ORIGINAL ARTICLE

Paediatric head and neck cancers in Nigeria: Implications for treatment planning in resource limited settings

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ABSTRACT

Background: The head and neck (H/N) is a common site for childhood cancers. This study examined all cases of H/N childhood cancers diagnosed in a major teaching hospital in Nigeria over 18 years to determine patterns of broad lineage cancer groups. **Materials and Methods:** Primary pediatric childhood malignancies diagnosed between 1990 and 2008 were analysed. Logistic regression models were fitted to determine significant clinical correlates of childhood cancer. **Results:** Lymphomas were the commonest cancers (49.5%). After controlling for site and age, there was no significant difference in the incidence of Burkitt's lymphoma (BL) by sex (P=0.423). The jaw bones (mandible and maxilla) were the commonest sites in the H/N for involvement of BL, with over 20 times the odds of occurrence when compared to other non-jaw sites of the H/N region (Adjusted Odds Ratio [AOR]=21.41, P<0.001). Among the jaw bones, there was no significant difference in the occurrence of BL (P=0.860). **Conclusion:** Lymphomas are the commonest cancer group among children in Nigeria. In resource limited settings where diagnoses depend majorly on clinical intuition, an awareness of predictors of a disease can shorten the time spent on arriving at a working diagnosis and guide the immediate choice of investigations and treatment.

Key words: Cancer, children, lymphoma, Nigeria

INTRODUCTION

Early childhood cancers constitute a serious condition with several psychological, medical and economic ramifications. The International Agency for Research on Cancer (IARC) estimates that annually, about 9.4 incident cancer cases per 100,000 occur in children younger than 15 years worldwide, with an age and sex adjusted mortality rate of about 5.4 cases/year per 100,000.[1] Approximately 3,413 cancers were diagnosed in children younger than 15 years in 2008 in Nigeria.[1] There is a heavy burden of head and neck (H/N) childhood cancers in sub-Saharan Africa is due to an interplay of factors such as extreme poverty and ignorance, which may result in either non-presentation, or delayed presentation for medical care at which point patients may have advanced disease. Additionally, it is posited that the contribution of viral infections to cancers remains considerably higher in Africa than in the rest of the world.[2] It is noteworthy that the Epstein-Barr virus has been strongly associated with endemic Burkitt's lymphoma (BL).

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Several studies have estimated the burden of H/N cancers in Nigeria, as well as documented the geographic and temporal trends in incidence.[3-5] However, very little is known about the clinic-pathologic correlates. This is of immense clinical importance as knowledge of the correlates of early-childhood cancers will better aid in their diagnosis, particularly in the setting of limited resources for a plethora of clinical investigations. Thus, this study was conducted to determine patterns of broad lineage cancer groups as well as correlates of H/N childhood cancers in Nigeria.

MATERIALS AND METHODS

This was a retrospective study using data from the University College Hospital (UCH) Ibadan between

1990 and 2008. Ethical clearance was obtained from the Institution's Ethical Review Committee. Biopsy report registers were obtained from the Departments of Oral Pathology and General Pathology. Records of all malignant lesions involving the oral and nasal cavities, the paranasal sinuses, oropharynx, nasopharynx, hypopharynx, larynx, trachea, ear and salivary glands were included. Malignancies involving the thyroid, eye and brain were excluded.

Statistical analysis

Categorical data were expressed as percentages and compared using Chi-square statistics. Continuous data were summarized using mean, standard deviation (SD) and confidence intervals. The data were further compared using Student *t*-test and/or one-way analysis of variance test as appropriate. The level of significance was set at the 5% alpha level. All analyses were conducted with Stata Statistical software V.11.

RESULTS

A hundred and one childhood malignancies were diagnosed during the 18-year study period. Overall, the male: Female ratio was 1.7:1. In terms of broad lineage groups, lymphomas were the most common group of cancers (49.5%), followed by epithelial malignancies (25.7) while mesenchymal tumours were the least common (24.7%). The most frequent childhood H/N cancers in descending order were BL (25.7%), embryonal rhabdomyosarcoma (16.8%), squamous cell carcinoma (SCC) (14.8%), non-Burkitt's non-Hodgkin's lymphoma (13.9%) and Hodgkin's lymphoma (9.9%). Other cancers included osteosarcoma (5.9%), mucoepidermoid carcinoma (MEC) (4.9%) and anaplastic carcinoma (2.9%). Figure 1 shows the distribution of childhood H/N cancers by site.

Lymphomas were the most common group of early-childhood malignancies diagnosed; accounting for close to fifty percent (49.5%) of all diagnosed cases [Table 1]. The odds of occurrence of lymphoma were highest in the 6-10 year age group; approximately, 5.3 times that in the 0-5 years group (P=0.026), and about 3.54 times the odds of occurrence when compared to the 11-15 age group (P=0.041).

