Young Adults Diagnosed with Leukaemia, by Subtype, during 2000-14 (CONCORD-3): Analysis of Individual Data from 258 Cancer Registries in 61 Countries. *The Lancet Child & Adolescent Health*, **6**, 409-431. https://doi.org/10.1016/s2352-4642(22)00095-5

[15] Ganzel, C., Wang, X.V., Rowe, J.M., Richards, S.M., Buck, G., Marks, D.I., *et al*. (2020) At Three Years, Patients with Acute Lymphoblastic Leukaemia Are Still at Risk for Relapse. Results of the International MRC UKALLXII/ECOG E2993 Trial. *British Journal of Haematology*, **191**, 37-43. https://doi.org/10.1111/bjh.16616

[16] Joko-Fru, W.Y., Parkin, D.M., Borok, M., Chokunonga, E., Korir, A., Nambooze, S., *et al*. (2018) Survival from Childhood Cancers in Eastern Africa: A Population-Based Registry Study. *International Journal of Cancer*, **143**, 2409-2415. https://doi.org/10.1002/ijc.31723

[17] World Health Organization (2020) Framework: WHO Global Initiative for Childhood Cancer. Cure All Framework: WHO Global Initiative for Childhood Cancer: Increasing Access, Advancing Quality, Saving Lives.

[18] Stones, D.K., De Bruin, G.P., Esterhuizen, T.M. and Stefan, D.C. (2014) Childhood Cancer Survival Rates in Two South African Units. *South African Medical Journal*, **104**, Article 501. https://doi.org/10.7196/samj.7882

[19] van Weelderen, R.E., Njuguna, F., Klein, K., Mostert, S., Langat, S., Vik, T.A., *et al*. (2021) Outcomes of Pediatric Acute Myeloid Leukemia Treatment in Western Kenya. *Cancer Reports*, **5**, e1576. https://doi.org/10.1002/cnr2.1576

[20] Mahmoud, M., Al Mahmasani, L., Charafeddine, M., Zahreddine, A., Moukalled, N., El Cheikh, J., *et al*. (2022) Impact of Insurance Status and Distance from Residence

to Treatment Center on the Outcomes of Patients Diagnosed with Acute Myeloid Leukemia. *Frontiers in Hematology*, **1**, Article 29. https://doi.org/10.3389/frhem.2022.1060029

[21] Borowitz, M.J., Wood, B.L., Devidas, M., Loh, M.L., Raetz, E.A., Salzer, W.L., *et al*. (2015) Prognostic Significance of Minimal Residual Disease in High Risk B-ALL: A Report from Children's Oncology Group Study AALL0232. *Blood*, **126**, 964-971. https://doi.org/10.1182/blood-2015-03-633685

[22] Berry, D.A., Zhou, S., Higley, H., Mukundan, L. and Fu, S. (2017) Association of Minimal Residual Disease with Clinical Outcome in Pediatric and Adult Acute Lymphoblastic Leukemia—A Meta-Analysis. *JAMA Oncology*, **3**, e170580.

[23] Abdelmabood, S., Fouda, A.E., Boujettif, F. and Mansour, A. (2020) Treatment Outcomes of Children with Acute Lymphoblastic Leukemia in a Middle-Income Developing Country: High Mortalities, Early Relapses, and Poor Survival. *Jornal de Pediatria*, **96**, 108-116. https://doi.org/10.1016/j.jped.2018.07.013