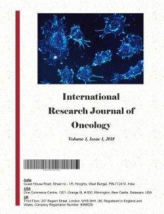

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Epidemiological Pattern of Adult Haematological Malignancies in a Tertiary Hospital in Cross River State

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Authors' contributions

This work was carried out in collaboration among all authors. Author AK, AI and NB designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors BOB, Ofonime Effiong, PE and IH managed the analyses of the study. Author Onyeulor Ebere and UGA managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Haematological malignancies are associated with increase morbidity and mortality in our environment. The pattern and distribution of diagnosed haematological cancers vary with age, sex, geographical location, and ethnicity. The epidemiology of adult haematological malignancies has not been described in our institution. This study aim to describe demographic distribution of affected persons and the types of haematological malignancies seen in our institution.

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Methods: This is a 10-year (2009-2018) retrospective study of all adult haematological malignancies seen at the University of Calabar Teaching Hospital, Calabar (UCTH). Data of year of presentation and diagnosis, age, gender, tribe, state of residence, place of origin of the patients and type of haematological malignancy were extracted from the hospital cancer, registry, and haematology medical records and from patients' case-notes. The data were collated into a Microsoft Excel 2016 spreadsheet and analysed with IBM SPSS Version 22. The results were presented using descriptive statistics (frequencies and percentages), and graphical charts.
Results: A total of 1314 cases of malignancies where seen during the study period. One hundred and thirty eight (10.5%) were adult haematological malignancies. Their ages ranged from 16 to 74 years. They include 73(52.9%) males and 65(47.10%) females with a male to female ratio of 1.1:1. Majority of the patients 105 (76.09%) are indigenes of Cross River State. The prevalence of lymphoid malignancies was higher than myeloid (76.81% vs 23.91%). Chronic lymphocytic leukaemia (CLL) was the commonest haematological malignancy (36, 26.09%) followed by Non-Hodgkin's lymphoma (NHL) 28 (20.29%) while Myelodysplastic syndrome (MDS) and Burkitt's lymphoma 2 (1.45%) each were the least.
Conclusion: This study has highlighted the burden and epidemiological pattern of HM in our institution and would serve as a term of reference for further studies on the topic and a tool for raising awareness on the disease burden.

Keywords: Hematological malignancies; epidemiology; Calabar.

1. INTRODUCTION

Haematological malignancies (HM) are heterogeneous group of neoplasm of clonal origin, arising from haemopoietic tissue (bone marrow and reticuloendothelial tissue) [1]. This spectrum of disease ranges from the pre-leukaemic (myelodysplasia), leukaemic, lymphoma to multiple myeloma. The etiology of these malignancies is largely unknown, however interplay of genetic mutations, environmental risk factors and infectious agents have been implicated in the pathogenesis of the disease.

Malignancies including HM are becoming public health challenge and disease of global priority due to the associated increase in morbidity and mortality [2]. Global prevalence of HM is estimated to account for 6.5% of all cancer world-wide [3]. Non-Hodgkin's Lymphoma (NHL) stands for 2.7% of all cancers and 2.4% of all mortality from cancer worldwide. Leukaemia accounted for 2.5% of all cancers and 3.2% of all deaths and Multiple Myeloma (MM) accounts for 0.8% of all cancers and 1.0% of cancer deaths, while Hodgkin's Lymphoma (HL) represented 0.5% of all cancers and 0.5% of cancer deaths [4]. However, there are variations in the epidemiology from one geographical region to another.

Hematologic malignancies make up a fifth of the most commonly occurring cancers and the second leading cause of cancer mortality [5,6]. Leukaemia was the fifth most common cause of cancer deaths in men and the sixth most common in women in the United States in a 5-year study between 2007 and 2011 [7] and in the United Kingdom, haematological malignancy is said to make up 63.2% with male 55.7% and female 44.3% [8]. In Sub-Sahara Africa it is third most common malignancy in males and sixth in females [9,10]. Similarly, in Nigeria it accounts for 17.4-18.05% of all cancer in Nigeria and it is the third and fifth in both male and female respectively [9,10]. A study conducted in Northern Nigeria showed prevalence 19.8% with male preponderance and chronic leukaemia predominantly [11]. Another study in the Southwest Nigeria reported a prevalence of 18.05% of all cancer with male preponderance and NHL predominantly [10]. Similar study conducted in Benin South-South of Nigeria, showed a prevalence of 17.4% with male preponderance and NHL predominantly [12]. There is paucity of information on the epidemiology of adult haematological malignancies in our environment, thus aim of this study was to describe the epidemiological pattern of HM in Calabar with a view to reawaken the consciousness of burden and pattern of distribution of adult haematological malignancies in the sub region.

