Management and Clinical Outcomes of Adult Acute Leukaemias at a Resource-constrained Suburban University Teaching Hospital in Southern Nigeria

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*Abstract: **Background:** Acute leukemias are aggressive diseases that are most rapidly fatal in the absence of treatment. Treatment is dependent on the type, age and overall performance status of the patient at diagnosis. This study determined the challenges involved in the management of acute leukemias and clinical outcomes while making recommendations relevant to improved care and survival outcomes for patients with acute leukaemias. **Methodology:** This longitudinal study involved adult patients managed for acute leukaemias at the Delta State University Teaching Hospital between March 2023 and February 2025. Treatment for AML comprised induction with daunorubicin and cytarabine and consolidation with high-dose cytarabine (HiDAC) while treatment for ALL was with prednisolone, cyclophosphamide, vincristine, daunorubicin, and HiDAC. The data were analyzed using SPSS Version23. **Results:** Twenty-two cases of acute leukaemiaswere diagnosed,with a prevalence of 15.5%. Acute lymphoblastic leukaemiawas the most common (12, 54.5%). Fifteen of the patients (68.2%) completed induction chemotherapy while seven (31.8%) did not. Six (40%) of the 15 who had induction chemotherapy, proceeded to undergo consolidation chemotherapy, while nine, (60%) did not. High rates of discharge against medical advice (DAMA) were observed in patients with acute leukaemias. Pre-induction rate was 85.7% while pre-consolidation rate was 44.5%. **Conclusion:** This study revealed poor survival rates amongst patients with acute leukaemias. Influencing factors included poor diagnostic tools, clinical, and environmental inadequacies, high rates of DAMA and inadequate supportive care. Improving management and clinical outcomes for patients with acute leukaemias requires a holistic overhaul of the entire chain of management of these patients.*

Keywords: Acute leukemias, treatment outcome, clinical outcome, Nigeria

Introduction

Leukaemias are a heterogeneous group of diseases characterized by the accumulation of malignant white blood cells in the bone marrow and peripheral blood as well as lymphoid tissues.Symptoms from these abnormal cells usually results from bone marrow failure and infiltration of tissues of the body. [1]When the DNA in white blood cells becomes mutated, they lose the ability to govern growth and division, resulting in leukemia. These abnormal cells are able to elude the body's immune system and proliferate uncontrolled, displacing healthy cells in the process. [2]

Leukaemias are traditionally classified as either acute leukaemias such asacute lymphoblastic leukaemia (ALL), and acute myeloid leukaemia (AML)or chronic leukaemias such as chronic lymphocytic leukaemia (CLL) and chronic myeloid leukaemia (CML), based on the rate of progression of the disease entity. The leukaemias are further subdivided into lymphoid or myeloid leukaemias depending on the cell of origin.

Acute leukaemias are usually aggressive diseases in which malignant transformation occurs in a haemopoietic stem cell or early progenitor cell. They represent the most rapidly fatal in the absence of treatment, of all hematological malignancies with a high mortality rate.[3,4,5]Acquired genetic damage results in an increased rate of proliferation, reduced apoptosis and a block in cellular differentiation. Together these events cause accumulation in the bone marrow of early haemopoietic cells known as blast cells.[1]The specific etiology of leukaemias is uncertain; with several potential risk factors, such as exposure to radiation, cytotoxic drugs, petro- and agrochemicals amongst others, linked to the development of acute leukemias.[6,7]

Although the global incidence of leukaemias is largely steady, there are regional variabilities related to ethnicity, environment, and lifestyle factors. Acute leukaemias accounts for between 9.9% to 13.6% of all haematological malignancies across various centers in Nigeria.[8,9,10]Generally, AML is the most common form of acute leukaemiain adults and becomes increasingly common with age, whereasALL is primarily a disease of childhood, with 75% of cases occurring in children under the age of 10 years at diagnosis.[1,11,12]Common symptoms of acute leukaemias include variable levels of fatigue, pallor, easy bleeding and bruising, frequent infections, bone and joint pain, as well as enlarged lymph nodes and organomegaly. [13, 14, 15]

Acute leukaemias are diseases if diagnosed early, can be more effectively managed, leading to better survival rates and quality of life. This is often not the case in Nigeria where studies have shown that patients with hematological malignancies usually present at an advanced stage with resultant poor clinical outcomes.[16,17]

Treatment of acute leukaemias is dependent on the type, age and overall performance status of the patient at diagnosis.[18] Options available includes chemotherapy, which entails three serial steps; remission induction therapy, intensification or consolidation therapy and maintenance therapy, targeted therapy, radiotherapy, immunotherapy and haemopoietic stem cell transplantation.[1,19,20]

Overall survival rates depend on the type, age and performance status of the patient at diagnosis. While treatment outcomes, survival rates and prognosis have continued to improve in the advanced countries,[18,20,21]this cannot be said to be so in low- and middle-income countries, such as Nigeria,due to poor awareness, late presentation of patients, high rate of discharge against medical advice, limited access to advanced diagnostic tools, grossly inadequate healthcare infrastructures, includingdeficient or absent supportive care and lack of access to advanced treatment options.[3,17,22,23]

The aim of the study was to highlight the challenges involved in the management of patients with acute leukaemias at the Delta State University Teaching Hospital, Oghara Delta State.

