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## Pediatric head and neck malignancies in sub-Saharan Africa

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### Abstract:

**Introduction:** Cancers are relatively rare in children however recent reports suggest that malignancies are becoming a major source of pediatric deaths.

**Method:** Using the database of the cancer registry of the University College Hospital, Ibadan we reviewed all newly diagnosed cases of head and neck cancers in children under 19 years old at the hospital between 1981 and 2008.

**Results:** A total of 1,021 cases of Head and Neck cancers were seen in children. The hospital based incidence of pediatric head and neck cancers is 36 cases per year. There were 627 males and 394 females [M:F ratio of 1.6:1] with mean ages of 8.21 and 7.70 years respectively. Boys were more affected than girls in all years of life while the peak age of onset for both sexes is the third year of life. The commonest anatomical site involved is the eye/orbit; other common sites were the nasopharynx, paranasal sinuses, nasal cavity and thyroid gland. Neural malignancies constitute the commonest malignancies seen (35.3%), other are lymphomas (33.1%), squamous cell carcinoma (9.1%) and soft tissue sarcoma (8.6%). Retinoblastoma is the commonest lesion seen among the patients with a slight male preponderance [M:F ratio of 1.2:1] Burkitt lymphoma (BL) is seen in all age groups but there is greater frequency in the older ages. The incidence of carcinomas is higher in the older age groups, relatively rare lesions like Hodgkins lymphoma and thyroid malignancies are almost exclusive to older children.

**Conclusion:** The pattern of head and neck malignancies in children in sub-Saharan Africa is changing; dominant lesions like lymphomas are being gradually replaced by other malignancies such as neural malignancies, soft tissue sarcomas and squamous cell carcinoma.

**Keywords** Pediatric, Head and Neck Malignancies, sub-Saharan Africa

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### Introduction

Cancers are relatively rare in children unlike the pattern seen in older age groups; nonetheless cancers have become a major cause of pediatric deaths in developed countries<sup>1</sup>. Childhood malignancies have been found only second to accidental trauma as the cause of deaths in children between 5 and 14 years in the developed world<sup>1</sup>. Another report from the United States identified cancers as the leading cause of mortality in children aged 1 to 14 years<sup>2</sup>. Head and neck cancers account for varying proportions of total cancers seen; globally this range between 5-50% of all cancers.<sup>3</sup> In the developed nations of Europe and North America it is as low as 5-8% while as high as 30% in a developing country like India.

About 85% of all cancers seen in children occur in developing countries<sup>4</sup>, this estimate is expected to increase above 90% over the next two decades<sup>5</sup>. The influence of

several factors such as cultural, genetics, demographics and access to health care contributes to differences in the burden of childhood cancer, from 3-10% of the total cancer burden in some regions to 1% in other developing regions<sup>5</sup>. Children constitute a significant proportion of the population in many developing countries, accounting for up to a third of the population in some instances<sup>6</sup>. In Nigeria, children [0-18 years] constitute more than half of the population, 52.4%<sup>7</sup> hence emphasizing the need to focus appropriately on this segment of the society.

The global focus on communicable diseases had diverted attention and allocation of resources away from childhood malignancies in many developing countries but with improvement in the management of infectious diseases childhood malignancies are emerging as a significant cause of death in these nations<sup>4</sup>. There is need to document data on childhood cancers in each country or region, this will be essential for planning medical services, treatment

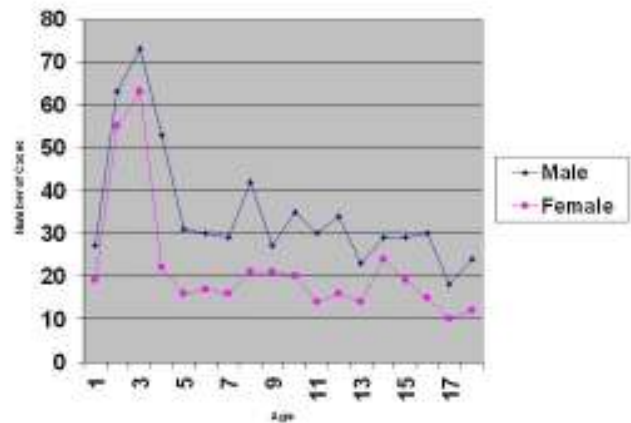
policies, resource allocation and for policy formulation. The aim of this paper is to review Head and Neck malignancies in children presenting for cancer treatment at the University College Hospital, Ibadan, Nigeria.

