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ADULT MALIGNANT LYMPHOMAS IN UNIVERSITY OF BENIN TEACHING HOSPITAL, BENIN CITY, NIGERIA- INCIDENCE AND SURVIVAL.

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SUMMARY

Background: The occurrence of malignant lymphomas is worldwide and its incidence has being increasing, ranked 12th among all cancers worldwide. We aim to determine the incidence and survival of the lymphoma patients in the Niger Delta region of Nigeria.

Study design: A study of 205 cases of lymphoma patients from 1993 to 2003. One-year survival was calculated using simple percentage of those alive and those that died before 1year of diagnosis.

Results: A total of 205 patients aged 18-72years were studied. Non-Hodgkin's Lymphoma (NHL) was the most frequent (83%) while Hodgkin's Lymphoma (HL) had an incidence of 17%. The 1year survival for patients with NHL and HL was 35.3% and 42.9% respectively. We found a strong association between haemoglobin (Hb) and white blood cell count (WBC) at presentation and 1year survival in NHL patients (P=0.0003;P=0.0001) and HL patients (P=0.0001;P=0.0104) respectively. Also, the mean Erythrocyte sedimentation rate (ESR) for lymphoma patients alive at 1year was significantly lower than those that died within 1year (P=0.0001). Duration of illness before presentation was found to influence 1year survival.

Conclusion: We conclude that NHL was the most common of the lymphoma seen in young adulthood in the Niger Delta region of Nigeria. A positive correlation between survival and duration of illness at presentation and haematological counts was found. The 1year survival is still very poor and this may not be unconnected with late presentation and other strong limiting factors.

Key words: Lymphoma; incidence; survival

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INTRODUCTION

Lymphomas are a heterogenous group of malignancies of B cells or T cells that usually originate in the lymph nodes but may originate in any organ of the body. The occurrence of lymphoma is worldwide, Non-Hodgkin's lymphoma (NHL) being the fifth most common cancer in United States and ranked 12th among all cancers worldwide.[1,2] Although lymphadenopathy in Africans is often inflammatory in origin,[3] lymphomas also constitute an important cause of lymphadenopathy in addition to increasing morbidity and mortality.[4] Hence, there are considerable differences in the recorded incidence in different geographic areas. Previous studies by Thomas et al[5] and Okpalla et al[6] in Ibadan, Nigeria highlighted the immunohistologic aspects of NHL while Adelusola et al in Ile-Ife highlighted patterns of lymphomas.[7]

In the last two decades, the incidence and survival period of lymphoma patients in the Niger Delta region of Nigeria known for its petrochemical industries has not been studied and also bearing in mind the increasing Westernized mode of behavior. We therefore aim to determine the incidence of the various types of lymphomas seen in this region and the epidemiology of the various lymphomas.

PATIENTS AND METHODS

All cases of adult lymphomas seen at the University of Benin Teaching Hospital (UBTH), a major referral center serving the Niger Delta region of Nigeria between December 1993 and November 2003 were

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reviewed. Clinical and demographic information of. 205 patients who required and did not require hospitalization were obtained from case files. Thses Include the age, sex, martial status, occupation and educational status including the duration of symptoms.Eligible patients were men and women above 18 years with accessible lymph nodes or other sites. Patients with lymphadenopathy due to metastatic carcinoma and those with incomplete biodata were excluded from the analysis.Diagnosis was established based on tissue samples that were studied by histological examination of a surgical biopsy from the lymph node or other accessible sites for biopsy by the Morbid Anatomy department of the same institution. NHL was classified according to the International Working Formulation (IWF).[8] Also, blood samples were collected for haematological indices that were done using automated coulter counter. The human immunodeficiency virus (HIV) status of the patients was noted and the positive ones confirmed by immunoblot test. One-year survival was calculated using simple percentage of those alive and those that died before 1 year of diagnosis

Data Analysis- The data obtained from this study was analysed using the instat package system. The statistical methods applied include frequency counts and cross tabulations using Yates correction whenever necessary. The haematological indices were estimated using the Mann-Whitney and one-way analysis of variance (ANOVA) for significant association with the various types of lymphomas.