The objective of the study was to determine the factors responsible for challenges involved in the management of acute leukaemias and make recommendations in order to improve care and survival outcomes for patients.

Methodology
Study area
The study was a longitudinal study carried out the Delta State University Teaching Hospital; a tertiary health institution located at Oghara, a suburban area in Ethiope-West local government area of Delta State, South – South Nigeria. It is a state government owned teaching hospital with over 300 bed capacity.It is affiliated with Delta State University, Abraka, and provides services from over 20 different medical disciplines. The department of Hematology and Blood Transfusion comprised of three consultant hematologists operating three outpatient clinics, hematology admissions, laboratory, and a blood bank.

Study population
The study population comprised of patients, 18 years and above, who presented via the Consultant out-patient Haematology clinics and Accident and Emergency wardand were diagnosed with either acute myeloid leukaemia or acute lymphoblastic leukaemia.

Data collection

Information was gathered from the patients who gave voluntary consent at the point of hospital admission and throughout the duration of management. Regular communication via phone calls was established between managing consultants and patients discharged by the consultant and those who discharged themselves against medical advice. Ethical approval was granted by the hospital ethics committee.

Sampling techniques and study duration

The participants were recruited consecutively between March 2023and February 2025 as the diagnosis was made. All diagnostic investigations –Full blood count, peripheral blood film, bone marrow aspiration; were carried out by the consultant hematologists according to standard procedures and protocols. Higher diagnostic investigations such as flow cytometry, cytogenetic and molecular studies were not accessible or too expensive for the patients to afford.

All the patients were admitted and managed in general open wards as there were no dedicated haematology wards or side rooms.Patients diagnosed with AML were treated with an anthracycline-based induction chemotherapy comprised of intravenous infusion of daunorubicin at $50mg/m^2$ once a day, on days 1 to 3 in combination with cytarabine at $100 mg/m^2/day$ given 12 hourly intravenouslyon days 1 - 7 based on the 7+3 protocol. Consolidation therapy using high-dose cytarabine (HiDAC) at $3,000 mg/m^2$ given every 12 hours on days 1, 3, and 5 following completion of induction therapy. Patients diagnosed with ALLhad three out of the five phases of chemotherapy protocol used at our center. Pre-induction was with oral prednisolone at $60mg/m^2/day$ on days 1 – 5, intravenous infusions of cyclophosphamide at $250mg/m^2/day$ on days 1 – 3 andvincristine at $1.4mg/m^2$ on day 1. Induction therapy was with oral prednisolone at $40mg/m^2$ on days 6 – 28, intravenous infusions on daunorubicin at $45mg/m^2$on days 6 – 8, and vincristine at $1.4mg/m^2$ on days 8,15, and 22. Early intensification, which commenced after complete remission, was with intravenous infusions of HiDAC at $3,000mg/m2$ every 12 hours on days 1 – 5. Unfortunately, none of the patients survived beyond this stage.

Prophylactic intrathecal therapy was administered to all the patients during each cycle of therapy. These included hydrocortisone, methotrexate, and cytarabine. Also, patients with central nervous system involvement, had additional intrathecal administration twice weekly until CSF clearance wasachieved.

All patients received supportive care, including anti-emetics, blood and blood products, and antimicrobial prophylaxis and treatment. However, some aspects weregrossly inadequate as patients were required to pay out of pocket for everything,A major challenge was the exorbitant cost of platelet concentrate, platelet agonists and haemopoietic stem cell transplantation services.

Data analysis

Data were analysed using Statistical Package for the Social Sciences (SPSS) version 23. The results were summarised using descriptive statistics (frequencies and percentages) and presented as figures andtables.

Results

Patient's characteristics are shown in table 1. Twenty-two cases of acute leukemiaswere diagnosed out of a total of142 patients with hematological malignanciesseen at the hospital during the period of this study. Thisputs the prevalence rateof acute leukemiasat our center at 15.5%.The patients were aged between 18 and 84 years oldwith a peak age at 18 to 30 years (45.5%), followed by the61 to 75 years age group (22.7%).Ten patients were single (45.5%), nine, married (40.9%) while three were widowed (13.6%).Most (45.5%) patients were self-employed, 36.4% were university students and 18.2% were retired patients.