## METHODS

This is a retrospective study based on records at the Ibadan cancer registry, University College Hospital, Ibadan (UCH). This population-based registry is the first cancer registry in Nigeria. UCH is the first teaching hospital established in Nigeria, and the first hospital in the country to acquire a Computed Tomography-scan facility and radiotherapy treatment facility. This resulted in the referral of patients from all over the country to UCH for both diagnosis and radiotherapy treatment.<sup>8</sup> Cases were actively located by the registry staff before being entered into a computer system running on CANREG 4. All cases of newly diagnosed Head and Neck malignancies (excluding tumors of the central nervous system) seen in children under 19 years of age who presented at University College Hospital, Ibadan between 1981 and 2008 were identified. The cases were selected using relevant codes from the International Classification of Diseases for Oncology ICD-10 Version 2010. Descriptive statistics were compiled for age at diagnosis, gender and histological diagnosis and sites of the tumors.

## RESULTS

A total of 4,560 cases of Head and Neck cancers were seen in the study period out of which 1,021 [22.4%] occurred in children. The hospital based incidence of pediatric head and neck cancers was 36 cases per year. There were 627 males and 394 females [M:F ratio of 1.6:1] with mean ages of 8.21 and 7.70 years respectively. Boys were more affected than girls in all years of life within the study limits. [Fig.1] The peak age of onset for both boys and girls in the study population is the third year of life. [Fig.1] Broadly, the peak incidence of cases was seen in the early part of 1980s with a gradual decline until 1999 and then increase in incidence of cases till the end of the study period, however this pattern was not rigidly consistent.[Fig.2] The annual distribution also showed that males were more affected every year than females. [Fig.2] The commonest anatomical site involved was the eye/orbit; other common sites were the nasopharynx, paranasal sinuses, nasal cavity and thyroid gland.[Table 1] The least involved anatomical sites were the oesophagus, hypopharynx and ear.[Table 1] Other sites such as lymph nodes, maxillofacial bones, oral cavity, soft tissues of the face and scalp were grouped together under Head and Neck NOS. [Table 1]



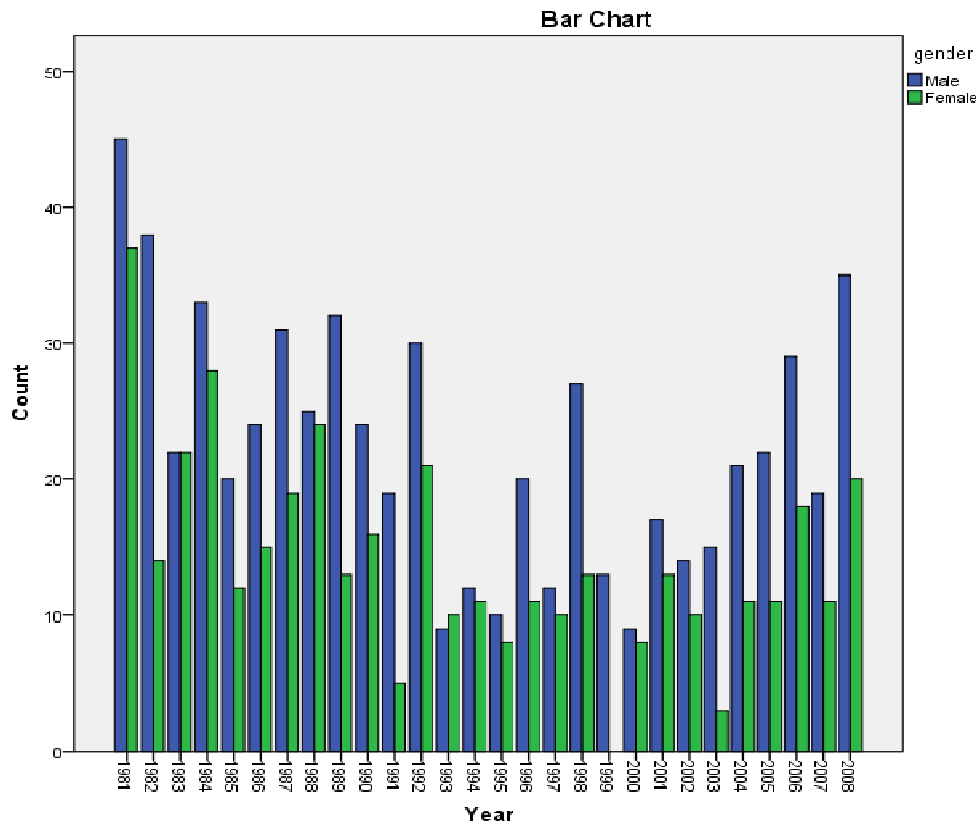
**Figure 1 Gender and age of patients at diagnosis**

