Pattern of Haematological Malignancies among Adult Nigerians Attending a Tertiary Hospital in South South Nigeria: Eight- Year Review

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ABSTRACT

Haematological Malignancies(HMs) are a major cause of morbidity and mortality worldwide. To the best of our Knowledge, there are no reports on the burden of these neoplasms in this environment. The objective of this study therefore was to determine the pattern of Haematological Malignancies in this region and compare with reports from other studies. A retrospective review of Haematological Malignancies in adult Nigerians in Uyo, Nigeria, was undertaken using records of patients managed in Haematology Department, University of Uyo Teaching Hospital (UUTH) over an 8-year period (January 1, 2008 to December 31, 2015. A total of 127 patients aged 20-79 years were diagnosed with Haematological Malignancies during the study period. The prevalence of the different Haematological Malignancies recorded: Prolymphocytic Leukaemia 1 (0.8%),Primary Myelofibrosis 2 (1.6%),Essential Thrombocythaemia 2 (1.6%), Polycythaemia Vera 8 (6.3%), Myelodysplastic Syndrome 4 (3.1%),Multiple Myeloma 14 (11.0%), Acute Myeloid Leukaemia 4 (3.9%), Acute Lymphoblastic Leukaemia 5 (3.1%), Chronic Myeloid Leukaemia 21 (16.5%), Chronic Lymphocytic Leukaemia 24 (18.9%), Hodgkin's Lymphoma 14(11.0%) and Non-Hodgkin's Lymphoma 34 (22.0%) .Non-Hodgkin's Lymphoma constituted the highest prevalence while prolymphocytic Leukaemia was the least seen. This study has shown that Haematological Malignancies are not uncommon in our environment Further research is required therefore to identify the potential risk factors, define the biology, molecular genetics and clinical outcome of these Malignancies in this region.

Keywords: Haematological Malignancies, Non-Hodgkin's Lymphoma, Prolymphocytic Leukaemia, Uyo

INTRODUCTION

Haematological Malignancies (HMs) comprise a wide spectrum of primary neoplasms of blood and lymphoreticular tissues that are of diverse incidence, prognosis and aetiology.[1]They account for 6-9% of all cancers and are the fourth commonest in males (after prostate, lungs and colorectal cancers) and in females (after breast, Lungs and colorectal cancers)[2].

HMs are clonal diseases and quite frequently are associated with chromosomal aberrations[1]. These malignant transformation usually occurs as a result of genetic mutations in somatic cells which can arise from a broad spectrum of environmental influences such as exposure to chemicals, drugs, ionizing radiation and microbiologic agents .The mode of presentation of these cancers vary tremendously between patients and this may be largely attributed to the biology and stage of the cancers. They are found in all racesand affect people of both sexes and all ages.

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Three principal categories of Haematological malignancies are recognized: the Leukaemias, the Lymphomas, and the Plasma Cell Neoplasms. Others are Polycythaemia Vera, Essential Thrombocythaemia, Primary Myelofibrosis and Myelodysplastic Syndrome[3]. These conditions are notoriously incurable and constitute a significant cause of morbidity and mortality globally[3]. There are substantial reports[1,2,3]. on the burden of Haematological Malignancies in the Oriental and Western world and some parts of Nigeria but information on the prevalence of these diseases in our environment is non-existent owing to absence of research on this subject. Studies[1,4] have shown that the pattern of some variants of HMs vary in different populations and geographic areas hence the need to determine the pattern of HMs in our environment and thereby (delete!!) highlight the magnitude of the problem to enable policy makers pay ardent attention to healthcare needs of Haematological Malignancy patients and encourage further research in this area.

MATERIALS AND METHODS

Study Site

The study was carried out at University of Uyo Teaching Hospital(UUTH), a tertiary health institution in Uyo, Akwa Ibom State,

South-South Nigeria. The hospital provides specialized healthcare services to the indigenes of Uyo and its environs.

Study Design

This was a cross-sectional, descriptive and retrospective hospital-based study involving the review of case records of Haematological Malignancy patients managed at Department of Haematology of UUTH over an 8-year period (January 1, 2008 to December 31, 2015).

Data Collection and Analysis

Information extracted from the records included: age, sex, final diagnoses from lymph node biopsy histology, peripheral blood film and bone marrow aspiration cytology reports. All the case notes of HM patients managed in our Department were retrieved and used for this study. (**Editorial Advice**: The above highlighted statement was retrieved from your explanation form and addedhere for you!Allow if you think its ok?) The data obtained were analysed using statistical package for Social Sciences (SPSS) Windows Version 11.5 and the results were presented in simple frequency tables.