2. MATERIALS AND METHODS

This is a 10-year (2009-2018) retrospective study of all adult haematological malignancies seen at

the University of Calabar Teaching Hospital, Calabar (UCTH), Calabar. The hospital is a 600-bedtertiary health institution that renders specialist care to its host community and environs. It serves as a referral centre for it neighbouring states that include Akwa-Ibom, and Ebonyi state as well Cameroon.

The study population consisted of all patients with haematological malignancies diagnosed at the University of Calabar Teaching Hospital from August 2009 to December 2018. Data were obtained from the Medical Records Department, haematology day-care clinic attendance register, the admission/discharge register, death register and the Cancer Registry domicile at the department of histopathology. The diagnoses of HM were made by medical consultants based on clinical and laboratory investigations of the patients included peripheral blood film and bone marrow examinations, histopathological assessment, immune-histology and immunohistochemistry on tissue specimen. Patients with inconclusive diagnoses were excluded from the study. Collected data include those who were diagnosed but were not managed in the hospital and those who passed on before their histology results were ready. Data that were collected included the date of presentation, the age, gender, tribe, state of residence, place of origin of the patients and type of malignancy. Adult was defined as ages of 16 and above.

The data were computed into Microsoft Excel 2016 spreadsheet and analysed with the IBM SPSS Version 22. The results were summarized using simple descriptive statistics (frequencies and percentages), and presented as tables and graphical charts.

3. RESULTS

A total of 1314 cases of malignancies were seen over the ten-year period (August 2009 to December 2018). One hundred and thirty eight (10.5%) were adult with haematological malignancies. Their ages ranged from 16 to 84 years. The modal age group was the 6th decade of life as in Table 1. They comprised 73(52.90%) males and 65(47.10%) females giving a male to female ratio of 1.1:1.

Majority of the patients 105 (76.09%) were indigenes of Cross River State while the remaining 33 (23.91%) hails from others parts of the country but were majorly resident in Cross River State as shown in Table 2. The annual incidence of HM was variable across the years of the study. The least was in 2012 and the highest peak was in 2017 as shown in Fig. 1. However, the annual incidence of HM was those seen in UCTH, Calabar.

The top five common HM during the study period were CLL 33 (23.9%), NHL 32 (23.2%), CML 24 (17.4%), HL 20 (14.5%) and MM 17 (12.3%). The least were Burkitt's and ALL both had a frequency of 2 (1.4%) each as shown in Fig. 2.

Table 1. Showing the various age range and frequency of haematological malignancies

Age range	Frequency	Percentage
10-19	8	5.80
20-29	20	14.49
30-39	15	10.87
40-49	19	13.77
50-59	36	26.09
60-69	24	17.39
70-79	14	10.14
80-89	2	1.45
Total	138	100

Table 2. Showing the location residence of the patients and frequency of haematological malignancies

Locality	Frequency	Percentage
Abi	4	2.90
Ikot ekpene	6	4.35
Bekwara	5	3.62
Boki	3	2.17
Calabar	43	31.16
Akwa ibom	16	11.59
Ikom	25	18.12
Obubra	6	4.35
Akampka	11	7.97
Obudu	8	5.80
Ugep	6	4.35
Yala	5	3.62
Total	138	100.00

Table 3 shows the distribution of HM by age. CLL recorded a peak in the 6th decade and none case was recorded before the fifth decade of life. CML was recorded in persons between the 3rd and 8th decade of life with a peak in the 4th decade. NHL was reported in all decades of life except in the 5th decade. Peak incidence was in the 6th decade. HL was seen across all age group except in the 6th decade and after the 7th decade of life. The two cases of MDS were seen after the 6th decade of life. All cases of ALL and AML were

reported in persons below 50 years of age. Similarly, Burkitt's lymphoma was reported in relatively younger age groups.

Table 4 shows the distribution of the haematological malignancies by gender and age. The prevalence of CLL, CML, MM and Burkitt's lymphoma were relatively higher in females while ALL, AML, MDS, Hodgkin's lymphoma and NHL were commoner in the males. Table 5 shows the distribution of various HM for each year of the study.

