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Pattern of childhood and adolescent malignancies at a tertiary health institution in South-east Nigeria : A ten year study

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Abstract: *Background:* Cancer remains a major cause of death in children and adolescents, and differs in adults in nature, distribution and prognosis[1]. A culture of case documentation is lacking in our environment and many cases go unreported.
Study objectives: To document the pattern of childhood and adolescent malignancies at a tertiary health institution in south-east Nigeria over a ten year period (January 2004 to December 2013)
Methodology: Details of all children and adolescents aged 18 years and below treated for malignancy were extracted from the cancer registry and the records unit of the histopathology department for the period beginning at January 2004 to December 2013 at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Nigeria. Information retrieved was verified against the hospital admission register, as well as the medical and histopathology records for all cancer patients over the period of interest.
Results: Eighty-five cases of childhood and adolescent malignancy were treated at NAUTH, Nnewi between January2004 and December 2013. Median age of the study population was 9years, with a range of 0.1–18years, more males (56.50%) than females (43.50%). Commonest tumours were the Lymphomas (11.76%) comprising Non-Hodgkin's lymphoma (80%), Hodgkin's lymphoma (10%) and Large-cell lymphoma (10%), the Leukaemias (11.76%) comprising Acute myeloblastic leukaemia (80%) and Acute lymphoblastic leukaemia (20%). Others were Rhabdomyosarcoma (11.76%), Nephroblastoma (11.76%), Retinoblastoma (5.88%), Ovarian tumours (4.71%), the Soft tissue sarcomas-excluding rhabdomyosarcoma (3.53%) and Osteogenic sarcoma (3.35%)'.
Conclusion: Study findings suggest that lymphoma, leukaemia, rhabdomyosarcoma and nephroblastoma are the commonest childhood and adolescent malignancies in south-east Nigeria.

Keywords: Childhood, Adolescent, Malignancy

Introduction

There is significant worldwide variation in the reported incidence of childhood cancer, which ranges from 80 to 150 per million children[2,3]. Also put at 1.0 – 2.5 per thousand children[4], childhood and adolescent cancers constitute approximately one percent of all cancers[5]. Annual number of new cases of childhood cancer reportedly exceeds 200,000 worldwide, with over 80percent of these occurring in the developing world[1]. Cancer remains a major cause of death in children and adolescents, and differs in adults in nature, distribution and

prognosis[1]. Children and adolescents in developing nations are afflicted by malignancies in addition to the perennial problems of infectious diseases and malnutrition. Data from Nigeria suggest that cancers in children constitute a small proportion of total admissions in paediatric wards[6]. Also, there are observable differences in the incidence of childhood cancer between northern and southern Nigeria, with higher incidence documented in the south[7, 8]. Study findings from Kenya, Tanzaniaand Ghana put childhood malignancies at 0.5 to 2% of overall malignancies[8].

Linet et al (1999)[9] reported leukaemia and CNS tumours as the commonest childhood malignancies in the United States, and together with skin cancers and retinoblastoma have shown further increase in prevalence over a 20 year period (1975-1995). On the contrary, lymphomas showed a downward trend in prevalence during the same period. Similarly, a study report from the United Kingdom[10] indicated a high prevalence of leukaemia compared with other childhood malignancies for Asian and Caucasian groups. However, a report[11] from a hospital based study done in northern and south-west Nigeria put lymphomas as the commonest childhood malignancy in both regions of the country, followed in northern Nigeria by retinoblastoma, nephroblastoma and leukaemia in descending order. In south-west Nigeria the prevalence of leukaemia was higher than that of retinoblastoma[11]. Also, Obioha et al[7] reported that lymphoma constituted nearly 40% of total cases of childhood malignancy in eastern Nigeria, followed by wilm's tumour, leukaemia and CNS tumours in descending order. A high incidence of lymphoma has been reportedly associated with poor living standards[7]. Also, childhood cancer, especially leukaemia which is prevalent in high income countries reportedly emerges as an important cause of morbidity with improvement in socio-economic conditions[12, 13]. This is so when infectious diseases and parasitic conditions are brought under control[12, 13].

