

An Audit of Acute Leukaemias at the University College Hospital, Ibadan, Nigeria

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Abstract

Objective: Acute Leukaemia refers to bone marrow precursive haemopoietic malignancy; comprising Acute Myeloid leukaemia (AML) and Acute lymphoblastic leukaemia (ALL). The current burden of acute leukaemia at the University College Hospital (UCH), Ibadan remains obscure and hence this study was carried out to determine the burden, prevalence and the general outcome of acute leukaemia seen between April 2003 and July 2008 in the tertiary hospital.

Material and methods: The case notes and departmental records (the "pink cards") of all acute leukaemia cases seen within the stipulated period at the University College Hospital (UCH) were examined. All cases included were diagnosed predominantly through clinical features, full blood count followed by microscopic examination of peripheral blood and marrow smears by a team of consultant haematologists.

Results: Records of fifty acute leukaemia cases were retrievable. Male female ratio was 2.1:1. Age range was 2-60 years with a mean age of 19 years. The population of AML (56%) slightly exceeds that of ALL. Male: Female ratio was 2:1 in each subtype. AML cases were older (mean age=21.4yrs, age range=4-60yrs) compared to ALL with a mean age of 20.4 years. L2-sub-type of ALL was most commonly diagnosed while for AML; M₂, followed by M₄ FAB sub-types were most commonly diagnosed.

Conclusion: Acute Leukaemias constitute a significant burden in our institution and the general characteristics are comparable to what obtains worldwide. The need for upgrade of facilities required for proper diagnosis and treatment remain a great challenge.

Keywords: Audit; Acute leukaemia; Prevalence; UCH Ibadan; Nigeria

Introduction

This study described the burden of acute leukaemias and the level of current diagnostic competence of acute leukaemias in this institution with the view to attract attention to facility upgrade and better survival of acute leukaemia cases in this institution.

Acute leukaemia; comprising Acute myeloblastic leukaemia (AML) and Acute lymphoblastic leukaemia (ALL), represents a clonal, malignant transformation of blood forming cells that arise from the bone marrow or the lymphoid organs, and which are often associated with fundamental genetic abnormalities. Acute leukaemias are characterized by persistent proliferation of haemopoietic progenitor cells in maturation arrest at a particular stage of development which is specific for each subtype of the leukaemia. The visible indicator of malignant transformation is associated chromosomal abnormalities which are also of clinical relevance. In view of the maturation arrest of precursor lymphoid or myeloid lineage, there is drastic reduction or absence of matured forms of affected lineage but undue proliferation and accumulation of the arrested progenitor cell. These aberrant cells, believed to have reduced apoptosis, overwhelm normal haemopoiesis, spill over into circulation and infiltrate organs and tissues. The clinical course is rapid and outcome is fatal, within three months, if untreated. Acute leukaemia represents a significant proportion of haematological malignancies worldwide.

This index retrospective study builds on previous publications on acute leukaemias [1-9] and it audits cases of acute leukaemias managed between April 2003 to May 2008 with the goal of, not only to determining the frequency, characteristics (types and subtypes) of acute leukaemias in Ibadan; but also to determine possible sustained increase in annual incidence of ALL and AML (reported as 3.7 and

1.9 per 10⁶ per year respectively) [7] and whether incidence of ALL continue to rise as predicted by Okpala et al. a decade ago [10].

Materials and Methods

This an audit of records of all patients with acute leukaemias seen over a six year period May 2003 to July 2008. At this period, records of 50 cases of Acute Leukaemia were retrieved and analyzed. The retrospective analysis included demographic data: age and sex, diagnosis and outcome.

The diagnosis of the acute leukaemia cases were made through clinical features, haematological investigations like the full blood count, meticulous peripheral blood film review and bone marrow aspiration smears examination (A diagnosis of acute leukaemia was made once the blast count \geq 20% and this is confirmed using cytochemical studies PAS, Sudan B black, myeloperoxidase) if and when possible. Other ancillary investigations were carried out to determine extent of disease and to monitor therapy.

Results

Over the five year period, a total of 50 cases of acute leukaemias were managed. There mean age was 20.4 years. There were thirty four

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Received March 04, 2013; Published March 23, 2013

Citation: Olaniyi JA, Umar GK (2013) An Audit of Acute Leukaemias at the University College Hospital, Ibadan, Nigeria. 2: 649 doi:10.4172/scientificreports.649

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(68%) males and sixteen (32%) females (M:F=2.1:1). Twenty eight (56%) were diagnosed as AML while twenty two (44%) were diagnosed as ALL cases. Table 1 showed the sex distribution of both AML and ALL cases. The male female ratio was 2.1:1 for each type. Table 2 and figure 1 showed the frequency distribution of the various subtypes of acute leukaemias. The figure indicates that an average of 5-6 acute leukaemia cases was managed per annum.