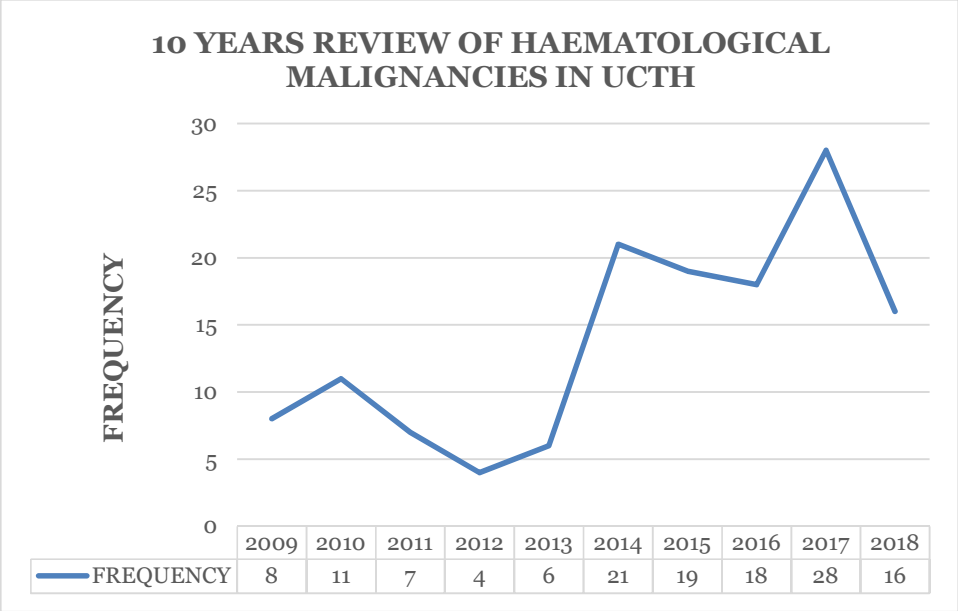

Fig. 1. Showing a 10 years review of haematological malignancies in UCTH

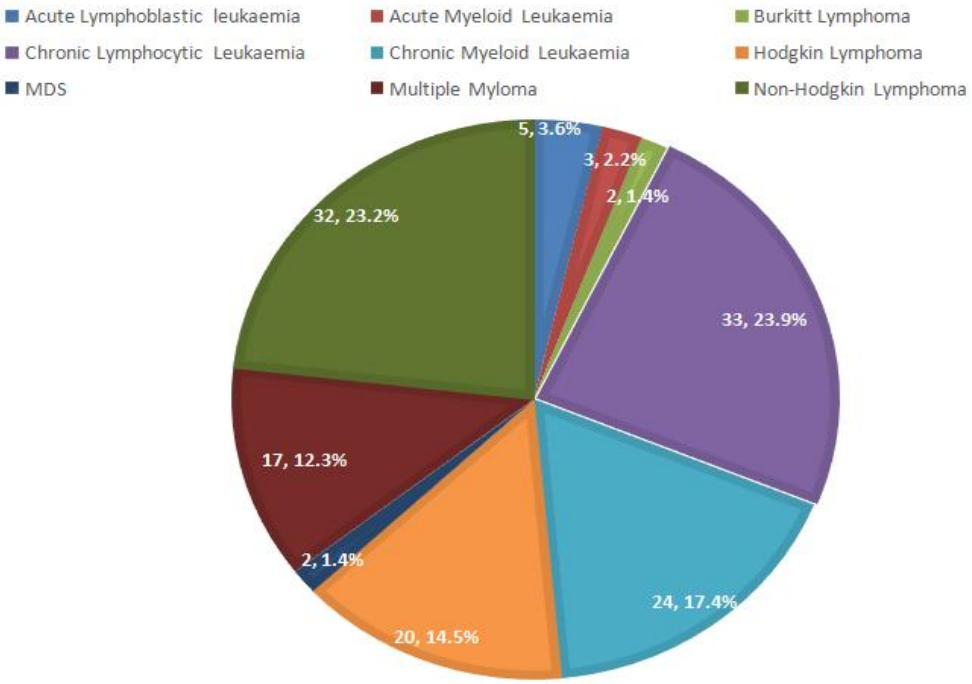

Fig. 2. Showing the prevalence of haematological malignancies in UCTH

Table 3. Showing the frequency and age range distribution of various haematological malignancies

Haematological malignancies	10-19	20-29	30-39	40-49	50-59	60-69	70-79	≥80
Acute lymphoblastic leukemia	2	1	0	1	0	0	0	0
chronic lymphocytic leukemia	0	0	0	7	11	8	8	2
Acute myeloid leukemia	0	1	1	1	0	0	0	0
Chronic myeloid leukemia	0	5	8	4	6	3	1	0
MDS	0	0	0	0	1	1	0	0
Multiple myeloma	0	0	0	4	6	6	1	0
Hodgkin's lymphoma	3	5	3	4	0	2	2	0
Non-hodgkin's lymphoma	2	5	3	0	13	3	3	0
Burkitt's lymphoma	0	1	1	0	0	0	0	0
Total	**7**	**18**	**16**	**20**	**37**	**23**	**15**	**2**

