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A prospective study of childhood malignancy in Enugu, Eastern Nigeria (2011-2013)

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Abstract: *Background:* The review of childhood cancers has most times been done in retrospect by most authors and this has its inherent limitations. Most reviews in Africa show that lymphomas are the commonest malignancies of childhood while acute leukemia ranks much lower.

Objective: To do a prospective audit of the pattern of childhood malignancies in Enugu, southeast, Nigeria.

Methods: Demographic and medical information on patients aged 1 -17 years admitted over a 36 month period for malignancies was obtained and recorded in pre-tested interviewed administered questionnaire. Data was analyzed using spss, 15 (Chicago II, USA) software.

Results: A total of 103 patients were admitted with diagnosis of

cancer with a male: female ratio of 1.3: 1 and median age of 7 years. Majority (63.1%) of patients were from the rural area with low socio-economic background. There was a decline in the incidence of childhood lymphoma from 40% about 25 years ago to 34% in the present study. Although lymphoma remains the leading childhood malignancy, sarcomas and acute leukemia rather than renal and eye tumors ranked second and third respectively among childhood cancers in the center.

Conclusion: There is a reversing trend in the pattern of malignancies of childhood in Enugu as acute leukemia becomes one of the leading malignancies of children.

Key words: childhood, malignancy, lymphomas, leukaemia

Introduction

Childhood cancer is a leading cause of death in developed countries of the world, but ranks lower than infections and malnutrition in the etiology of childhood mortality in Sub Saharan Africa¹. The pattern of childhood cancer is almost the same in America and Europe with leukemia and brain tumors predominating^{2,3}. Although some studies^{4,5,6} show that lymphomas are more common in developing countries, the true pattern of childhood cancer may not be available in those countries (due to improper record keeping, lack of diagnostic facilities, belief systems and non-presentation to the health facility). A previous study done by Onwasigwe et al from our center 12 years ago also showed that lymphoma constituted about 40% of all childhood malignancies with Burkitt's lymphoma constituting over 60% of the lymphomas while leukemia was the fifth commonest childhood malignancy⁷. A similar pattern with lymphoma as the predominant childhood malignancy was also noted in Kano, Northwestern and Ife, Southwestern Nigeria by Shehu et al⁸ in 2012.

Most of these studies on the pattern of childhood malignancies are retrospective and the peculiar limitation of

retrospective studies may affect the result. The present study is prospective and aims to identify any change in the pattern and socio-demographic characteristics of patients with childhood malignancies at The University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu, Southeast Nigeria.

Subjects and Methods

The study was conducted in the pediatric medical wards of the University of Nigeria Teaching Hospital, Ituku-Ozalla, Enugu over a three year period (2011- 2013). It was a cohort study of children aged 1- 17 years with a histologically confirmed diagnosis of cancer and was approved by the hospital Health Research and Ethics committee with informed consent obtained from the patients' caregivers. The Hospital has facilities for biopsy, histopathological and cytological investigations as well as well-equipped laboratory for haematological, biochemical and microbiological investigations. Treatment facilities available include chemotherapy, surgery, radiotherapy and palliative care. Information regarding patient's age, gender, socioeconomic class, place of

residence, symptoms, type of cancer and its anatomical location was obtained using investigator administered questionnaire. Place of residence was categorized into urban or rural communities. Rural community refers to a community where families reside in relatively small areas and their main occupation and interests are farming and fishing while urban community is large with people engaged in varied occupations such as manufacturing, commerce, professional works such as law, medicine and engineering; or government jobs. Socio-economic classification was done using Ogunlesi et al classification⁹. Socioeconomic classification by Ogunlesi et al is based on the highest educational attainment, the occupation and income of parents and is classified 1 to 5 with class 1 being the highest level.

Statistical analysis

Data was analyzed using a combination of statistical software (SPSS 15, Graphpad prism 5). Categorical variables were presented in form of tables and graphs while discrete variables were presented as means or medians. Also frequencies of categorical variables were compared using chi square while means of discrete variables were compared using Student's t-test. Level of significance was set at $p < 0.05$.

