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Analysis of Full Blood Count and Bone Marrow Aspirations at Presentation in Children Diagnosed with Acute Leukaemias – A Single Centre Experience in Southern Nigeria

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Authors' contributions

This work was carried out in collaboration between both authors. Author KIK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Author GKE managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Acute leukaemias are the most common malignant neoplasms in childhood, presenting with a variety of nonspecific symptoms. Though many of the recent more sophisticated methods of diagnosis have important prognostic implications, they are often not available in low- and middle-income countries.
Objective: To review the full blood count and bone marrow aspirations at presentation in children diagnosed with acute leukaemias at a teaching hospital in southern Nigeria.
Methodology: A retrospective survey of children with acute leukaemias admitted into the Paediatric Oncology unit of the University of Port Harcourt Teaching Hospital (UPTH), from January 2014 to December 2020. Their clinical profile, full blood count and bone marrow aspirations were analyzed using SPSS version 25.0

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Results: Forty-three children aged 8 months to 17 years, with a median age of 9 years, were diagnosed with acute leukaemia within the period under review, 28 (65.1%) were males and 15 (34.9%) females, giving a M:F ratio of 1.9:1. Commonest clinical features at presentation were fever (n=28, 65.1%), pallor (n=18, 41.9%) and gum bleeding (n=16, 37.2%); while 38 (88.4%) of them presented with anaemia, 20 (46.5%) had leukocytosis and 36 (83.7%) had thrombocytopoenia with a median platelet count of $42x10^9$/L and circulating blasts were present in the peripheral blood film of most of the patients. Acute lymphoblastic leukaemia (ALL) was the diagnosis in 30 (70%) children, and AML in 9 (21%). The bone marrow was hypercellular in 30 cases (69.8%) and erythropoiesis was depressed in 39 (90.7%) children.
Conclusion: At the UPTH, children with acute leukaemias were mostly males. Fever, pallor and gum bleeding were the commonest symptoms with most of them having circulating blasts. Acute lymphoblastic leukaemia was the commonest type and bone marrow was mainly hypercellular with depressed erythropoiesis.

Keywords: Full blood count; Bone marrow aspiration; Children; Acute leukaemia; Southern Nigeria.

1. INTRODUCTION

Acute leukaemias are a group of clonal haematological malignancies characterized by accumulation of immature blood cells (blasts) in the peripheral blood and/ or bone marrow, resulting in a disruption of normal marrow function and, ultimately, marrow failure [1-2]. They are the most common malignant neoplasms in childhood, accounting for approximately 31% of all malignancies that occur in children younger than 15 years of age [2].

The aetiology of childhood leukaemia is unknown, although several genetic and environmental factors are associated with it, and it is universally fatal without effective therapy [2-3]. However, with advances in medicine, its 5-year survival rates have steadily improved, from below 10% in the 1960s to over 90% today in high income countries, while in sub-Saharan Africa, where its true incidence remains unknown, its survival rate rarely reaches 15% [4-6].

The clinical features, laboratory findings and responses to therapy depend on the type of leukaemia. Affected children typically present with a variety of nonspecific symptoms (such as fever, pallor, malaise, or bleeding), which are rapid in onset and progression, and many of which can be easily confused with infectious diseases, such as malaria, resulting in under-diagnosis [4,7]. Other features include anaemia, recurrent infections and bleeding diathesis secondary to anaemia, neutropenia and thrombocytosis due to bone marrow infiltration with the blasts [2].

The diagnosis of acute leukaemias requires the demonstration of ≥ 20% blast in the bone marrow, however in the presence of certain cytogenetic abnormalities the diagnosis may be made with lower blast counts [1].

Based on the type of blasts, they are broadly classified into acute lymphoblastic leukaemia (ALL), the most common type of childhood leukaemias (77%) and acute myeloblastic leukaemia (AML), accounting for approximately 11% of them [1,3]. Rarely, acute leukaemias can have features of both ALL and AML. These are called mixed lineage leukaemias, acute undifferentiated leukaemias, or mixed phenotype acute leukaemias (MPALs, which in children, are generally treated like ALL and usually respond to treatment like ALL [8-9]. Recently with more sophisticated methods of diagnosis, the 2016 World Health Organization (WHO) classification of acute leukaemias utilizes immunophenotyping to determine cell lineage, and cytogenetic or molecular genetic studies to define sentinel abnormalities [1-2]. Though many of these tests have important prognostic implications, they are often not available in Low- and Middle Income Countries (LMICs).

In many resource limited settings like ours, the diagnosis of acute leukaemias still relies on peripheral blood and bone marrow findings. Thus, this study was carried out to review the full blood count findings and bone marrow diagnoses of children with acute leukaemias at a tertiary health facility in southern Nigeria.