As shown in table 2, eighteen (36%) of the acute leukaemias were of age ≤ 10 years and only one (2%) was within age bracket 41-50 years. However, unlike ALL, AML peaks at age brackets 31-40 years and at >50 years.

Figure 2 indicates that AML subtypes M₀ (naught), M₃ and M₇ were not diagnosed. And five (unclassified) cases (10%) of Acute leukaemia cases would have benefited from advanced studies like flow cytometry for confirmation of diagnosis. Most commonly diagnosed was M₂ followed by M₄.

Figure 3 showed that 68% of ALL were diagnosed as L2-subtype during the period and only 9% were diagnosed as L3 i.e. (L2>L1>L3).

During the study period, cytochemical stains were not available for routine use and hence further definition of diagnosis using cytochemistry was not done.

Discussion

Acute leukaemia arises from a genetically abnormal lymphoid/myeloid precursor cell that is arrested at a particular stage of maturation, generates an abnormal clone within the marrow which

	ALL	AML	Total
Number (n)	28	22	50
M:F	2:1	2:1	2.1:1
Mean Age	19 yrs	21.4 yrs	20.4 yrs
Age range	3-54	2-60	2-60

Table 1: Demography of Acute Leukaemias.

Age range	Frequency		
	AML	ALL	Total
<-10	10 (35.7%)	8 (36.4%)	18 (36%)
11-20	5 (17.8%)	4 (18.2%)	9 (18%)
21-30	4 (14.3%)	7 (31.8%)	12 (24%)
31-40	7 (25%)	1 (4.5)	8 (16%)
41-50	0	1 (4.5)	1 (2%)
>50	2 (7-1%)	1 (4.5)	3 (6%)
	28 (56%)	22 (44%)	50 (100%)

Table 2: Frequency of Acute Leukaemias.

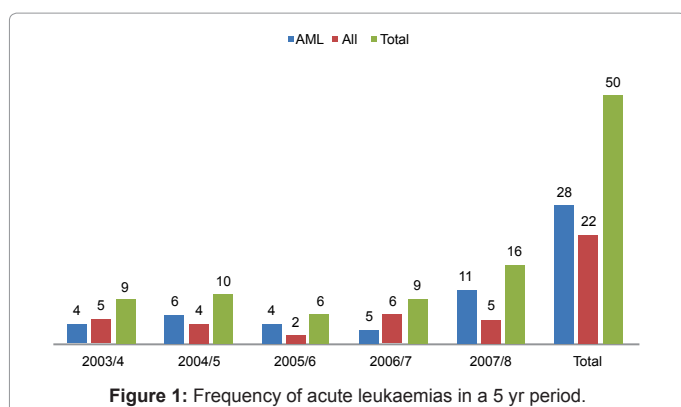


Figure 1: Frequency of acute leukaemias in a 5 yr period.

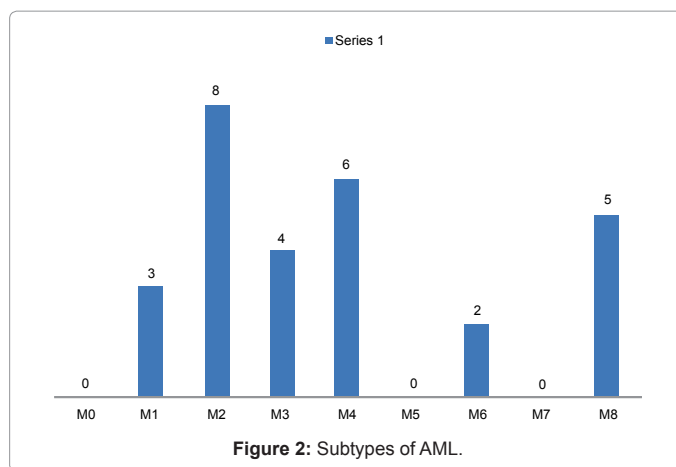


Figure 2: Subtypes of AML.

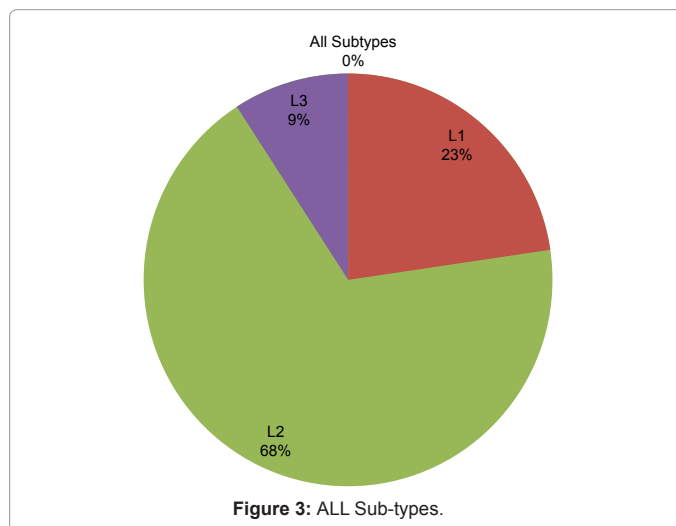


Figure 3: ALL Sub-types.

rapidly overpopulates the marrow, spread to peripheral blood and infiltrates tissues and organs. Therefore, acute leukaemias present as bone marrow failure due to the very heavy marrow infiltration by the abnormal clone of blast cells with resultant very minimal residual normal marrow.