Result

A total of 103 patients were admitted with diagnosis of cancer over the study period. The patients' median age was 7 years (range: 1-17) with a male: female ratio of 1.3:1. Majority (56.3%) of the affected children belonged to the lower socioeconomic class. Table 1 shows the general characteristics of the patients.

Gender	Male	Female
	58(56.3%)	45(43.7%)
Age	<5 36(34.9%)	5-10 38(36.9%)
		11-15 24(23.3%)
		>15 years 5(4.9%)
Socio-economic class	I 7(6.8%)	II 9(8.7%)
		III 32(31.1%)
		IV 36(35%)
		V 19(18.4%)
Place of domicile	Rural 38(36.9%)	Urban 65(63.1%)

In the study, sixty five (63.1%) of the patients admitted with cancer were from the rural area compared with 38 (36.9%) from the urban area. The pattern of childhood malignancies over the period was shown in table 2. It showed that lymphoma was the most prevalent (34.0%), followed by the sarcomas (17.5%), acute leukemia (15.5%) and renal tumors (13.6%).

Burkitt's lymphoma constituted 48.6% of the lymphomas and 16.5% of all malignancies among the patients. The age of patients with this malignancy ranged from 4-14 years with peak and mean ages of 5 and 7.25 (± 2.23) years respectively. Eight (47.1%) of the patients were males while nine (52.9%) were females with male: female ratio of 0.9: 1

Sixteen (94.1%) of the 17 patients with Burkitt's lymphoma were from the rural area and 88.2% were from the low socioeconomic class. 41.2% of the patients presented with jaw mass, 52.9% with intra-abdominal mass while 5.9% presented with paraplegia and intra-abdominal mass.

Hodgkin's disease constituted 22.8% of the lymphomas and 7.8% of childhood malignancies. All the patients were males with age range 8-16 years and peak age of 13 years. 62.5% were from the urban area while 37.5% were from rural area. 37.5% each were from the middle and lower socioeconomic group while 25.0% were from the high socioeconomic group. Six (75.0%) presented as neck mass while one (12.5%) each presented as intra-abdominal and thigh masses. Ten (28.6%) of the lymphomas was non-Hodgkin's lymphoma and made up 9.7% of all the malignancies. Most (80.0%) of the patients were ten years and above with a male: female ratio of 1.5: 1 and majority (80.0%) from the rural area. Four (40%) of the NHL presented as intra-abdominal mass, five as head and neck masses while one case presented as breast mass.

Eighteen patients (17.5%) were diagnosed of sarcoma of which rhabdomyosarcoma constituted the majority (66.7%). Other sarcomas included osteosarcoma, angiosarcoma, fibrosarcoma, Kaposi sarcoma and embryonal liver cell sarcoma.

Among the acute leukemia, 68.8% was acute lymphoblastic leukemia while 31.2% was acute myeloid leukemia. The mean age of the patients was 9.8 (3.7) years with age range of 4 to 17 years. The male: female ratio was 1.3:1. Ten (62.5%) resided in the urban area while 37.5% resided in the rural area and majority (68.8) belonged to the low socioeconomic class. In terms of symptoms at presentation, (14/16) presented with fever, 4 (25%) with bleeding disorder, 3 (19.0%) with bone and or body pains, one with bilateral proptosis of the eyes, one with hearing impairment, 4 (25%) with head and neck masses and one with intra-abdominal mass. All the patients were pale on presentation.

Renal tumor was the third commonest tumor (13.6%), affecting children 1to 5 years of age with peak age incidence of 2-3 years and male: female ratio of 0.6: 1. Majority (92.8%) who had it were from the middle and low socioeconomic group. Four (30.8%) of the patients had elevated blood pressure that required anti-hypertensive medication.

The fourth commonest tumor was retinoblastoma (12.6%). It affected mostly the under five year olds with peak age incidence 2-3 years. Seven (53.8%) of the 13 subjects were females with a M:F of 1: 0.9 Majority (69.2%) of the affected patients resided in the rural area and 61.5% were of low socioeconomic class while 38.5% were of middle class. Majority (69.2%) of the patients presented with unilateral orbital mass, 23.1% (3/13) presented primarily with leukocoria while one patient presented with multiple scalp masses and bilateral orbital mass.