In high income countries, improvement in the survival for children with cancer has been documented (75 - 80% long term survival), and is considered one of the great medical achievements of the last 50 years[5]. However, over eighty percent of cases of childhood malignancy live in low to middle income countries were survival for childhood cancer ranges from ten to thirty percent. In developing nations, an estimated 100,000 children die each year from malignancies, with no chance of a cure, adequate pain relief or other supportive care[2,3]. Poor outcome in low income countries may be due to late detection, misdiagnosis, poverty, non-availability of drugs, co-morbidities, refusal or abandonment of treatment sometimes due to superstition, as well aspoorly equipped health facilities[4,6,11]. A culture of case documentation is lacking in many developing countries and several cases go unreported[1]. Also, various environmental factors negatively impact on accurate documentation of childhood and adolescent malignancies, such as parental cultural practices, the traditional belief system, influence from religious bodies, and economic considerations. These influence parents of affected children to shun conventional medical centers and resort to traditional practitioners, churches and patent medicine dealers for treatment. Also, in poor resource settings, diagnosis of some childhood and adolescent cancers may be done clinically, and treatment commenced without histology or cytological confirmation. These all result in inaccuracy of diagnosis and under reporting of malignancy in this age group. The incidence of childhood and adolescent malignancy and assessment of disease pattern are best estimated from hospital archives orhistopathology records, as there is often no reliable nationwide population based cancer registration[5].

There is the need to update and document the current pattern of childhood and adolescent malignancies within the south-east Nigerian environment. This will create necessary awareness among parents, medical practitioners and relevant authorities about the most prevalent malignancies in this age group. Greater awareness among relevant groups will facilitate advocacy for more effective institutional healthcare planning and resource allocation for the management of the affected individuals in this environment. Our retrospective hospital based study is under taken for this purpose. The objective of this study was therefore to determine the pattern of childhood and adolescent malignancies at a tertiary health institution in south-east Nigeria over a ten year period (January2004 to December 2013).

Materials and Methods

Using a pre-designed data sheet, details of all children and adolescents aged 18 years and below treated for malignancy were extracted from the cancer registry and the records unit of the histopathology department for the period January 2004 to December 2013 at Nnamdi Azikiwe University Teaching Hospital (NAUTH), Nnewi, Nigeria. The information retrieved was verified against the hospital admission register obtained from the hospital medical records department as well as histopathology records for all cancer patients over the period of interest. The overall age and sex distribution of the affected individuals were described using percentages, and the relevant data displayed in tables. Inclusion criteria were both genders, age eighteen years and below, and malignant nature of tumour confirmed on histology or cytology. Patients with borderline histological or cytological findings were excluded.

Results

Eighty-five cases of childhood malignancy confirmed on either histology or cytology were treated at NAUTH, Nnewi in the period between January 2004 and December 2013. The study population had an age range of 0.1 years to 18 years, and a median age of 9 years. More males (56.50%) than females (43.50%) were diagnosed with malignancies during the study period. Table 1

shows the annual numbers for childhood and adolescent malignancies, paediatric /adolescent hospital admissions and overall malignancies during period of study. Paediatric and adolescent malignancies constituted 0.9% of paediatric and adolescent hospital admissions and 5.6% of overall malignancies treated during the same period. As shown in the graphical illustration (figure1), the year to year incidence of childhood and adolescent malignancies peaked at 2.56% of hospital admissions for this age group in 2005, and at 7.69% and 9.35% of overall malignancies managed at NAUTH (2005 and 2012 respectively). As seen in Table 2; Commonest tumours were the Lymphomas (11.76%) comprising Non-Hodgkin's lymphoma (80%), Hodgkin's lymphoma (10%) and Large-cell lymphoma (10%), the Leukaemias (11.76%) comprising Acute myeloblastic leukaemia (80%) and Acute lymphoblastic leukaemia (20%). Others include the Rhabdomyosarcoma (11.76%), Nephroblastoma (11.76%), Retinoblastoma (5.88%), Ovarian tumours (4.71%), the Soft tissue sarcomas-excluding rhabdomyosarcoma (3.53%) and Osteogenic sarcoma (3.35%). These are illustrated in the histogram (Fig 2). Table 2 also shows the frequency distribution of childhood and adolescent malignancies in relation to patient's gender. Lymphomas showed equal gender ratio (1:1),however, retinoblastoma and ovarian malignancies were more prevalent among females (ratios 2:3and 0:4 respectively). More prevalent among males were leukaemia (3:2%), nephroblastoma(3:2%), rhabdomyosarcoma (7:3%), other soft tissue sarcoma (2:1%) and osteogenic sarcoma(2:1%).

Table 1: Yearly numbers of childhood malignancies, paediatric /adolescent hospital admissions and overall malignancies and percentages

Year	No of childhood malignancies	No of paediatric admissions	Childhood malignancies as % of paediatric admissions	Total number of malignancies	Childhood malignancies as % of overall malignancies
2004	5	358	1.40	129	3.88
2005	10	390	2.56	130	7.69
2006	12	496	2.42	227	5.29
2007	13	732	1.78	257	5.06
2008	9	1818	0.50	171	5.26
2009	6	1580	0.38	133	4.51
2010	9	1687	0.53	156	5.77
2011	4	928	0.42	83	4.82
2012	10	951	0.05	107	9.35
2013	7	458	1.53	126	5.56
Total	85	9398	0.90	1519	5.60

Fig 1: Year by year number of childhood malignancies in relation to overall malignancies and paediatric/adolescent hospital admissions

Fig. 2: bar chart showing proportion of various paediatric malignancies.