Neural malignancies as a group constitute the commonest malignancies seen in the study population (35.3%), this was followed by lymphomas (33.1%), squamous cell carcinoma (9.1%) and soft tissue sarcoma (8.6%).[Table 2]

The frequency distribution of these common malignancy groups is shown in Figure3. Retinoblastoma was the commonest lesion seen among the patients with a slight male preponderance [M:F ratio of 1.2:1] [Table 2]. The classification of the lesions according to age groups in Table 3 showed that retinoblastoma was typically seen in younger patients; the mean age of retinoblastoma patients was 3.37years. Rhabdomyosarcoma was seen in all age groups except in the very young. Burkitt lymphoma was seen in all age groups but a greater frequency occurred in the older age groups. The incidence of carcinomas was higher in the older age groups, relatively rare lesions like Hodgkin's lymphoma and thyroid malignancies are almost exclusive to older children. The pattern of distribution of the two commonest lesions: Retinoblastoma and Burkitt lymphoma is shown in Figure 4.

## DISCUSSION

Epidemiological data on pediatric head and neck cancers in sub-Saharan Africa is rare. Other studies on head and neck from the region lumped together all age groups in their data set. The hospital based incidence seen in this study is similar to reports of head and neck malignancies from other centers in south-west Nigeria<sup>9,10</sup> however other studies from Nigeria have reported higher incidences.<sup>11</sup> University College Hospital Ibadan had the first cancer registry in Nigeria and the first radiotherapy facilities for the management of malignant lesions. This factor in addition to the longer duration of the study period may explain the difference in incidence seen from other studies.



**Figure2. Annual frequency of malignancies based on gender**

**Table 1. Anatomical site by gender.**

	Male	Female	Total
<b>Head and Neck NOS</b>	293	160	453
<b>Paranasal Sinues</b>	18	9	27
<b>Nasal Cavity</b>	16	8	24
<b>Nasopharynx</b>	47	17	64
<b>Salivary glands</b>	2	3	5
<b>Thyroid</b>	6	5	21
<b>Hypopharynx</b>	2	0	2
<b>Oropharynx</b>	2	2	4
<b>Eye/Orbit</b>	232	176	408
<b>Ear</b>	2	1	3
<b>Larynx</b>	7	1	8
<b>Oesophagus</b>	0	1	1

Table2. Frequency of head and neck malignancies.

	Male	Female	Total	Mean Age	Proportion %
Adenocarcinoma	2	0	2	17	0.2
Hodgkin's lymphoma	8	3	11	13.36	1.1
Non-Hodgkin's lymphoma	27	9	36	11.28	3.5
Burkitt lymphoma	191	100	291	9.74	28.5
Mucoepidermoid carcinoma	4	1	5	12.6	0.5
Neuroblastoma	1	2	3	3.33	0.3
Retinoblastoma	200	155	355	3.37	34.8
Other neural malignancies	2	0	2	1.5	0.2
Osteosarcoma	7	5	12	13.58	1.2
Chondrosarcoma	0	2	2	14	0.2
Ewing sarcoma	1	0	1	14	0.1
Other skeletal sarcomas	4	6	10	9.2	1
Rhabdomyosarcoma	49	25	74	7.88	7.2
Non rhabdomyosarcoma soft tissue sarcoma	9	5	14	8.64	1.4
Squamous cell carcinoma	70	23	93	13.63	9.1
Follicular thyroid carcinoma	2	6	8	14.5	0.8
Medullary thyroid carcinoma	1	1	2	16	0.2
Papillary thyroid carcinoma	2	6	8	10.5	0.8
Other malignancies	11	9	20	11.1	2
Neoplasm malignant	36	36	72	10.6	7.1
<b>Total</b>	<b>627</b>	<b>394</b>	<b>1021</b>	<b>8.01</b>	<b>100</b>