RESULTS

One hundred and twenty-seven (127) patients were diagnosed with Haematological Malignancies during the study period. There were 69(54.3%) males and 58(45.7%) females giving a male to female ratio of 1.2:1, their ages ranged from 20-79 years. Among the Haematological Malignancies, NHL was the most frequent constituting 22.0%of the cases followed by Chronic Lymphocytic Leukaemia (18.9%) and Chronic Myeloid Leukaemia (16.5%). Others include Hodgkin's Lymphoma (11.0%), Multiple Myeloma (11.0%), Polycythaemia Vera (6.3%) Acute Myeloid Leukaemia (3.9%), Acute Lymphoblastic Leukaemia (3.1%), Myelodysplastic Syndrone(3.1%) Essential Thrombocythaemia (1.6%),and Primary Myelofibrosis (1.6%), as well as Prolymphocytic Leukaemia (0.8%), Table 1.Haematological Malignancies such as plasma Cell Leukaemia, Hairy Cell Leukaemia and Hairy Cell Variant were not diagnosed during this period.

Acute Lymphoblastic Leukaemia, Acute Myeloid Leukaemia and Hodgkin's Lymphoma were more frequently observed in young adults, Non-Hodgkin's Lymphoma and Chronic Myeloid Leukaemia were more commonly encountered in older adults while Chronic Lymphocytic Leukaemia, Multiple Myeloma, Essential Thrombocythaemia and Polycythaemia Vera were seen more in older adults ,middle- aged and elderly patients. Prolymphocytic Leukaemia, Myelodysplastic Syndrome and Primary Myelofibrosis were found in the elderly only (Table 2).

Table 1: Frequency, Median Age at Diagnosis and Sex Distribution of the Study Population

S/No.	Diagnosis	Median age at Diagnosis (years)	Frequency n (%)		Total n (%)
			Male	Female	
1	Acute Lymphoblastic Leukaemia(ALL)	26	3(2.4)	1(0.8)	5(3.2)
2	Acute Myeloid Leukaemia(AML)	25	3(2.4)	2(1.5)	4(3.9)
3	Chronic Myeloid Leukaemia(CML)	42	9(7.1)	12(9.4)	21(16.5)
4	Chronic Lymphocytic Leukaemia(CLL)	57	10(7.9)	14(11.0)	24(18.9)
5	Prolymphocytic Leukaemia(PLL)	66	1(0.8)	-	1(0.8)
6	Hodgkins Lymphoma(HL)	30	8(6.3)	6(4.7)	14(11.0)
7	Non-Hodgkins Lymphoma(NHL)	47	18(14.2)	10(7.9)	28(22.1)
8	Multiple Myeloma(MM)	59	8(6.3)	6(4.7)	14(11.0)
9	Myelodysplastic Syndrome(MDS)	71	2(1.6)	2(1.6)	4(3.2)
10	Polycythaemia Vera(PV)	56	4(3.1)	4(3.1)	8(6.2)
11	Essential Thrombocythaemia(ET)	57	2(1.6)	-	2(1.6)
12	Primary Myelofibrosis(IpMF)	69	1(0.8)	1(0.8)	2(1.6)

Table 2: Age-specific distribution of Haematological Malignancies in UUTH

Age group (??)	AML n(%)	CML n(%)	ALL n(%)	CLL n(%)	NHL n(%)	HL n(%)	MM n(%)	MDS n(%)	PLL n(%)	IpMF n(%)	ET n(%)	PV n(%)	Total cases n(%)
20-29	4	3	3	-	4	6	-	-	-	-	-	-	20
30-39	-	4	-	-	7	5	-	-	-	-	-	-	16
40-49	1	9	1	1	8	-	5	-	-	-	-	-	25
50-59	-	2	-	13	1	1	2	-	-	-	2	7	28
60-69	-	2	-	7	4	2	5	1	1	2	-	1	25
70^{+}	-	1	-	3	4	-	2	3	-	-	-	-	13s
Total Cases	5	21	4	24	28	14	14	4	1	2	2	8	127

DISCUSSION

To our understanding, this is the pioneer work on the pattern of Haematological Malignancies in this environment. From our results, Malignant lymphomas are the most common Haematological Malignancies (33.1%) in Akwa Ibom State. Of this, NHL was the most prevalent accounting for 22.0% of the HM cases while HL constituted 11.0%. The median age at presentation of NHL was 47 years. This is similar to the work by Mohd[5] et al in Bangladesh in which a slightly higher median age of48 years was reported. However HL was observed to be more common in patients aged 20-29 and 30-39yrs. Similar pattern was also observed in India[6] and Southern Nigeria[7] . The high prevalence of lymphoma reported in our work corresponds to incidence rates in Europe, Africa and other parts of the world[7,8,9].