Rhabdomyosarcoma, the fifth commonest tumor

(11.7%) in this study shows a male predominance (72.7%) and affected mostly patients from the low socioeconomic class (81.8%). However, the age group varied widely from two to 16 years. Nine (75.0%) of the twelve subjects presented with head and neck masses, 16.7% as intra-abdominal masses and 8.3% as mass on the anterior chest wall.

Other tumors included neuroblastoma 2(1.9%), osteosarcoma 2(1.9%), chronic myeloid leukemia 2(1.9%), reactive sinus hyperplasia with generalized lymphadenopathy 2(1.9%) and germinoma, Kaposi sarcoma, fibrosarcoma, angiosarcoma, embryonal liver cell sarcoma 1 (0.97% each).

Among 21 patients whose tumors were staged, 15 (71.4%) presented with stage 4 disease and only one with stage 1 (4.7%) disease.

Table 2: Frequency of childhood malignancies

Tumor	N (103)	%
Lymphomas	35	34.0
BL	17	48.6
NHL	10	28.6
HD	8	22.8
Acute leukemia	16	15.5
ALL	11	68.8
AML	5	31.2
Renal tumors	14	13.6
Retinoblastoma	13	12.6
Rhabdomyosarcoma	12	11.7
Others	13	12.6

Others: angiosarcoma (1), chronic myeloid leukaemia (2), embryonal liver sarcoma (1), germinoma (1), fibrosarcoma (1), Kaposi sarcoma (1), neuroblastoma (2), osteosarcoma (2), sinus histiocytosis with generalized lymphadenopathy (2)
BL= Burkitt's lymphoma; NHL= Non-Hodgkin's lymphoma; HD= Hodgkin's disease

Discussion

The study showed sex predilection to cancer with a male to female ratio of 1.3:1. This is comparable with 1.4:1 documented in Ile Ife by Shehu et al⁸. However, the ratio was less than 2.4:1 noted in Northern Nigeria by Shehu et al as well as 1.8:1 from central Sudan¹⁰. This difference may be related to socio economic and cultural factors as it has been observed that there is low cancer registration among girls in countries or regions of the world with low female education rates and poor health system indicators¹¹.

The pattern of childhood tumors in Africa has been characterized by high prevalence of lymphoma and low prevalence of leukemia^{7,12}. This is in contrast to the pattern in developed parts of the world where leukemia predominates^{13,14}. In the present study, although lymphoma is still more prevalent, it seems to be on a decline with prevalence of 34%, in contrast to about 40% reported earlier by Obioha et al¹⁵ from our center about 25 years ago and 42.8% by Huda et al in Gezira, Central Sudan¹⁰. Specifically, Burkitt's lymphoma was noticed to be decreasing in incidence as it constituted 16.5% of the childhood malignancies when compared with 19.4%

by Olesina et al in Ibadan and 19.6% by Tijani et al in Lagos, Western Nigeria^{16,17}. This decline in the incidence of lymphoma may be associated with improvement in general living condition of the people as well as improvement in the control of malaria; as poor living conditions and high incidence of malaria and Epstein-Barr virus infection are known risk factors for the occurrence of lymphoma, especially Burkitt's lymphoma¹⁸. There is also a reversal of sex incidence of Burkitt lymphoma from a male: female ratio of about 2:1 to 0.9:1¹⁹. The reason for this reversal may be due to increasing awareness of the people on the need to pay equal attention to the education and health care of their male and female children which may have increased the cancer registration rate of girls.

The sarcomas constituted the second commonest childhood malignancy (17.5%) in this study and this collaborated with the study by Ocheni et al⁶ (15.2%) in 2005. The rising relative frequency as previously documented by Ocheni et al²⁰ is maintained with rhabdomyosarcoma remaining the most common childhood sarcoma.