Table 4. Showing the frequency and sex distribution of various haematological malignancies

Haematological malignancies	Frequency		Total (%)
	Male (%)	Female (%)	
Acute lymphoblastic leukemia	4 (5.48)	0 (0.00)	4 (2.90)
Chronic lymphocytic leukemia	17 (23.29)	19 (29.23)	36 (26.09)
Acute myeloid leukemia	3 (4.11)	0 (0.00)	3 (2.17)
Chronic myeloid leukemia	11 (15.07)	16 (24.62)	27 (19.57)
Myelodysplastic syndrome	2 (2.74)	0 (0.00)	2 (1.45)
Multiple myeloma	4 (5.48)	13 (20.00)	17 (12.32)
Hodgkin's lymphoma	10 (13.70)	9 (13.85)	19 (13.77)
Non-Hodgkin's lymphoma	22 (30.14)	6 (9.23)	28 (20.29)
Burkitt's lymphoma	0 (0.00)	2 (3.08)	2 (1.45)
Total	73 (52.90)	65 (47.10)	138 (100)

Table 5. Showing various haematological malignancies and yearly distribution

Haematological malignancies	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Acute lymphoblastic leukemia	0	1	0	1	0	0	1	0	1	0
Chronic lymphocytic leukemia	2	4	3	1	2	6	4	3	7	4
Acute myeloid leukemia	0	0	1	0	0	1	0	0	0	1
Chronic myeloid leukemia	2	2	0	0	4	3	2	8	4	2
MDS	0	0	0		0	0	0	0	0	2
Multiple myeloma	1	1	0	1	0	3	0	3	3	5
Hodgkin's lymphoma	0	1	1		0	4	4	1	5	3
Non-hodgkin's lymphoma	1	2	1	1	0	4	8	3	6	2
Burkitt's lymphoma	0	0	0	0	0	0	0	1	1	0
Total	8	11	7	4	6	21	19	18	31	16

4. DISCUSSION

In this study, Adult HM constitutes 10.5% of all malignancies recorded during the period of review. This was similar to rates published in studies conducted in Morocco [13-15] and was slightly higher than the study in United States which reported prevalence of 9.3% [16]. The

difference in prevalence of HM reflects the wide variation in the epidemiology of HM. The variability of risk factors from one locality to another, health seeking behaviour, availability of consultant specialist to make appropriate diagnosis contribute to the prevalence rate of the community. Availability and accessibility to cancer preventive and control measures may to contribute to the relatively lower rate reported in the US.

The study also showed that adult haemalological malignancy were more in those residing in Calabar urban followed by Ikom, Akwa Ibom, Akamkpa respectively with least observed in Boki. This pattern maybe attributed to their relative proximity to the health facility and occupational exposure. For instance the hospital is located at Calabar Municipality giving ease of access to those living within the hospital environs whereas, Ikom is approximately 6 hours drive to the state capital where the facility is situated. The predominant occupation in Ikom is cocoa farming and this increases the exposure of the population to organo-phosphorus compounds, insecticides, and pesticides. The same applies to other cities involved in this study.

We showed the annual pattern of distribution of adult HM during the period of review. A peak was observed in 2017 with least incidence in 2012 and the widest difference between consecutive years was between 2016 and 2017. The variation in annual incidence may be attributed in part to frequent industrial actions in the hospital that limits patient access to specialized care. The increase in the recent years was partly due to increased awareness of the availability of haematologist in the institution. The institution now runs a resident programme in haematology and has recruited more haematologists making it easier to access such specialized services.

This study revealed that the age range of adult HM was 16 - 84 years with individual malignancies having varying peak ages. This was similar to the study conducted in Morocco but was at variance with other studies conducted elsewhere in Nigeria [13,17,18]. Majority of the adult HM was observed among patients age >40 years (70.3%). This is biologically explainable due to the multiple hit theory, which suggest that the cumulative effect of genetic assault manifest over time [21,22].