Omoti *et al.*[7] and Tenge *et al.*[10] in Niger-Delta area of Nigeria and Kenya respectively, also reported that lymphoma was the most frequent haematological malignancy in their studies Similarly, Khan et al[11] in a study of 922 patients with childhood cancers in Northern Pakistan, observed that lymphoma was the most common Haematological Malignancy in both sexes. A comparable study carried out in equatorial belt of Africa showed that lymphoma was among the top-ten tumours in the geographical region where pathogens and environmental factors have been recognized suggesting that they may play a crucial role in lymphomagenesis[12]. Bhurgri *et al.*[13] reported an increasing incidence and time trends in a population-based study conducted in Karachi. However, the incidence of lymphoma as observed in the Kuwait cancer control centre registry was said to have declined[14]. This variation in time trends may be due to varying genetic susceptibilities and exposure to environmental agents. Contemporary evidence suggests that factors and conditions that trigger either chronic antigenic stimulation and cytokine production coupled with persistent malarial infestation and Epstein-Barr virus infection (EBV) or immune suppression may provide a preferential ambiance for development of malignant lymphomas[15].

As true as the foregoing is, the increasing incidence rate of lymphoma may also be partly explained by improved healthcare services in the country engendering hitch-free patients' access to tertiary hospitals and the availability of robust diagnostic techniques vis-à-vis better histologic evaluation by Pathologists who play a pivotal role in diagnosis.

Previous studies indicate that incidence rates for leukaemia are higher among Caucasians compared to Blacks but recent reports reflect a lack of disparity in the incidence rates between the two races[8,9]. In our study, we observed a pattern of an increasing prevalence rate in the Chronic Leukaemias compared to the Acute Leukaemias. This increasing trend may be attributed to a number of factors: improved sentience on the part of the patients together with accessibility of Haematologists and well-equipped diagnostic facilities. Also, we have observed that the penchant for traditional remedies in lieu of orthodox therapies sustained and fuelled by ignorance, illiteracy, poverty, daunting socio-economic challenges and tenacious customs have been on the decline in the past years. Furthermore, coastal areas of Akwa Ibom (oil-producing state) is prone to environmental pollution from frequent oil spillages with their attendant health hazards. These areas may also serve as dumping grounds for industrial/radioactive wastes that emanate from neighbouring Rivers state.

The Chronic Leukaemias (36.2%) were the second most common HMs after the

Lymphomas in this study. Chronic Lymphocytic Leukaemia (CLL) was the most frequently encountered Chronic Leukaemia (18.9%) with a median age of 57 years and more females being afflicted than males. This is similar to the finding in Benin City,[3] a large urban centre in Southern rain forest area of Nigeria. The reason for the female preponderance could be related to the fact that some females are educationally, socially and economically empowered like their male counterparts and therefore are more likely to seek medical attention when the need arises. It may also be because there are more females than males in Nigeria as shown by the census figures.[16] CLL is the commonest Leukaemia in Western adults(25-30% of the all Leukaemias) with a median age of 70 years.[17] However, reports from Bangladesh and India revealed a lower median age of 60 years[5,18] Notable in our study was that the median age of patients at the time of presentation was similar to the Asian figure but younger than that reported in the American study. The observation of more CLL cases among the middle-aged persons in our series may be ascribed to the reduced population of the elderly in our environment as only few people in our population live up to 70 years and beyond. The reason for the disparity in the age incidence between our environment and the Western Societies is not far-fetched; the life expectancy in Nigeria is lower (53years) than the life expectancy in the United States (77.7years) and other developed countries[19].

Chronic Myeloid Leukaemia(CML) and Prolymphocytic leukaemia were the other chronic leukaemias recorded in this study .The latter is an extremely rare entity[3], little wonder we had only one case (0.8%). This is however inconsistent with the work reported by Omoti[7] *et al* in Benin City, Southern Nigeria where a frequency of 5.6% (n=22) was reported for PLL in their review of 391 haematological malignancies. CML was found to be less common than CLL in this study. This is in contrast to other studies in Africa[3,20]. CML accounts for 15% of adult Leukaemias in the West and males are affected approximately 1.5times as often as females. Male predominance has been documented in most studies[19,21,22]. However, in our study the reverse was the case. Its incidence is known to rise slowly with age to reach a median of about 60 years[23]. The median age of patients with CML in Nigeria and other African countries with a similar demographic pattern is 38 years[24]. In our study we reported a median age of 42years. This disparity could be partly due to the difference in sample size.