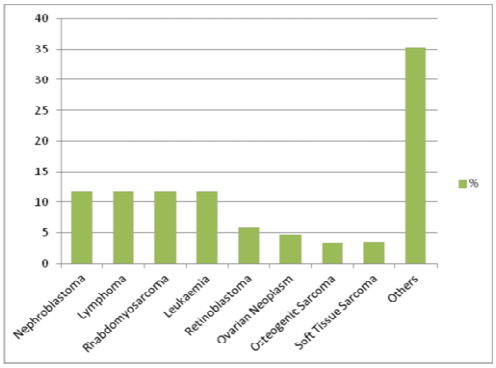

Table 2: Paediatric malignancies and proportions in relation to gender

Tumour	No	Male	Female	M:F Ratio
Nephroblastoma	10	6	4	3:2
Lymphoma	10	5	5	1:1
Rhabdomyosarcoma	10	7	3	7:3
Leukaemia	10	6	4	3:2
Retinoblastoma	5	2	3	2:3
Ovarian Neoplasm	4	0	4	0:4
Osteogenic sarcoma	3	2	1	2:1
Soft tissue Sarcoma	3	2	1	2:1
Others	30	18	12	3:2
Total	85	4 (56.5%)	37 (43.5%)	48:37

Table 3 shows the age range and the median age for patients diagnosed with the commonest malignancies, ranging from a median age of 3 years for patients diagnosed with nephroblastoma and retinoblastoma, to 5.5, 7.5, 10 and 10.5 years for rhabdomyosarcoma, leukaemia, ovarian malignancies and lymphoma respectively. Patients diagnosed with osteosarcoma and soft tissue sarcoma (excluding rhabdomyosarcoma) had median ages of 14 and 17 years respectively.

Table 3: Age range and median age for patients diagnosed with the commonest malignancies.

Tumour	Age range (yrs)	Median age (yrs)
Nephroblastoma	0.1 - 8	3
Lymphoma	1.7 – 18	10.5
Rhabdomyosarcoma	0.2 – 16	5.5
Leukaemia	1.8 – 18	7.5
Retinoblastoma	3 – 4	3
Ovarian neoplasm	0.4 – 13	10
Osteosarcoma	12 – 15	14
Soft tissue sarcoma	16 - 17	17

Discussion

Our study findings show a peak in 2005 for new cases of childhood and adolescent malignancies in relation to paediatric and adolescent hospital admissions and the overall malignancies respectively. However, the chart also shows a reduction in the incidence of cancers in the

subsequent half decade thereafter, and a second peak in 2012 in relation to paediatric admissions. The first peak in 2005 was likely due to a generally increased parental awareness about access to conventional treatment for childhood and adolescent malignancies at our institution. However, the second peak in 2011 appears to correspond to period of newly-introduced, improved, diagnostic facilities and availability of trained personnel for the evaluation of a variety of cancer patients, especially at the radiology and pathology departments of this institution.

This study shows that paediatric and adolescent tumours constitute 5.6% of total malignancies, slightly higher than reported from Bangladesh (4.4%) 5 and India (3.58%)[14], and much higher than reported in the United States (0.8%)[15]. Differences may be due to our hospital based data which may be unrepresentative of the true cancer burden, or as noted by Jabeen et al[1], children and adolescents form a larger proportion of the population of developing countries due to lower life expectancy than in the developed world. Our study population was 56.5% male and 43.5%female, giving a male to female ratio of 1.3:1, similar to the 1.5:1 reported by Agboola et al[16] in favour of males among children diagnosed with malignancy in Sagamu, south-west Nigeria. However a gender ratio in favor of young males over females presenting in hospital with cancer in the south-east Nigerian setting may also be reflective of the traditionally higher value that parents in the region place on males.

This study showed that the four most common cancer groups in our series were tied. They were the lymphoma group (11.76%), comprising non-Hodgkin's lymphoma (80%), Hodgkin's lymphoma (10%) and large cell lymphoma (10%), and the group of Leukaemia (11.76%), comprising acute myeloblastic (80%) and acute lymphoblastic leukaemias (20%) respectively. Others are Nephroblastoma (11.76%)and rhabdomyosarcoma (11.76%). These differ from study findings thirty years earlier in the same region of Nigeria in1982 by Obioha et al[7], who found a much higher proportion of lymphomas (40%),followed by nephroblastoma (14%), leukaemia (12.9%) and CNS tumours (9.7) among childhood malignancies. They also reported an association between lymphoma and poor living standards, as well as a lower incidence of lymphomas and higher incidence of leukaemia than previously reported from other parts of Nigeria and Africa[7]. Our study findings suggest a relative reduction in the proportions of lymphoma and leukaemia, and an associated increase in the proportions of nephroblastoma and rhabdomyosarcoma among childhood and adolescent malignancies in this environment. Improved diagnostic facilities, greater number of trained health workers, improved living conditions and an increased parental awareness about childhood malignancies resulting in a wider variety of cases presenting in hospitals, may all account for changes in disease pattern within the region over the years. Our study finding are also at variance with those from the United States were leukaemia (30.2%), CNS cancers (21.7%) and lymphoma (10.9%) are the commonest childhoodmalignancies[15], possibly also due to the aforementioned factors, especially better living conditions. The pattern of childhood cancer in Europe is reportedly similar to that in the United States[1].