BL was the most common childhood malignancy accounting for about a fourth of all cases (25.7%). The median age of diagnosis for BL for boys and girls was 10 and 12 years

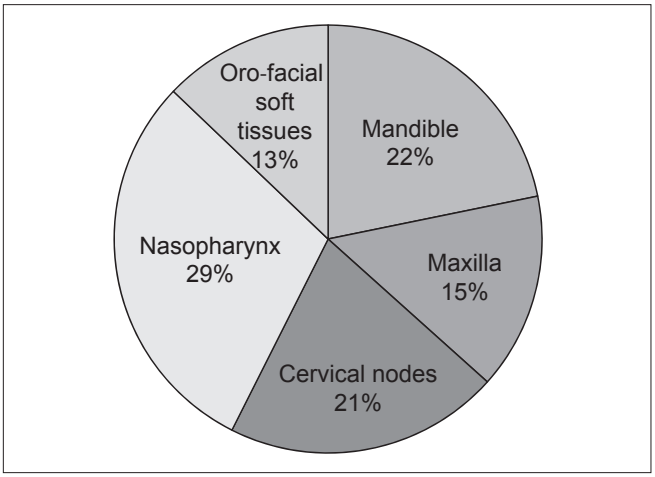

Figure 1: Distribution of tumours by site

Table 1: Demographic and clinic-pathologic characteristics of study participants

Cancer type	Total *N* (%)	Male:Female ratio	0-5 years *n* (%)	6-10 years *n* (%)	11-15 years *n* (%)
Lymphoma, *n* (%)	50 (49.5)				
Burkitt's lymphoma	26 (25.7)	1.6:1	4 (15.4)	12 (46.2)	10 (38.5)
Non-Burkitt's lymphoma	14 (13.9)	3:1	3 (21.4)	7 (50.0)	4 (28.6)
Hodgkin's lymphoma	10 (9.9)	4:1	0	3 (30.0)	7 (70.0)
MesenchymaL, *n* (%)	25 (24.7)				
Rhabdomyosarcoma[§]	18 (17.8)	2:1	10 (55.6)	6 (33.3)	2 (11.1)
Osteosarcoma	6 (5.9)	1:2	0	0	6 (100.0)
Malignant peripheral nerve sheath tumour	1 (0.9)	0:1	0	0	1 (100.0)
Epithelial, *n* (%)	26 (25.7)				
Squamous cell carcinoma	15 (14.8)	1:1.4	4 (26.7)	1 (6.7)	10 (66.7)
Anaplastic carcinoma	3 (2.9)	1:2	0	0	3 (100.0)
Mucoepidermoid carcinoma	5 (4.9)	3:1	0	1 (20.0)	4 (80.0)
Nasopharyngeal carcinoma	1 (0.9)	1:0	0	0	1 (100.0)
Papillary mucinous adenocarcinoma	1 (0.9)	1:0	0	0	1 (100.0)
Melanoma	1 (0.9)	1:0	1 (100.0)	0	0

[§]Includes one case of alveolar rhabdomyosarcoma; the rest were embryonal variants

respectively. After controlling for site and age, there was no significant difference in the incidence of BL by sex (P=0.423). The jaw bones (mandible and maxilla) were the commonest sites in the H/N region for involvement of BL. The odds of occurrence of BL in the jaw bones were over 20 times when compared to other non-jaw sites of the H/N region (Adjusted Odds Ratio [AOR]=21.41, P<0.001) [Table 2]. Among the jaw bones, there was no significant difference in the occurrence of BL (P=0.860).

SCC was the commonest epithelial malignancy and accounted for 14.8% of all cases diagnosed. The mean age for diagnosis of SCC was 10.1 years (SD±4.5 years). 80% of diagnosed SCC cases were situated in the nasopharynx, the remainder occurring in the oro-facial soft-tissues. One case each of melanoma and nasopharyngeal cancer was diagnosed over the 18-year study period.

MEC accounted for about 4.9% of the cases diagnosed during the study period. The parotid glands were the commonest sites for epithelial salivary gland tumours with 75% of MEC cases involving primarily the parotid gland. The mean age of diagnosis of MEC was 12.2 years (SD±2.7 years). One case of papillary mucinous adenocarcinoma was diagnosed during the entire study period.

Embryonal rhabdomyosarcoma was the most common mesenchymal malignancy (16.8%). The mean age of diagnosis was 4.9 years (SD±3.3 years). Close to 50% of cases of embryonal rhabdomyosarcoma occurred in the nasopharynx. Other sites included the mandible (23.5%), oro-facial soft-tissues (17.6%) and cervical lymph nodes (11.8%). The odds of developing embryonal rhabdomyosarcoma were highest in the 0-5 year category, over 48 times when compared to the 11-15 year category (AOR=48.41, P=0.001). The alveolar variant of rhabdomyosarcoma was rare, diagnosed only once during the 18-year study period. Osteosarcoma accounted for 5.9% of cases diagnosed and occurred equally in the mandible as in the maxilla. There was a higher predilection for females, with a male: female ratio of 1:2 cases in our cohort.