RESULTS

A total of 205 patients aged 18-72years with a diagnosis of either NHL or HL was established based on histological examination of an excised lymph node biopsy over a ten-year period (1993-2003). This comprises of 135 females (65.9%) and 70 males (34.1%) with a male-to-female ratio of 1:1.9. A total of 395 haematological malignancies were seen during the study period giving a proportion of 51.9% of lymphomas. Among the lymphomas, NHL was themost frequent with an incidence of 83% while HL had an incidence of 17% (table1). According to the IWF classification, the intermediate (41.2%) and high grade (29.4%) lymphomas were the commonest histologic types. A total of three patients (1.5%), all NHL patients were HIV seropositive. The age distributions at presentation for the lymphomas are also shown in table 1. Lymphoma incidence was low after 70years of age in this study.The mean haematological indices for the lymphomas at presentation are shown in table 2. There was a statistically significant difference in the haematological values for the lymphomas at mainly with the 'B' symptoms (unexplained fever >38%, night sweats and loss of >10% body weight within 6months preceding diagnosis), anaemic symptoms and cervical lymhadenopathy. The most commonly used chemotherapeutic regimen was CHOP (cyclophosphamide 650mg/m^2 days 1 and 8, doxorubicin 45mg/m^2 days 1 and 8, vincristine 1.4mg/m^2 days 1 and 8 and prednisolone 100mg/day for days 1-7).

The 1year survival for patients with NHL and HL was 35.3% and 42.9% respectively. The haematological values at presentation were found to influence the outcome of survival after chemotherapy was started (table3). We found a strong association between haemoglobin (Hb) and white blood cell count (WBC) at presentation and 1year survival in NHL patients (P=0.0001; P=0.0003) and HL patients (P=0.0001; P=0.0104) respectively. Also, the mean erythrocyte sedimentation rate (ESR) for lymphoma patients alive at 1year was significantly lower than those that died within 1year (P=0.0001). The duration of illness before presentation was also found to influence the 1year survival. The average duration of illness before presentation for those alive at 1year for NHL and HL was 8.75 and 6.53 months while for those that died before 1 year was 14.8 and 11.9 months respectively.

DISCUSSION

The occurrence of lymphoma in previous studies has shown that it causes many deaths worldwide and its incidence has increased in many parts of the world in recent decades.[9] The increasing incidence of NHL is poorly understood but improved diagnostic techniques, chronic antigenic stimulation, effects of human immunodeficiency virus (HIV) Epidemic and immunosuppressive therapies accounts for only one third of the increase.[10] Recent work suggest that common exposures which influence immune Competence, albeit at a much weaker level may also be a risk factor including other attributable factors responsible for the increasing incidence.[11]

The predominance of NHL (83%) over HL (17%) observed in this study agrees with previous findings of Okpalla et al,[6] Adelusola et al,[7] in Nigeria and other studies in the diaspora[1,2] where the incidence of HL is constantly lower than that of NHL. The mean age of NHL patients was 41.4years and for HL it was 32.4years. The low incidence of lymphomas after the age of 70years is because only few people in our population live beyond this age.This also supports the epidemiological and Biostatistre programme in Bethesda, USA where analysis by age group revealed a substantial decrease in incidence at older age and increase among young

Table 1: **The incidence, sex and age distribution of Lymphomas at the time of diagnosis.**

Variables	Types of Lymphomas NHL n=170			HL n=35		
Incidence (%)	83			17		
Sex (M:F)	60:110			10: 25		
Age (years)	M	F	Total	M	F	Total
18-19	5	10	15	0	5	5
20-29	20	10	30	5	5	10
30-39	20	25	45	5	10	15
40-49	10	10	20	0	0	0
50-59	0	35	35	0	4	4
60-69	0	20	20	0	0	0
>70	1	4	5	0	1	1

Table 2: **Haematolological indices of the lymphomas at the time of diagnosis.**

	Haemoglobin (g/dl) ±SEM	*Total leucocyte count ($x10^9$/l) ±SEM*	*Platelet count ($x10^9$/l) ±SEM*	*ESR (mm/hr)*
NHL	9.3(±2.3)	10(±6.5)	262(±224)	67.4(±41)
HL	8.0(±2.1)	7(±3.5)	212(±76)	69.0(±40)

Table3: **The mean haematological counts in patients with lymphomas at presentation and outcome at 1year of therapy.**