The lymphoma group showed equal gender ratio, and equal proportions seen below and above the age of 10 years. However, below 10 years of age, lymphomas predominantly occurred between 5 -9years, which is in agreement with study findings in Bangladesh by Jabeen et al[1]. Leukaemia on the other hand was diagnosed more among males than females in the ratio of 3:2, with the largest affected group aged 5 – 9years. This is at variance with findings in Bradford by Mckinney[10] and in Bangladesh byJabeen[1] who both reported leukaemia as most common under age of 5 years. This difference may be due to delayed case presentation among the Nigerian study population, as well as differences in the forms of leukaemia that may be prevalent at different age groups in the UK, Bangladesh and Nigeria. Nephroblastoma was more common in boys (M:F = 6:4) and occurred exclusively among individuals below the age of 10 years, with peak age at 0 – 4 years. This is consistent with sprevious literature on the disease[17, 18]. The rhabdomyosarcoma group was separated from other soft tissue sarcomas due to their high relative frequency of occurrence. They are most commonly seen at 5 - 9 years of age, and show a wide difference in gender ratio (M:F = 7:3). The group of soft tissue sarcomas in exclusion of rhabdomyosarcomas constitute 3.35% of childhood malignancies, affecting more males than females (2:1) and more prevalent in adolescents (10 – 18years). Adigun et al[19] at Ilorin, Nigeria, reported soft tissue sarcomas including rhabdomyosarcoma as infrequent, accounting for 6.5% of all cancers in children aged 0 - 15 years. However, Tanko et al[8] at Jos, Nigeria, reported rhabdomyosarcoma as the commonest childhood malignancy (31%), exceeding non-Hodgkin (19.5%) and Burkitt lymphoma (13.8%).Various environmental influences, diet and cultural habits, as well as public awareness about childhood malignancies may all account for the suggested variation in the incidence of soft tissue sarcoma in the different regions of Nigeria. In this study, retinoblastoma was the 5th commonest malignancy (5.88%), seen exclusively in children aged 0 – 4 years with a gender ratio of 3:2 in favour of females. Our finding is partly similar to that of Jabeen et al[1] in Bangladesh who reported 70% of Retinoblastoma occurring below the age of 5 years and second only to lymphoma among childhood malignancies. Agboola et al[16] also reported Retinoblastoma (21%) as second only to lymphoma among children diagnosed with malignancies at Shagamu, Nigeria. A future population based study in south-east Nigeria may be needed to determine the actual regional prevalence of retinoblastoma. Ovarian malignancies (4.71%) occurred equally among females aged above and below the age of10 years. This is in partial agreement with the study report by Junaid [20] who also described ovarian tumours as relatively uncommon, with larger proportion occurring at 10 years and above among children aged 0 – 20 years in south-west Nigeria. Osteogenic sarcoma (3.35%) occurred exclusively in children aged 12 - 18 years, with median age of 14 years

and a gender ratio of 2:1 in favour of males. Parkin etal[21] had earlier put bone tumours at 5% of all childhood malignancies worldwide, with osteogenic sarcoma comprising a large proportion of this.

Numerous histological and cytological entities not individually mentioned in this text are relatively few as individual cases and are grouped as 'Others'. They collectively constitute 35.29% of the study population, and considered individually as rare in our environment (see footnotes). The CNS tumours are not featured in this study, possibly due to a dearth of relevant facilities for proper overall neuro-paediatric diagnosis and clinical management at the centre during the period of study.

Conclusion

Findings from this hospital based study suggest that lymphoma, leukaemia, rhabdomyosarcoma and nephroblastoma are the commonest malignancies afflicting children and adolescents in the south-east region of Nigeria.

Authors' contribution
Okocha EC, Aneke JC, Onyiora IV, Anyiam DC, Uka CO, Onwukamuche ME, Ndukwe CO. Data retrieval/ review and manuscript preparation:
Ulasi TO, Umeh EO, Ebubedike UR, Ezeudu CE, Ekwunife OH, Ugwu JO: Literature review and manuscript preparation.
Ebubedike UR, Umeh EO, Uka CO: Data analyses
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