Original Research Article

Pattern of childhood acute leukemia presentation at a tertiary hospital in Nigeria: a five-year review

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ABSTRACT

Background: Acute leukemia is the most common childhood malignancy but its occurrence in low- and middle-income countries are under-reported. Its pattern of presentation varies depending on several factors. The objective of this report is to determine the pattern of presentation of acute leukemias in children at a tertiary hospital in Nigeria.
Methods: A retrospective cross-sectional study of children managed for acute leukemia at the Paediatric Department in a 5-year period. Of 31 patients, 27 had adequate records, which were reviewed. Data collected include patient's demographics, clinical features and treatment outcome.
Results: There were 16 males and 11 females, aged 8 months to 16 years (mean 7.45 years ±4.75 SD). The pattern of clinical features were fever (85.2%), pallor (92.6%) and splenomegaly (51.9%). The specific leukemia type ratio for Acute Myeloid leukemia (AML) and Acute lymphoblastic leukemia (ALL) was 1: 2.9. The parents of three patients took their children away before commencement of treatment, one patient completed treatment and 6 (22.2%) died before completing treatment. Nearly half of the patients were lost to follow up to seek alternative care while 9 (33.3%) of the patients were in remission at last follow up. Lost to follow-up was found not to be significantly associated with socioeconomic status, age and sex respectively.
Conclusions: Acute lymphoblastic leukemia remains the predominant type of childhood leukemia in our setting. Majority of the patients presented with fever and pallor moreover the default to follow-up plagues treatment completion.

Keywords: Acute Leukemia, Follow-up, Outcome, Presentation

INTRODUCTION

More than 80 percent of global annual cancer diagnoses are in resource-poor countries.[1] Globally leukemias are the most common childhood malignancies, accounting for about 30% of all paediatric malignancies with acute lymphoblastic leukemias constituting about 76% of all cases of acute leukemia.[2-5] In developing countries like Nigeria, leukaemia accounted for about 10.2 to 12.9% of childhood malignancies.[6] Several factors have been postulated to be associated with development of acute leukemia, but causal relationship remains to be substantiated.[7]

Many advances have been made in understanding the molecular biology, presentation and management of acute leukemia in the past few decades.[8] Acute leukemias are heterogeneous group of haematological malignancies in which there are clonal expansion of immature precursors (blasts) in the bone marrow. The blast cells are either

myeloid or lymphoid and these are further classified as B cell or T cell. The blasts progressively replace the normal hematopoietic tissue and invade other organs of the body. Therefore, the pattern of presentation of acute leukemia is quite variable depending on the disease nature and its extent.

The observed variations in acute leukemia epidemiology and pattern of clinical presentation between resource-rich and resource-poor countries are postulated by William et al to be due to the differences in lifestyle/socioeconomic status. The common presentations of acute leukemia include fever, fatigue, pallor, bleeding, infection, lymphadenopathy and hepatosplenomegaly.[8,9,10] Majority of the presenting clinical features are as a result of infiltration of organs, bone marrow and extramedullary sites. The initial presentation of leukemia is usually nonspecific which may include anorexia, fatigue and irritability with progressive bone marrow failure leading to pallor, bleeding, fever and infection. About 40% present with abnormal bleeding while 24% may present with significant bone and joint pains.[8] A greater proportion of children with acute leukemia have clinical features for some weeks prior to presentation.

Remarkable progress has been made in diagnosis and treatment of childhood cancers especially in resource-rich countries, but most resource-poor countries still lag behind. With effective chemotherapy, most children with cancers can now be expected to have long term survival rate of about 80%, though more than 80% of African children still die without assess to treatment.[11] According to Hadley et al challenges like resource deficiencies and difficult healthcare access leading to loss to follow-up compromise management of childhood tumours. We aim to determine the pattern of presentation of acute leukemias in children at a tertiary hospital in Nigeria.[11]

METHODS

This is a retrospective cross-sectional study of children managed for acute leukemia at the paediatric department of a tertiary hospital in a 5- year period from January 2012 to January 2017. The study was done at National Hospital Abuja which is located in the Central business district of the federal capital territory, the Capital of Nigeria. This is a fair representative of the country's multicultural and ethnic background. The institution is a referral centre that provides tertiary healthcare to neighbouring cities and boundary states like Kaduna, Niger, Plateau, Nasarawa and Kogi at the North, West, East, South-East and South-West respectively.