2. MATERIALS AND METHODS

The study was conducted at the University of Port Harcourt Teaching Hospital (UPTH), an 800-bedded federal tertiary health institution and a major referral centre, serving Rivers and the neighbouring States in southern Nigeria.

It was a retrospective study of children who were diagnosed with acute leukaemias and admitted into the Oncology unit of the Paediatric Department, which caters for children aged 0–17 years, from January 2014 to December 2020. Patients were identified from nurses' records and data on each patient collected from hospital notes. Variables studied included clinical profile, full blood count at presentation and bone marrow aspiration findings.

The diagnosis of acute leukaemia was based on bone marrow finding of >20% blasts and classification was according to the French American British – FAB classification system which is based on morphology [10]. In very few cases, immuno-histochemical markers were employed in the process of diagnosis for those who could afford it. Ancillary investigations which also aided in diagnosis included complete blood cells count, peripheral blood smear and bone marrow cytology. Some investigations like immunohistochemistry, karyotyping or molecular biology were not available in our facility.

Data were analyzed using SPSS software version 25 (IBM, Armonk,NY). Results were expressed in charts and tables.

3. RESULTS

There were 43 children diagnosed with acute leukaemia within the 7 year period under review, with a median age of 9 years (age range: 8 months to 17 years) of which 28 (65.1%) were males and 15 (34.9%) females, giving a male to female ratio of 1.9:1.

The commonest clinical features at presentation were fever (n=28, 65.1%), pallor (n=18, 41.9%) and gum bleeding (n=16, 37.2%). Other features are presented in Table 1. Central nervous system (seizures, paraplegia) were seen in 2 (4.7%) cases each. The mean duration of symptoms prior to presentation was 56 days (inter quartile range [IQR] 65.5 days).

Thirty-eight (88.4%) of the children presented with anaemia i.e. haemoglobin concentration (Hb conc) <10g/dL; the mean Hb conc was 7.0 (+/- 1.9g/dL) (Table 2). Leukocytosis was seen in 20 patients (46.5%), another 20 (46.5%) had normal white blood cell (WBC) count, while 3 (7.0%) had leukopoenia. The median WBC was 10 X 10^9/L (IQR 36.5 X 10^9/L). There were 13 patients (30.2%) with neutropenia (absolute neutrophil count (ANC) <1.5 X 10^9/L). The median platelet count was 42 X 10^9/L (range 4 – 276 X 10^9/L) and thrombocytopoenia was present in 36 cases (83.7%). Six patients (14.0%) had pancytopenia. On the peripheral blood film, 39 (90.7%) had circulating blasts; median blast count was 51% (range 2 – 99%).

Table 1. Clinical features of children with leukaemia at presentation

Clinical features	Frequency	Percent
Fever	28	65.1
Pallor	18	41.9
Gum bleeding	16	37.2
Hepatosplenomegaly	14	32.6
Bone pains	12	27.9
Lymphadenopathy	11	25.6
Fatigue	10	23.3
Weight loss	7	16.3
Cough	5	11.6
Difficulty in breathing	5	11.6
vomiting	5	11.6
jaw swelling	3	7.0
Convulsions	2	4.7
Headaches	2	4.7
Haematuria	2	4.7
Paraplegia	2	4.7
Swollen red eyes	2	4.7
Others (n=1 each): Dysphagia, Gingival hypertrophy, Joint swelling, leg swelling, Priapism, Skin rash, Squint	7	16.1

Acute lymphoblastic leukaemia was the diagnosis in 30 children (70%); while 4 (9%) had unspecified acute leukaemia diagnosis (see Fig. 1). Of the 30 with ALL, 18 (60%) had L1 phenotype, 10 (33.3%) had L2, while only 2 (6.7%) had L3 phenotype. There were 9 (21%) children with AML, of which 2 (22.2%) had M1 phenotype; 4 (44.4%) were diagnosed with M2 phenotype; 2 (22.2%) had M4/M5 phenotype; and 1 patient (11.1%) had M7. There were 4 cases (9%) diagnosed as acute leukaemia without further classification into AML or ALL (unspecified).

The bone marrow was hypercellular in 30 cases (69.8%), hypocellular in 6 (14.0%) and normocellular in 7 (16.2%). Erythropoiesis was depressed in 39 (90.7%) children while megakaryopoiesis was depressed in 33 (76.7%) and absent in 7 (16.3%). Table 3 gives the details of bone marrow findings of children with acute leukaemias in this study.