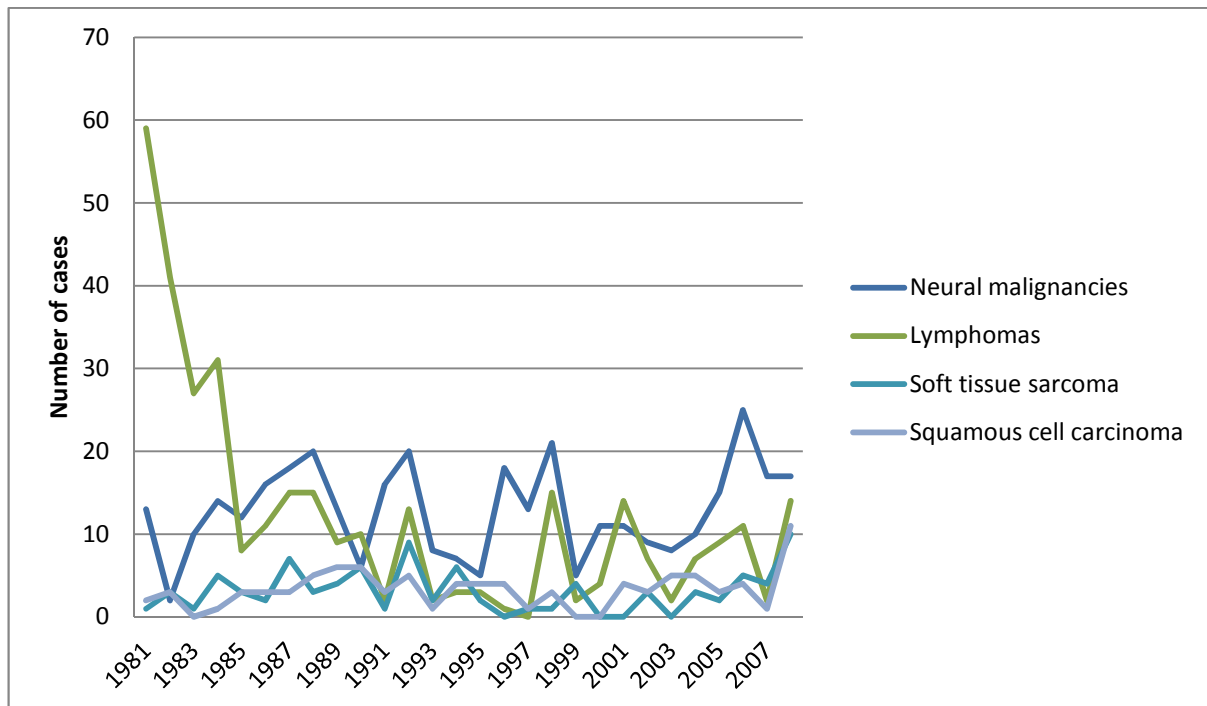


Figure3. Annual distribution of common malignancy groups

Table 3. Head and Neck Malignancies in each Age Group

0 – 1year	N	2–5yrs	N	6–10yrs	N	11–18yrs	N
Retinoblastoma	32	Retinoblastoma	289	BL	141	BL	119
RMS	5	BL	29	Retinoblastoma	25	SCC	75
BL	2	RMS	27	MN	24	MN	35
Non-rhab STC	2	MN	12	RMS	18	RMS	24
Other SS	1	SCC	6	SCC	11	NHL	22
Other NM	1	NHL	4	NHL	10	Other malignancy	11
SCC	1	Neuroblastoma	3	Other SS	5	Osteosarcoma	10
Other malignancy	1	Non-rhab STC	2	Papillary TC	5	Retinoblastoma	9
MN	1	Other SS	1	Non-rhab STC	4	HL	8
		Other NM	1	Follicular TC	2	Non-rhab STC	6
		Other malignancies	1	Osteosarcoma	2	Follicular TC	6
		MC	1	MC	1	Papillary TC	3
						Other SS	3
						MC	3
						Medullary TC	2
						Adenocarcinoma	2
						Chondrosarcoma	2
						Ewing sarcoma	1