The following information were retrieved from the case notes: patient's demographics, clinical features and treatment outcome. Those with inadequate records were excluded from the study. Socioeconomic class was determined using the Olusanya's classification.[12] All the patients had bone marrow studies done which were prepared and read by the haematologist according to

specified standards. Bone marrow aspiration was done using disposable bone marrow aspiration needles (Medax size 21G). About 0.5mls of aspirate was taken and smears were made (8-10 slides). The smears were air dried and fixed with methanol. Four marrow and two peripheral blood slides were stained with Romanosky stain. Cytochemical stains were done for 4 slides (Periodic acid Schiff, Non-Specific Esterase and Myeloperoxidase). The slides were reported and treatment options then suggested.

All data obtained for each patient were entered into database SPSS version 21 (SPSS, Inc., Chicago, IL, USA). A descriptive analysis was performed and associations between variables using Fisher's exact test were done with statistical significance set at p-value <0.05. Ethical approval was obtained from the institutional review board. Data were analysed using SPSS version 21.

RESULTS

A total of 27 patients were studied giving an annual case per year to about 5.4 cases per year. Acute leukemia in this study accounted for 17.9% of all childhood tumours seen within the study period.
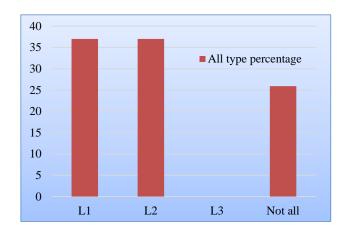

Figure 1: Acute lymphoblastic leukemia subtype distribution.
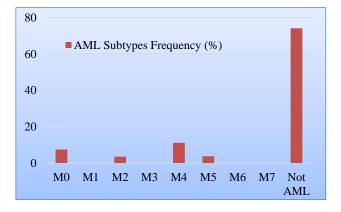

Figure 2: Acute Myeloid leukemia subtypes frequency distribution.

The demographics for the participants (Table 1) showed that there were 16 males and 11 females, M: F of 1.5: 1 and aged range 8 months to 16 years (mean 7.45±4.75 years).

Forty-eight percent of the patients were referred from other tertiary health centres while 40.7% were from secondary health centres.

Table 1: Demographic characteristics of patients.

Variables						F	P-value§
Age							
Age range	8 months-16 years						
Age mean	7.45±4.75 years						
Age group at diagnosis (years)							
	Total	**0-4**	**5-9**	**10-14**	**14-19**		
Sex						0.80	0.95
Male	16 (59.3)	5	6	3	2		
Female	11 (40.7)	4	3	3	1		
Total	27 (100)	9	9	6	3		
Source of referral							
Primary/private healthcare	3 (11.1)	-	1	1	1		
Secondary healthcare	11 (40.7)	5	3	2	1		
Tertiary healthcare	13 (48.1)	4	5	3	1		
Total	27 (100)	9	9	6	3		
Socioeconomic status						7.55	0.24
Upper class	7 (25.9)	2	1	3	1		
Middle class	14 (51.9)	6	6	2	-		
Lower class	6 (22.2)	1	2	1	2		
Total	27 (100)	9	9	6	3		

§ P-values for sex and socioeconomic status were not significantly associated with age group

Middle class was the predominant socio-economic status of caregivers (51.9%) then followed by upper class (25.9%).

Table 2: Frequency (%) distribution of initial presenting clinical features.

Clinical features	Number	Frequency (%)
Pallor	25	92.6
Abnormal bleeding	17	63
Bone pain	14	51.9
Fever	23	85.2
Lymphadenopathy	19	70.4
Hepatomegaly	20	74.1
Splenomegaly	14	51.9

The predominant pattern of presenting clinical features (Table 2) was pallor (92.6%), fever (85.2%), and splenomegaly (51.9%).

Pallor was the most common presenting clinical feature for both acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) (Table 3). The specific leukemia type ratio for acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) was 1:2.9.

Table 3: Frequency (N) distribution of initial presenting clinical features with respect to Acute Leukemia type.

Clinical features		Diagnosis		Total
		ALL	**AML**	
Pallor	Yes	19	6	25
	No	1	1	2
Abnormal bleeding	Yes	11	6	17
	No	9	1	10
Bone pain	Yes	12	2	14
	No	8	5	13
Fever	Yes	18	5	23
	No	2	2	4
Lymphadenopathy	Yes	14	5	19
	No	6	2	8
Hepatomegaly	Yes	17	3	20
	No	3	4	7
Splenomegaly	Yes	12	2	14
	No	8	5	13

Figure 1 and Figure 2 show the distribution of ALL and AML subtypes respectively. Concerning the outcome variables (Table 4), the parents of three patients took their children away before commencement of treatment, one

patient completed treatment and 6 (22.2%) died before completing treatment.