4. DISCUSSION

This study showed a male preponderance among children diagnosed with acute leukaemias, while fever, pallor and gum bleeding were the commonest presenting clinical features, with most children having thrombocytopaenia and high average level of bone marrow blasts. The most frequent diagnosis was ALL (70%) however, 9% of children were diagnosed with unspecified acute leukaemia due to limitation of resources for further investigations for specific disease classification, and the majority of the bone marrow were hypercellular.

The male preponderance obtained in this study is similar to other studies, including a previous survey in the same centre where acute leukaemias were found to be the most common childhood malignancies, accounting for 23% of all cancers in children below the age of 15 years [5-7]. The mean duration of symptoms prior to presentation was 56 days, which reflects a delay from onset of symptoms to presentation at our center. Besides, the commonest symptoms these children presented with were fever and pallor, which are similar to previous reports [2,6,7]. In a malaria endemic region like ours, these symptoms are often assumed to be due to malaria, a major cause of anaemia in tropical areas, and the widespread practice of self-treatment of febrile illnesses may be contributing factors to delayed presentation to the hospital [11]. Blasts may penetrate the central nervous system, thereby causing features such as seizures, loss of consciousness, paraplegia, etc. This is seen more in patients with ALL than AML [12]. Two of our patients had seizures and 2 others had paraplegia at the time of presentation, they both had ALL.

With regards to the full blood count parameters, these were as expected for patients with acute leukaemia, with majority having anaemia, leukocytosis and thrombocytopaenia [2]. Although leukocytosis was common, there were some patients who had pancytopaenia. In the diagnosis of acute leukemia, the total white cell count may be high, normal or low - with or without the presence of blasts in the peripheral blood. Despite those who had pancytopaenia, circulating blasts were present in the peripheral blood film of most (>90%) of the patients in this study, with higher average blast count observed in children with AML (91.3%) than those with ALL (51%). This is however at disparity with the report of Togo et al in Mali, who found higher average level of circulating blasts (80%) in children with ALL. The duration of ill-health before diagnosis may account for the difference [6].

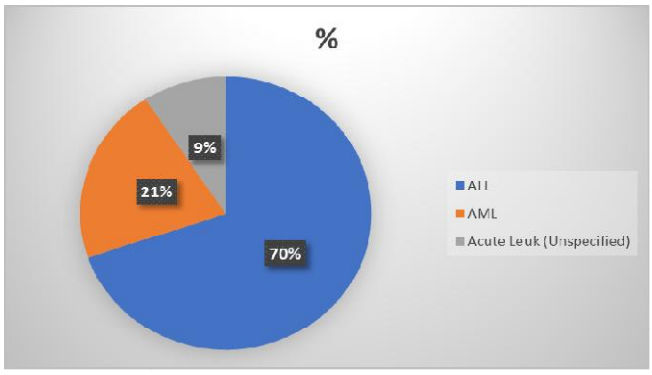

Fig. 1. Acute leukaemia diagnoses in children

Table 2. Median full blood count parameters of children with acute leukaemia at presentation

	Acute Leuk (not specified) [n= 4]		AML [n= 9]		ALL [n=30]		All Patients [n=43]	
Counts	**Median**	**Range**	**Median**	**Range**	**Median**	**Range**	**Median**	**Range**
Hb Conc. (g/dL)	7.6	6.8-8.3	6.7	3.7-12.7	6.85	3.3-10.6	6.9	3.3-12.7
WBC ($x10^9$/L)	4.5	2.1-6.9	11.1	4.8-98.0	17.9	3.5-657.3	10	2.1-657.3
ANC ($x10^9$/L)	0.8	0.7-0.8	3.1	1.8-14.8	2.4	0.4-45.3	2.4	0.4-45.3
ALC (x109/L)	3.7	1.3-6.1	13	2.0-75.0	8.2	2.4-117	8.17	1.3-117
Platelets ($x10^9$/L)	113	61-165	25.5	8-196	42	4-276	42	4-276
ESR (mm/Hr)	95.5	77-125	58	24-101	84	22-150	54	22-150
Blast count (%)	63	18-81	91.3	2-80	54.5	11.5-99.0	51	2-99

Hb conc: haemoglobin concentration; WBC: white blood cell; ANC: absolute neutrophil count; ALC: absolute lymphocyte count; ESR: erythrocyte sedimentation rate