There is also male preponderance with male to female ratio of 1:1.1. This finding is similar with the general observation in scientific publication that the prevalence of most HM is commoner in male than female [5]. Onwasigwe et al. [23] also reported similar finding in Enugu South Eastern Nigeria. However when the HM were considered individually, females had higher prevalence of CLL, MDS and MM. Our finding was similar to reports from France and United Kingdom where male to female ratio was 1.2:1 and 1.3:1 respectively [19,20]. The high prevalence of CLL in female was similar to what was reported in the North Central and South Western parts of Nigeria by Babatunde et al. [10] and Salawu et al. [19]. In addition, a similar study conducted in South-South Nigeria showed female preponderance.

The median age for CLL was 54.5 years. This was higher than those observed in Asian [24-26] and western countries [27-29] with female preponderance, which was similar to other studies conducted within Nigeria [10,19,20] but at variance with other studies conducted within and outside Africa [13].

Lymphoid malignancies were 76.81% [20]. This is at akin with other studies conducted within and outside Africa [13,17,18]. In this study, chronic leukaemia was more than acute leukaemia. This finding was similar to reports by previous published studies [30-32]. CLL was the most common (26.09%) followed by NHL (20.29%), CML (19.57%), HL (13.77%), MM (12.32%), ALL (2.90%), AML (2.17%) with MDS and Burkitt's lymphoma having same value (1.45%) this is similar to a study conducted in Morrocco, Northern Africa [13] but at variance with other studies within Nigeria the variation could be attributed to the various study design [9,10,12].

Acute leukaemia had a male preponderance with ALL making up 2.90% and AML 2.17% this differed from other studies reported in Northern and Southern Nigeria [9,10]. Similar prevalence of ALL was reported by Elidrissi et al. [13] but a higher prevalence of AML. This highlights the slight variation from one locality to another.

NHL was the second most common lymphoid malignancy constituting 20.29% with a median age of 55 years and male preponderance. This is similar to the study conducted by Babatunde *et al* in the North-Central of Nigeria and somewhat similar to study conducted outside Nigeria [10], in Eastern Morocco. Other Nigerian based studies [13,19,20] which reported a higher prevalence for NHL.

CML accounted for 19.57% of HM with female more affected than male in the ratio 1.3:1. The median age was within the 30-39 years. This is similar to the observation by Higlaund et al. [33] but was at variance with other studies conducted in South Africa and Nigeria by Louw and Boma et al. respectively [34,35].

MM accounted for 12.32% of all adult HM with male to female ration of 1:3.25. This was slightly higher than other study conducted elsewhere in Nigeria but similar to study conducted by Elidrissi et al. in Morocco [13]. The relatively higher prevalence in our study may be attributed to the fact that Cross Riverarians are predominantly farmers some of whom are exposed to agrochemicals including organophosphates. The people are also exposed to petrochemical pollutions as an oil producing state These agents have been implicated to have a causal relationship in pathogenesis of myeloma.

Hodgkin's lymphoma (HL) accounted for 13.8% of all adult HM with male to female of 1.1:1. HL affects all age groups but had bimodal peaks. The first peak was in young adults (20-29 years) and the second and highest peak 40-49 year. This contrasted studies of develop countries with age peaks of 20-34 years and 55-74years. The variation may be associated with variation in exposure to infection with EBV in children between these countries [37,38]. Association of HL with malaria endemicity may also contribute to the differences in the epidemiological pattern. Our findings were similar to those of Babatunde et al. [10] and Oluwasola et al. [39]. However Omoti et al in South-South Nigeria and some studies in Europe reported relatively lower peaks [20,36].

MDS contribute 1.45% of HM with modal age at onset of 50-69 years. MDS is usually a diagnosis of exclusion and there is paucity of information on MDS in our environment. A high index of suspicion is necessary for its diagnosis as it presents commonly as refractory anaemia, which may be misunderstood for other differentials of chronic anaemia. Salawu et al. [19] reported a somewhat similar prevalence of 1.9%. Also in Europe, a prevalence of 1.24% but a lower value was reported in Northern Africa [13,37].

The strength of this study was that it was the first study from our institution on the epidemiology of HM. However; it has several limitation inherent in the study design. Being retrospective in nature, information bias in inevitable. A number of cases may have been missed out due to lack of proper documentation. It is possible that the study may have underestimated the burden of HM in our environment because the health sector suffered repeated prolonged industrial actions which may have limited patients' access to care.

5. CONCLUSION

This study has highlighted the burden and epidemiological pattern of HM in our institution and would serve as a term of reference for further studies on the topic and a tool for raising awareness on the disease burden. There is need for further studies to establish causal relationship between HM and environment exposures in our sub region.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The research was approved by the Health Research Ethics Committee of the University of Calabar Teaching Hospital.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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