	Outcome Alive	Dead	P value
NHL	(n=60)	(n=30)	
Hb(g/dl)	10.8(±1.9)	8.5(±1.6)	0.0001
WBC($x10^9$/l)	8.4(±5.0)	14.0(±6.0)	0.0003
Platelet count ($x10^9$/l)	316.0(±203)	273.0(±291)	ns
ESR(mm/hr)	44.7(±34)	96.8(±43)	0.0001
HL	(n=15)	(n=20)	
Hb(g/dl)	10.4(±1.3)	6.4(±0.6)	0.0001
WBC ($x10^9$/l)	3.9(±1.7)	6.2(±3.2)	0.0104
Platelet count ($x10^9$/l)	187.0(±5.2)	206(±9.9)	ns
ESR (mm/hr)	51.1(±23)	116.9(±22)	0.0001

*NHL-Non-Hodgkin's Lymphoma; HL-Hodgkin's Lymphoma.
*ns-not significant

Adults in some industrialized countries.[12] Less developed countries continue to show high rates in young adults.[12]

That lymphoma is frequent in males has been reported[2] but there was a female dominance in this study. The characteristic bimodal age incidence found in the Western world was also seen: one peak in

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. Although NHL can occur at any age, the incidence rises considerably with age while in HL the incidence rises abruptly in adolescence and peaks in the third decade as shown in this study. This age incidence observed might be due to the interplay of both environmental and genetic factors, as has been suggested by family and population studies in HL.[13] In this study, majority of the patients (73.2%) at the time of diagnosis had an Hb level of less than 10g/dl. This is not surprising because anaemia has been known to be a common finding in haematological malignancies including

Lymphoma among our patients. The probability of occurrence of anaemia in cancer patients depends on well-defined number of variables.[14] These include the type, stage and duration of the malignancy, intensity of treatment protocol and the occurrence of intercurrent infection.[14] Also, most of the patients (59%) presented with elevated ESR of greater than 50mm/1hour at the time of diagnosis. Elevation of the ESR is most common in advanced disease and correlates with constitutional symptoms.

A considerable number of the patients presented with the expected haematological counts. There was a statistically significant difference between the types of lymphomas and the various haematological counts studied (P<0.0001). Patients with lower Hb values and higher WBC had a significantly lower remission rate with a poor outcome. This was shown in the strong association between the Hb and WBC at presentation and 1year survival in NHL patients (P=0.0001 and P=0.0003) and HL patients (P=0.0001 and P=0.0104) respectively. The ESR for the lymphoma patients alive at 1year was significantly lower than those that died within 1year (P=0.0001). This reveals the aggressive nature of the disease, as elevated ESR is commonly associated with advanced disease. Also, the incidence of HIV among the lymphoma patients in this study was 1.5%, and when compared to the 3.5% HIV seroprevalence in the general population of our locale[15], further shows the association and effects of HIV and lymphoma.[10]

We also found in this study that the overall 1year survival for patients with NHL and HL was 35.3% and 42.9% respectively. The 5year survival could not be estimated, as most of the patients did not live up to this number of years as well as poor follow up. The poor survival time observed in our lymphoma patients probably underscores the lack of access to advanced/high-tech therapy as seen in the technologically advanced world. Many of the patients are unable to afford the high cost of treatment. Many fail to turn-up for treatment after diagnosis only to reappear pre-terminally. Other limiting factors responsible for the poor survival rate in our environment include illiteracy and ignorance, poor economy, absence of a functioning national health insurance scheme and often times lack of blood components support even in some tertiary health center.

This poor survival rate was also found to be similar to the average survival time of 344 days in Dakar, Senegal where only 4 patients (37%) and 2 patients (1.8%) out of 107 cases were alive at 3years and 5years respectively.[16] Also, in a Singaporean institution the 1year survival for B cell lymphoma was found to be 42%.[17]

The average duration of illness was found to significantly influence the survival time in each patient as already been documented in this study. The shorter the duration of illness before presentation the better the outcome in chemotherapy-treated patients. This further emphasizes that early presentation and prompt diagnosis with treatment will improve the survival outcome of our patients.

In conclusion, we found that NHL is the most common of the malignant lymphomas seen in the Niger Delta region of Nigeria and this agrees with other studies. We also found a positive correlation between survival and duration of illness at presentation and between the haematological indices. The 1year survival is still very poor and this may not be unconnected with late presentation and other strong limiting factors.

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