Table 2: Two-sided *P* values, adjusted odds ratios and 95% confidence intervals for predictors of Burkitt's lymphoma among pediatric patients in Ibadan, Nigeria[a]

Categories	AOR	*P*>z	95% CI	
Site				
Non-jaw sites*	1			
Jaws	21.41	<001	6.23	73.58
Age				
0-5 years*	1			
6-10 years	3.9	0.118	0.71	21.4
11-15 years	1.76	0.472	0.37	8.31
Sex				
Male*	1			
Female	1.69	0.423	0.47	6.11

[a]Logistic regression model for occurrence of Burkitt's lymphoma with clinical site, age and sex as predictors, *Refers to reference groups, AOR – Adjusted Odds Ratio; CI – Confidence Interval

DISCUSSION

In the present study, lymphomas accounted for 49.5% of childhood H/N neoplasms. This is in agreement with a study in Ife, Nigeria by Amusa *et al.*[4] that also reported lymphomas as the most predominant childhood H/N malignancy Lymphomas are malignant neoplasms of lymphoid lineage that are broadly classified as either Hodgkin's lymphoma or non-Hodgkin's lymphoma. Childhood non-Hodgkin lymphomas are further classified as lymphoblastic lymphomas, small non-cleaved cell lymphomas (or BLs/Burkitt-like lymphomas) and large cell lymphomas.[6,7]

We found that the odds of occurrence of lymphoma were highest in the 6-10 year age group; approximately, 5.3 times that of the 0-5 year group, and about 3.5 times when compared to the 11-15 age group, furthermore, the odds of occurrence of lymphomas among males were 3.2 times that among females. BL accounted for approximately a quarter (25.7%) of all cases. Similar findings have been documented in other studies with BL reported as the commonest tumour of childhood, peaking in 6 or 7 years of life.[8,9] A study in Uganda on generalized BL reported that 2.4% of cases were 0-2 years of age; most (69.1%) were 3-8 years of age and 28.4% were 9-14 years of age. They also noted that children with tumours involving the face or head were younger (6.4 years) than children with tumours involving abdominal and/or other unspecified sites (7.5 years).[10]

Embryonal rhabdomyosarcoma was the second most common childhood H/N cancer accounting for 16.8% of all cases. In a 19 year review from Ibadan, the embroyonal variant was found to be the commonest type, constituting 61.5% of all cancers, this however included other sites apart from the H/N.[11] They, nevertheless, found the H/N to be the commonest site for rhabdomyosarcomas in children under 15 with a frequency of 50.6%. In our study, the odds of developing embryonal rhabdomyosarcoma were highest in the 0-5 age category, over 48 times when compared to the 11-15 year age category. Indeed, it has been reported that children aged 2-6 year tend to have H/N rhabdomyosarcoma, whereas adolescents aged 14-18 year tend to have primary tumours in the extremity, truncal, or paratesticular locations.[12] Rhabdomyosarcoma typically occurs in two distinct age groups: Children 5 years of age and below, who are most likely to have the embryonal form of disease; and adolescent children aged 14-20, who more often have alveolar rhabdomyosarcoma.[13]

SCC accounted for 14.8% of all cases diagnosed. The mean age for diagnosis of SCC was 10.13 years (SD±4.50 years).

Adeyemi *et al*,[3] reported that H/N carcinomas constituted 21.4% in their study of patients less than 16 years of age. In our study, 80% of diagnosed SCC cases were situated in the nasopharynx. A retrospective analysis in Louisiana identified 40 children and adolescents with nasopharyngeal carcinoma between 1948 and 1992. Thirty-two patients had lymphoepithelioma ("class III nasopharyngeal carcinoma" in the WHO classification system) and eight had SCC.[14] The occurrence of epithelial malignancies of the nasopharynx is rare in children but when present, lymphoepithelioma predominates.[15] Nasopharyngeal carcinoma has a bimodal age distribution. A small peak is observed in late childhood (adolescence), and a second peak occurs in people aged 50-60 years. Our study suggests an earlier onset than previously estimated.

Implications for policy and clinical practice

Our study provides a framework for differential diagnosis for H/N tumours. Particularly, in poorer regions of the world where diagnoses depend majorly on clinical intuition, an awareness of clinical correlates, which are well predictive of a disease condition can help to shorten the time spent in arriving at differential diagnoses of childhood H/N cancers and also guide the immediate choice of investigations to perform after the most likely working diagnosis is made.

This study also highlights the need for a robust health care system in Nigeria. In a country with about 70% of the population below the poverty line, out-of-pocket payments for cancer treatment are simply out of the reach of those who need it the most.[16] The National Health Insurance Scheme (NHIS) in Nigeria currently does not cover costs associated with diagnosis, chemotherapy and/or surgical management of cancers. NHIS should be expanded to include these components.

Limitations

The results of this study were based on data from only one teaching hospital in Nigeria. However, similar results have been documented in several other regions of sub-Saharan Africa, thus suggesting that the findings are indeed consistent.

CONCLUSION

Lymphomas are the commonest cancer group among children in Nigeria. Age is a strong predictor of broad lineage categorization of H/N malignancy.

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