Acute leukaemias including Acute Myeloid Leukaemia (AML) and Acute Lymphoblastic Leukaemia (ALL) reported in our study accounted for 3.9% and 3.1% of the HM cases, respectively. Adult AML are frequently reported in North America, Europe and Oceania, while in Asia and Latin America the cases are few and far between[2,8,17,25]. AML is the commonest Acute Leukaemia in adults in Western Countries and accounts for 29% of Leukaemias in US[24]. Its incidence is also known to increase slowly with age(median 65 years).In our study, we observed that most of the AML cases occurred in persons aged 20-29 years (Table 2). The median age at presentation (25 years) in our study is lower than in Western countries[24] but similar to that in India (30 years)[26]. The lower life expectancies prevailing in both countries (Nigeria & India) may likely be a plausible reason for the lower age incidence recorded in both studies. ALL affects people of all ages but it displays a bimodal incidence peak at ages less than 20 years and over 50 years[24]. In our study, we could not demonstrate the former due to the exclusion of that age group but we observed that 75% of the ALL patients whom we managed were young adults (20-29yrs) with a median age of 26 years (tables 1 & 2). However, approximately 60% of the cases in Western Societies are diagnosed in children younger than 20 years of age (overall median age of 14 years)[24].

The median age at presentation of Multiple Myeloma in this study was 59 years. This is younger than previously reported in some studies especially in the Western hemisphere where it has been widely reported that it affects primarily the elderly(median 66 years)[24,25,27]. However our finding is in consonance with the observations of other investigators in Bangladesh[5] and India, [26] who found the median ages at diagnosis to be 55years and 55-56 years, respectively. This is also similar to a study done in Benin City, Nigeria where a median age of 54 years was obtained, and work done by Salawu[28] *et al.*, in Ile-Ife in which they got a slightly higher median of 60 years. The reason for the disparity between the Western studies and ours may be hinged on the interaction of a medley of factors such as genetic, racial, socio-economic and other environmental influences.

Myelodysplastic Syndrome (MDS) is relatively a condition affecting the elderly. In our work, MDS constituted 3.1% of the HMs and 100% of the patients were elderly (median age 69 years). This is similar to the studies done in southern Nigeria[3] and Western countries[25]. However, our finding was in dissonance with a study carried out in India where a much lower median age of 46.1 was reported[29]. However, Mohd[5] *et al*. in Bangladesh in their review of 225 patients with Haematological Malignancies reported that MDS accounted for 4.5% of HMs and 76.9% of the patients were older than 50 years of age (median age 57 years). This observation agrees with a study in Japan[30]but is in disagreement with our finding. The disparity in the age incidence between our region and the Asian countries could be partly due to a broad range of genetic polymorphisms, environmental and racial factors as well as other demographic variables.

The prevalence of non-Leukaemic Myeloproliferative Neoplasms (PV,ET and I°MF) was low in our report. This observation is consistent with reports from earlier studies. [19,31,32,33] Polycythaemia Vera and Essential Thrombocythaemia affected significantly the middle-aged patients while primary Myelofibrosis was more prevalent in the elderly. This observation is also in agreement with previous reports.[19,31,32,33,34] PV was commoner than I°MF in this study. This finding is however at variance with what was reported in Benin City[3], Southern Nigeria. Variation in sample size between the two studies may account for this disparity.

Multiple studies [8-11,13,14] have shown that Haematological Malignancies are gender-skew whiffed, frequently affecting males more than females. Our work however revealed a varying picture. The prevalence of CLL and CML in women was 1.4 and 1.3 times respectively, that in men. Equal percentages were recorded between the sexes in MDS, PV and I°MF) while male predominance was observed for the other malignancies.

The reasons for the well-known phenomenon that HM incidence is generally higher in men than women are unclear but may include hormonal effects, unstable genetic apparatus with attendant susceptibility to mutational changes, higher prevalence of smoking and heavier alcohol consumption, and higher environmental-and occupational-related risk factor exposure in men compared to women[13,14].

CONCLUSION

This study has shown that Haematological Malignancies are not uncommon in our environment. The distribution of the various HMs in the study is similar to that reported within and outside Nigeria. The lower number of cases observed for most of the malignancies may be a reflection of the lesser population of Uyo when compared to the bigger cities we correlated our findings with. This study points to a number of issues that are worthy of further research particularly when disparities observed between our work and studies done elsewhere are taken into cognizance. Further large scale studies are necessary therefore to identify the potential risk factors, define the biology, molecular genetics and clinical outcome of these malignancies in this region.

Note: Make sure all abbreviated names of journals in your ref. section carry the std abbreviationsas stipulated by their publishers.

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