It is noteworthy that leukemia which has hitherto been reported in many studies to have low incidence in Africa is the third commonest childhood malignancy in the present study displacing renal tumor and retinoblastoma in the trend^{21,22}. Onwasigwe and colleagues had earlier reported leukemia as the fifth commonest childhood malignancy in Enugu in 2002 while Ocheni et al from same centre in 2005 and Ochicha et al in Kano, Northern Nigeria in 2012 reported leukemia to be the fourth and third commonest childhood malignancy respectively^{7,6,23}. This shows that in our study centre, leukemia rose from being fifth commonest malignancy in 1989, to fourth in 2005 and now third. Tables 3 & 4 compares studies of childhood malignancies in the centre from 1976 to present study period and it is noted that there is an increasing frequencies of sarcomas and acute leukemia rising from 7.6% in 2005 to 15.5% in the current study period. It is also noted that the annual cancer incidence has been decreasing from the first study to the fourth with a rise from 14.4% observed by Ocheni et al⁶ in the 1999-2004 review to 34.3% in the present study. The present increase in cancer incidence may be because of improved diagnostic techniques or because the current study was prospective and cases of cancer were actually looked out for. It is also observed that the sex incidence has been relatively stable.

Table 3: Comparison of annual incidence of childhood malignancies from 1976-2013

Author	Year of study	Annual Incidence	Age incidence	Peak age	M:F ratio
Agugua	1976-1980	116.4			
Obioha et al	1978-1982	51.4			
Onwasigwe	1989-1998	31.3			1.3
Ocheni et al	1999-2004	14.4			1.5
Current	2011-2013	34.3	1-17	5-10	1.3

Table 4: Comparison of relative frequencies of childhood malignancies (1976-2013)

Type of cancer	Agugua (1976-1980)	Frequency (%) Obioha (1978-1982)	Onwasigwe (1989-1998)	Ocheni (1999-2004)	Current (2011-2013)
All lymphoma	49.4	39.3	38.3	41.2	34.0
Burkitt's lymphoma	37	26.5	25.3	24.1	16.5
Acute Leukemia	5.5	12.9	8.6	7.6	15.5
Renal tumour	5.6	3.0	1.9	5.1	13.5
Retinoblastoma	2.9	6.2	12.1	7.6	12.6
Sarcomas	10.4	4.3	14.7	15.2	17.5

The rising incidence of leukemia may be linked with improved diagnostic techniques and exposure to high tension electricity cables due to rapid electrification of urban centers²⁴. Report by Draper et al²⁵ in England and Wales noted an increased risk for development of childhood leukemia in children who were delivered within 200 meters from power lines. Other studies from Canada²⁶ and Sweden²⁷ also found increased risks for childhood leukemia in children residing close to power transmission lines. However, some other studies from Denmark²⁸, Norway²⁹ and United States³⁰ did not show increased risk for childhood leukemia in children living near high-voltage power lines. Most affected patients in this study resided in the urban area. Also similar to the study by Huda et al in Central Sudan. Leukemia affected mostly children above 5 years in our centre unlike in America and Europe where most affected children are less than five years^{10,31}.

The renal tumors and retinoblastoma remain disease of the under five children (because they are embryonal tumours), affecting mostly children of low socioeconomic class. However, it is noted to be affecting more females than males unlike in western countries of the world where the sex incidence is similar³¹. The reason for this apparent tilt towards female gender preference may need to be authenticated by further studies.

Among patients whose disease was staged, majority presented at an advanced stage and this has been the pattern in most parts of Africa³². Advanced stage disease is usually as a result of delay in presentation to cancer treatment centre due to parents or health system delay. Parents may delay to present their wards because of misconception (either cultural or religious) about the disease or due to financial constraint while the health system may delay due to poor referral services or lack of diagnostic facilities. Delay may also be due to intrinsic characteristics of tumor itself (such as slow growth or absence of systemic symptoms) which will definitely culminate in delay in diagnosis and poor prognostication³³. In conclusion, although lymphomas remain the commonest childhood malignancy in Enugu, the prevalence seems to be on the decline with an increasing incidence of sarcomas and acute leukemia and this may be related to increasing urbanization and more inclination to Western life style. In general, males are more affected by cancer with majority of the patients from the rural area and of low socio-economic status as well as presentation with advanced stage disease.

Authors contributions

Conception and design of study by IJ and AN, data collection by OU, data analysis and writing of manuscript by BF. All authors read and approved the final manuscript.

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