ALL (12, 54.5%) was the most common diagnosis made, while AML diagnosis was made for 10 (45.5%) patients. ALL was found to be the most common acute leukemia in patients younger than forty years (83.3%) while AML was commoner in the elderly (50%).

Fifteen of the patients (68.2%) had induction chemotherapy while seven (31.8%) did not. Six (40%) of the 15 who had induction chemotherapy, proceeded to undergo consolidation chemotherapy, while nine, (60%) did not. At the end of follow-up all twenty-two (100%) patients were dead.

Table 1: Patients Characteristics

	Frequency	Percentage
Gender		
- Male	11	50.0
- Female	11	50.0
Age		
- 18-30 years	10	45.5
- 31-45 years	2	9.1
- 46-60 years	3	13.6
- 61-75 years	5	22.7
- 76-84 years	2	9.1

Mean ± SD (years)	43.6 ± 22.1	
Marital status		
- Single	10	45.5
- Married	9	40.9
- Widowed	3	13.6
Occupation		
- Retired	4	18.2
- Self-employed	10	45.5
- Student	8	36.4
Diagnosis		
- ALL	12	54.5
- AML	10	45.5
ALL Age Frequency		
- < 20 years	4	33.3
- 20-30 years	4	33.3
- 31-40 years	2	16.7
- 41-50 years	0	0.0
- 51-60 years	0	0.0
- > 60 years	2	16.7
AML Age Frequency		
- < 20 years	0	0.0
- 20-30 years	2	20.0
- 31-40 years	0	0.0
- 41-50 years	2	20.0
- 51-60	1	10.0
- > 60 years	5	50.0
Use of Induction Chemotherapy		
- Yes	15	68.2
- No	7	31.8
Use of Consolidation Chemotherapy		
- Yes	6	40.0
- No	9	60.0
Outcome		
- Dead	22	100.0

Figure 1highlights the reasons some patients did not undergo induction chemotherapy.. Discharge against medical advice (DAMA) (6 patients, 85.7%) accounted for the leading reason for not undergoing induction chemotherapy.

One patient (14.3%) died before the commencement of induction chemotherapy, shortly after being diagnosed.
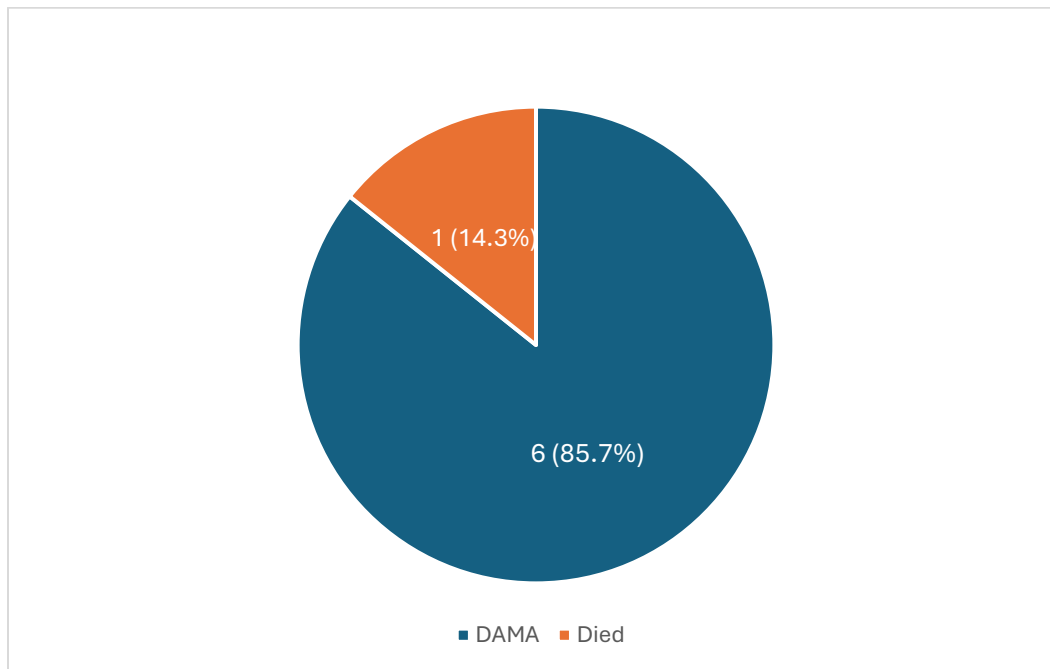

Figure 1: Reasons for not undergoing induction chemotherapy.