The main goal of diagnostic modalities vis-à-vis morphology, cytochemistry, cytogenetics and immunophenotyping (antigen assessment using monoclonal antibodies) is to be able to place the clone within one of the bone marrow cells and to be able to predict prognosis. During the period of study, morphology was the main diagnostic tool and very occasionally complimented with cytochemistry.

Acute leukaemia affects all age groups and all races; this study align with previous studies [10] indicating a rising incidence of acute leukaemias in this catchment area of Nigeria. However, there are now at least four new Teaching Hospitals (≤ 120 km proximity) around this center and still this population of acute leukaemia was recorded within 5 years.

The incidence of acute Leukaemia varies geographically, but is usually 20-30 million per year [11]. In this index study, we found a yearly frequency rate of 6-16 Acute Leukaemias per year (Figure 1) and like the earlier reports [10], male: female ratio of 2.1:1.

In the past, the prognosis was universally bad, with deaths in a view

weeks for most untreated cases. However, well organized intensive chemotherapy has brought significant remission and cure rates. Also, the advent of bone marrow transplant has further improved the outlook of acute leukaemias. Regrettably in Nigeria, achieving first remission remains difficult and early death is still characteristic [9]. This poor outcome could be attributed to poverty, poor supportive management in terms of blood and blood products and inability to adequately prevent and control infections at the phase of chemo-induced hypoplasia, inability to apply standard chemotherapy either because patient could not afford/sustain provision and lack of facility for stem cell transplant.

This index study showed that significant proportion of acute leukemia occurred at ≤ 10 years of age, with diagnosis of AML exceeding ALL (Table 2 and Figure 2), then declines steadily as age advances except for upsurge of AML at ages 31-40 years and >50 years age brackets. This may suggest a close link with inherited disorders associated with acute leukaemia as against acquired genetic disorders associated with environmental carcinogens. Only 2% of the acute leukaemias were diagnosed at age bracket 41-50 yrs (Figure 2). The study again showed that using only morphology alone has a serious limitation in making accurate diagnosis in that five cases of AML could not be definitely placed in any FAB class. It is also noteworthy that M_0 , M_5 and M_7 were not diagnosed during the study period. The use of advanced technology like Flow-cytometric immunophenotyping would have assisted to clearly defined each leukaemic clone i.e. demonstrate subtypes of acute leukaemia and reveal the rare biphenotypic and bilineage acute leukaemias. As regards ALL, the most commonly diagnosed was L2-subtype, constituting 68% and this is in agreement with previous study [10]. The preponderance of L2 subtype (68%) and L3 subtype, which are of bad prognosis, might be a significant contributory factor to the generally very poor survival outcome.

It is obvious that our diagnostic methods need upgrading in order to excellently define cases of acute leukaemia vis-à-vis using cytochemistry, flow-cytometry and molecular studies. Flow-cytometric immunophenotyping is actually the best in full immunological characterization of acute Leukaemias to identify cluster of differentiation antigens, thereby defining level of maturation of lymphoid/myeloid leukaemic clone and also resolves the ambiguity of mixed-lineage and bi-phenotypic acute leukaemias [12].

All these are pointers to urgent need for human resource development, facility upgrading, and implementation of National Health Insurance to fully cover cancer care or at least substantially subsidize cancer therapy. An upgraded cancer care center that has what it takes, including facility for bone marrow transplant, is needed per geopolitical region in Nigeria. These will go a long way in improving

survival and enhance possible cure of these malignancies and thereby reduce drastically death burden from cancer in Africa.

Death burden from cancer remains unacceptably high in Africa. Of 7.6 million deaths from cancer worldwide in 2008, 64% of these deaths occurred in developing countries. Also in 2002, of 6.2 million cancer deaths 55% were from the developing world [11,13]. This index study evaluated the burden of acute leukaemias, which is associated with dismal outcome, in Ibadan, Nigeria. This is to re-direct our search-light to non-communicable diseases to become the major focus of medical prevention, care and research as in advance economies [14].

Acknowledgement

The authors appreciate and acknowledge the contribution of Consultant staff of Department of Haematology, University College Hospital Ibadan, Nigeria viz-a-viz Prof YA Aken'Ova, Prof. WA Shokunbi, Dr. TR Kotila, Dr. TS Akigbola, Dr. FA Fasola and involved Resident Doctors in the total care of these patients.

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