Table 4: Primary outcome variables.

Outcome variables	No.	%
Discharged to follow-up	19	70.4
Lost to follow-up	14	51.9
Left against medical advice	3	11.1
Completed treatment	1	3.7
Remission	9	33.3
Mortality	6	22.2

Table 5: Relationship between age, sex and socioeconomic status (SES) with lost to follow-up.

Variables		Lost to follow-up		Total	P-value
		Yes	No		
Age group	0-4	5	4	9	0.31
	5-9	3	6	9	
	10-14	5	1	6	
	15-19	1	2	3	
Total		14	13	27	
Sex	Male	8	8	16	0.81
	Female	6	5	11	
Total		14	13	27	
SES	Upper class	3	4	7	0.78
	Middle class	7	7	14	
	Lower class	4	2	6	
Total		14	13	27	

Table 6: Socioeconomic status and mortality based on diagnosis.

		Diagnosis		Total	P-value §
		ALI	AML		
Socioeconomic status	Upper class	4	3	7	0.52
	Middle class	11	3	14	
	Lower class	5	1	6	
Total		20	7	27	
Mortality	Yes	5	1	6	0.08
	No	7	-	7	
	Lost to follow-up	8	6	14	
Total		20	7	27	

Nearly half of the patients were lost to follow-up to seek alternative care which was found not to be significantly associated with socioeconomic status, age and sex with p-values of 0.78, 0.31 and 0.81 respectively. However, 9 (33.3%) of the patients were in remission at the last follow up.

DISCUSSION

Annually, about 5.4 cases per year of acute leukemia were found in present study and constitute 17.9% of all childhood tumours. In Nigeria, reliable national figures are not readily available due to paucity of population-based childhood tumour registry.

However, Babatunde et al in Ibadan, Nigeria and Ali et al in Egypt reported that in their studies acute leukemia accounted for 10.2% and 29.3% respectively of total childhood malignancies.[6] Present study showed that ALL accounted for majority of leukemia with 74%, which is in keeping with other studies.[13] However, Ochicha et al reported a higher prevalence of AML than ALL in their study in Northern Nigeria.[13,14]

In the last decade, statistics show that in the developed nations, there has been an increase in the incidence of malignancies but due to under reporting in resource-poor countries this statistic are not available. There appears to be an increase in number of cases diagnosed per year but giving the short duration of the study such assertion had to be with caution.

The male to female ratio of 1.5:1 observed in this study is similar to other studies that reported male preponderance.[5,6,13] Fleming in his review of leukemia in Africa attributed these observed disparities in leukemia epidemiology to inadequate record keeping, poor laboratory services, under-diagnosis by clinicians and poor access to healthcare service.[15]

Most of the patients were in the middle or upper socioeconomic class and the association between demographic variables (sex, socioeconomic class) and age groups was not statistically significant.

We found no association between socioeconomic status and acute leukemia diagnosis although Williams et al reported an association between high socioeconomic class and prevalence of acute leukemia.[9] Eden in his review reflected on the importance of genetic-environmental interaction in the aetiology of childhood leukemia.[5] The common clinical features patients presented with were pallor, fever, hepatomegaly and lymphadenopathy which are similar to other reports.[8]

All of the observed symptoms were commoner in patients with ALL than AML, though our small sample size may have contributed to our findings. For patients with ALL, majority presented with pallor, fever and hepatomegaly while pallor and abnormal bleeding were the commonest amongst patients with AML. Nine of the patients went into remission (33%) and six deaths were recorded (22%). Mortality was not significantly associated with acute leukemia subtype in this study.

The death rate due to acute leukaemia is still unacceptably high in Nigeria. Most patients diagnosed did not however complete their treatment. They were either lost to follow up or refused treatment. In a similar study by Ahmad et al more than half of their patients with childhood malignancy did not complete their treatment.[16] These high percentages in both studies could be due to the financial burden associated with the treatment of the disease, ignorance and poor supportive therapies in terms of blood and blood products.

Magrath et al in their study reiterated the significance of public enlightenment, health professional training and strengthening of health systems through international collaborations and health insurance in the care of childhood cancers in resource-poor countries.[17] Our major finding was that demographic variables; age, sex and socioeconomic status were not significantly associated with major outcome variables; loss to follow-up and mortality from acute leukemia.