Figure 2 highlights the reason some patients did not undergo consolidation chemotherapy. Four (44.5%) discharged themselves against medical advice while five (55.5%) died during induction.
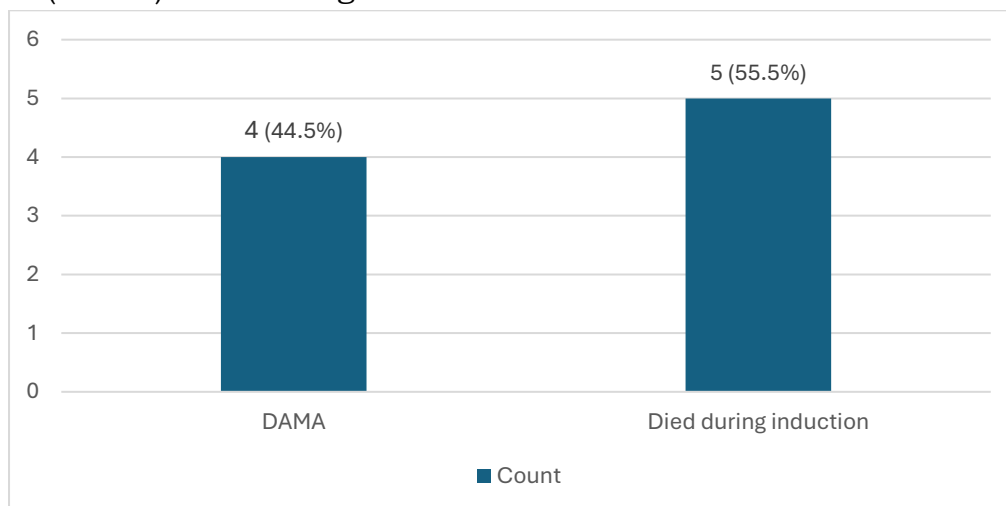

Figure 2: Reasons for not using consolidation chemotherapy

Discussion

Twenty-two cases of acute leukaemias with a prevalence rate of 15.5% were diagnosed during the study period. The documentation of the prevalence rate of acute leukemias in Nigeria has not been optimal due to the absence of a national cancer registry. However, available individual center-based studies highlights regional disparities leaving acute leukaemia burden in vast areas unknown and undocumented.[9,24,25,26]The absence of functioning and comprehensive cancer registries in Nigeria has significantly impacted national cancer control efforts by hindering identification of local causes of cancers, effective control measures and planning. It also hinders effective resource allocation and policy development.[27]

In our study, we found that ALL was commoner in the young adults while AML was commoner in the older adults with increased incidence in the elderly patients. This is in tandem with numerous previous local and international studies.[1,9,11,16,28]

The results of this study revealed the high level of discharge against medical advice (DAMA) in patients with acute leukaemias. Pre-induction rate was 85.7% while pre-consolidation rate was 44.5%. Similar contextual studies with which these findings can be compared have not been found. However, a previous study done at the same center, reported a significant DAMA rate of 39% amongst patients with hematological malignancies with financial constraints being the major reason behind these discharges.[22] The high rate of DAMA amongst patients with acute leukaemias posed a significant impediment to the management and overall survival of these patients at our center. Due to failure to commerce or complete treatment, these patients received care that was inadequate, deteriorated clinically without intervention, with ultimately adverse outcomes.[22,30]

Mortality rate amongst patients with acute leukaemias at our center during the period of this study was sadly 100%. The high rate of mortality recorded in this study is is with the low survival and mortality rates reported by several other studies involving both in adults and children.[3,19,30,31,32]The high mortality rates at our resource-limited center could beattributedto a myriad of factors. These included the high rate of DAMA, treatment related mortality, lack of adequate supportive care, especially blood and blood products, lack of infections control and prophylaxis, and use of cytotoxic chemotherapy. Also, not being able to afford or lack of access to up-to-date diagnostic/evaluation tools, targeted therapeutic agents and haemopoietic stem cell transplantation all contributed to the overall poor outcomes.

Conclusion

Survival rates among patients with acute leukaemias in this study were low. A complex of intertwined clinical, environmental and socioeconomic factors influenced management options and survival out comes in our resource constrained center. To improve clinical outcomes, impediments such as lack of proper population-based cancer registration centers and lack of adequate and up-to-date diagnostic tools must be addressed. Furthermore and more importantly, adequate and far-reaching insurance cover and establishment of foundations focused on the provision and/or subsidization of diagnostic tools, treatments, adequate supportive care and haemopoietic stem cell transplantation services must be prioritized. With these, out-of-pocket payments with the resultant negative impact of DAM would be effectively nipped in the bud.

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