Table 3. Bone marrow findings for children with acute leukaemias

		Acute Leukaemia (not specified)* [n= 4]		AML [n= 9]		ALL [n=30]		All Patients [n=43]	
Mean Bone marrow Blast Count		**89.5%**		**71.7%**		**88.2%**		**83.2%**	
BM Features		**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**
Cellularity									
	Normocellular	1	25	2	22.2	4	13.3	7	16.3
	Hypercellular	2	50	5	55.6	23	76.7	30	69.8
	Hypocellular	1	25	2	22.2	3	10.0	6	14.0
Erythropiesis									
	Normoactive	0	0.0	2	22.2	1	3.3	3	7.0
	Depressed	4	100	7	77.8	28	93.3	39	90.7
	Hyperplasia	0	0.0	0	0.0	1	3.3	1	2.3
	Normoblastic	0	0.0	1	11.1	7	23.3	8	18.6
	Micronormoblastic	4	100	5	55.6	15	50.0	24	55.8
	Megaloblastic	0	0.0	1	11.1	4	13.3	5	11.6
	Mixed Micro + Megalo	0	0.0	0	0.0	4	13.3	4	9.3
	Dysplasia	0	0.0	2	22.2	0	0.0	2	4.7

		Acute Leukaemia (not specified)* [n= 4]		AML [n= 9]		ALL [n=30]		All Patients [n=43]	
Mean Bone marrow Blast Count		**89.5%**		**71.7%**		**88.2%**		**83.2%**	
BM Features		**Number**	**%**	**Number**	**%**	**Number**	**%**	**Number**	**%**
Myelopoiesis									
	Normoactive	0	0.0	0	0.0	3	10.0	3	7.0
	Depressed	4	100.0	0	0.0	27	90.0	31	72.1
	Myeloid Hyperplasia	0	0.0	9	100.0	0	0.0	9	20.9
	Auer Rods	0	0.0	3	33.3	0	0.0	3	7.0
	Dysplasia	0	0.0	2	22.2	0	0.0	2	4.7
	BM Eosinophilia	0	0.0	2	22.2	0	0.0	2	4.7
Lymphopoiesis									
	Normoactive	0	0.0	0	0.0	7	23.3	7	16.3
	Depressed	4	100	9	100.0	0	0.0	13	30.2
	Lymphoid Hyperplasia	0	0.0	0	0.0	23	76.7	23	53.5
	Dysplasia	0	0.0	0	0.0	0	0.0	0	0.0
Megakaryopoiesis									
	Normoactive	0	0.0	0	0.0	3	10.0	3	7.0
	Depressed	2	50.0	6	66.7	25	83.3	33	76.7
	Absent	2	50.0	3	33.3	2	6.7	7	16.3
	Hyperplasia	0	0.0	0	0.0	0	0.0	0	0.0
	Dysplasia	0	0.0	1	11.1	0	0.0	1	2.3

The bone marrow findings in our patients were similar to other studies. Hypercellular marrow with depressed erythropoiesis and megakaryopoiesis associated with high blast counts were common. Erythropoiesis was mostly micronormoblastic, this may be due to increased hepcidin and IL-6 found in anaemia of chronic disorders which interferes with erythroblast uptake of iron from the bone marrow macrophages due to destruction of ferroportin [13]. Acute myeloblastic leukaemia may sometimes be associated with dysplasia. Only a few cases had dysplasia of the erythropoietin, myeloid or megakaryocytic cell line- however, dysplasia was only noted in patients with AML.

In a resource limited setting like ours, diagnosis of acute leukaemia is still largely dependent on morphology, based on the FAB classification of acute leukaemia which classifies ALL into 3 subtypes and AML into 8 subtypes [10]. Acute lymphoblastic leukaemia is the commonest childhood leukaemia, this was the case in this study (70%), and in previous reports, though AML was more prevalent in some African series [5-7,14]. Though useful in making a preliminary diagnosis of acute leukaemias, morphology has its limitations and is subject to both intra- and inter-observer differences [15]. Thus, there may be misdiagnosis of acute leukaemias if further investigations such as immunophenotyping and cytogenetic analysis are not done.

It could be difficult to differentiate myeloblasts from lymphoblasts using Romanowsky stains alone in the absence of cytochemical stains. Moreover, WHO recognizes biphenotypic acute leukaemias or acute leukemia of ambiguous lineage which have both lymphoid and myeloid blasts [8,16]. This was found in 4 (21%) patients in this study. It is possible that the lack of facilities for further classification of the type of acute leukaemia they had, may account for this finding, rather than the children having biphenotypic acute.

5. CONCLUSION

Children diagnosed with acute leukaemia in our hospital were predominantly males, presented late, with fever, pallor and gum bleeding as their commonest symptoms. Most of them had circulating blasts, ALL, and hypercellular marrow with high bone marrow blast count and depressed erythropoiesis. Provision of facilities for immunophenotyping and cytogenetic studies are recommended for adequate diagnosis and classification of acute leukaemias in children.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Ethical approval for the study was obtained from Medical Ethics Committee of the hospital.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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