However, Hossain et al found significant variations in survival by age of presentation. The disparity in our finding may be explained by our relatively small sample size in relation to the study of Hossain et al.[18]

Flow cytometry and cytogenetic studies are not readily available in our country hence limits adequate sub-classification of leukemias. The retrospective nature of the study and small sample size limits its findings and analysis as many factors that could have influenced acute leukemia presentation, management and outcome were not determined. Our results could also have been limited by the effects of unmeasured confounders.

CONCLUSION

Acute lymphoblastic leukaemia remains the predominant type of childhood leukaemia in our setting. Majority of the patients presented with fever and pallor; moreover, loss to follow-up plagues treatment completion. There is need for massive enlightenment, training and retraining of personnel at the lower health facilities to ensure early referral.

Funding issues also need to be addressed as the commonest cause of loss to follow up or refusal to accept treatment is the cost implication of the treatments. Further studies will need to be done to substantiate the above assertion and other possible causes of loss to follow-up that may negatively influence treatment completion.

ACKNOWLEDGEMENTS

REFERENCES

1. Kaatsch P. Epidemiology of childhood cancer. Cancer Treat Rev. 2010;36:277-85.
2. Center M, Siegel R, Jemal A. Global cancer facts and figures. Atlanta: American Cancer Society. 2011:1-52.
3. Howlader N, Noone AM, Krapcho M. SEER Cancer Statistics Review, 1975–2010. National Cancer Institute, Bethesda, Md, USA; 2010.
4. Smith MA, Ries L, Gurney J, et al. Leukemia. In: Ries L, Smith, M, Gurney J, et al, editors. Cancer Incidence and survival among children and adolescents: United States SEER Program 1975-1995. Bethesda, MD: National Cancer Institute, SEER Program; 1999:17-34.
5. Eden T. Aetiology of childhood leukaemia. Cancer Treatment Rev. 2010;36(4):286-97.
6. Babatunde TO, Ogun GO, Brown BJ, Akang EE, Aken'Ova YA. Pattern of childhood leukaemia in University College Hospital, Ibadan. Afr J Med Med Sci. 2014;43(2):135-8.
7. Puumala SE, Ross JA, Aplenc R, Spector LG. Epidemiology of Childhood Acute Myeloid Leukemia. Pediatr Blood Cancer. 2013;60(5):728-33.
8. Bashir M, Zaman S, Rafatullah WF, Shoaib M, Biland B. Hematological and clinical presentation of acute leukemias at Khyber Pukhtoonkhwa. Gom J Med Sci. 2010;8:134-40.
9. Williams CKO, Foroni L, Luzzatto L, Saliu I, Levine A, Greaves MF. Childhood leukaemia and lymphoma: African experience supports a role for environmental factors in leukaemogenesis. Ecancer. 2014;8:478.
10. Rubnitz JE, Gibson B, Smith FO. Acute myeloid leukemia. Hematol Oncol Clin N Am. 2010(24):35-63.
11. Hadley LGP, Rouma BS, Saad-Eldin Y. Challenge of pediatric oncology in Africa. Seminars in Pediatric Surg. 2012;21:136-41
12. Olusanya O, Okpere E, Ezimokhai M. The importance of social class in voluntary fertility control. West Afr J Med. 1985;4:205-12.
13. Ali AM, Sayed HA, Sayed DM, Mikhail NN. Pattern of pediatric tumors at pediatric department in South Egypt Cancer Institute: thirteen years report. J Pediatr Child Nutr. 2016;2(2):100-12.
14. Ochicha O, Gwarzo AK, Gwarzo D. Pediatric malignancies in Kano, Northern Nigeria. World J Pediatr. 2012;8(3):235-9.
15. Fleming AF. Epidemiology of the leukemias in Africa. Leukemia Rese. 1978;3(2):51-9.
16. Ahmad HR, Faruk JA, Abdullahi M, Olorunkooba AA, Ishaku H, Abdullahi FL, et al. Pattern and outcomes of childhood malignancies at Ahmadu

bello university teaching hospital, Zaria. Sub-Saharan Afr J Med. 2016;3:127-31.

17. Magrath I, Steliarova-Foucher E, Epelman S, Ribeiro RC, Harif M. Paediatric cancer in low-income and middle-income countries. Lancet Oncol. 2013;14:e104-16.

18. Hossain MJ, Xie L, McCahan SM. Characterization of pediatric acute lymphoblastic leukemia survival patterns by age at diagnosis. J Cancer Epidemiol. 2014;2014.