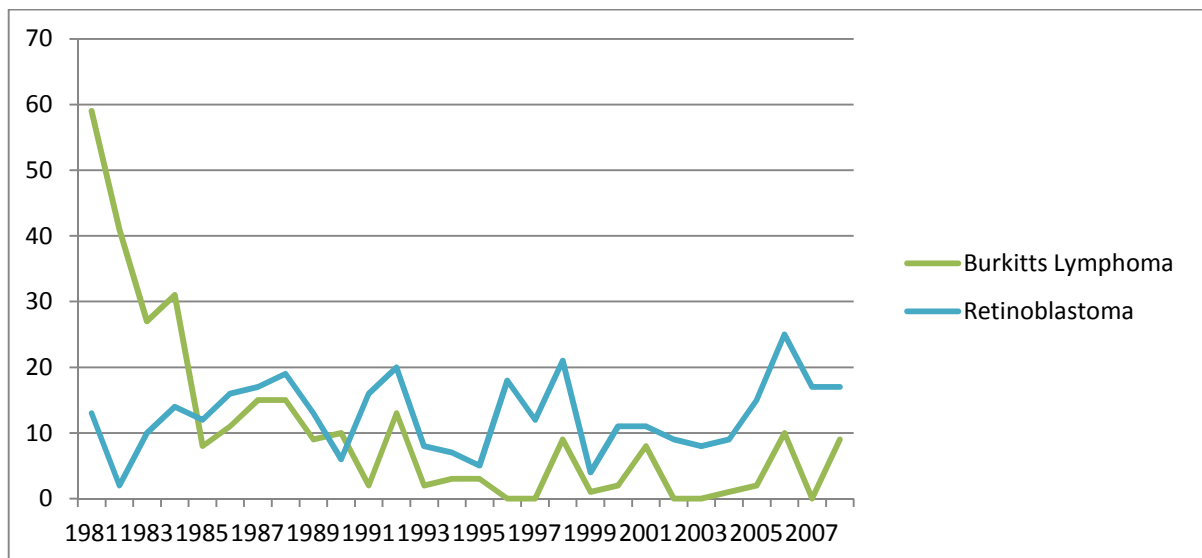


Figure 4. Pattern of the two commonest lesions

The gradual annual decline seen in the incidence and the subsequent increase may be related to the economic history of the country. An economic downturn was experienced in the early 1980s with a rapid increase in inflation rate <sup>12,13</sup> but the advent of democratic rule coincided with economic recovery. Available data suggests that economic growth in Nigeria has been growing since then.<sup>14</sup> Since health related costs for most

households in Nigeria are an out of pocket expense it may likely explain the trend of increased diagnosis in time of economic prosperity.

There is a clear male predilection for pediatric head and neck malignancies in this study population. This is seen in all ages and for all types of lesions considered. This is in contrast to reports from the United States which suggests girls were more affected than boys in head and neck

neoplasms.<sup>15</sup> Even though among adult patients with head and neck cancers males are more affected than females, social habits like drinking alcohol, cigarette smoking and work related hazards like exposure to hardwood can explain the gender difference in adults however the reason for the male predilection in our children is unknown.

The site of the lesion was not specified in most of the cases; excluding this however the eye/orbit is where majority of the lesions occurred. This is probably accounted for by the high prevalence of retinoblastoma seen in the dataset. The nasopharynx, paranasal sinuses and nasal cavity are also common sites for head and neck tumors in these patients. This indicates the predilection of numerous malignancies such Burkitt lymphoma, squamous cell carcinoma and salivary gland lesions for these sites.

Neural malignancies and lymphomas are the leading causes of pediatric head and neck malignancies seen; this pattern has remained consistent with reports from other authors.<sup>15,16</sup> The incidence of retinoblastoma was fairly consistent throughout the study period. It has been argued that this consistency suggests that non-genetic factors may play a significant role in the cause of the lesion since inheritable cancers only constitute a small part of pediatric lesions.<sup>15,17</sup> Several factors have been implicated in the development of cancers in children, some such as ionizing radiation have been proven while other factors like environmental pollution and exposure to electromagnetic fields are but not proven yet.<sup>15,18</sup>

In Africa, the association with infectious diseases have been noted to be responsible for the high incidence of non-Hodgkins lymphoma (NHL).<sup>19,20</sup> Burkitt lymphoma is a B-cell NHL which has been associated with Epstein Barr virus and *P.falciparum* infection.<sup>21-24</sup> Since it was described 50 years ago by Denis Burkitt<sup>25</sup> Burkitt lymphoma has remained one of the commonest childhood cancer seen in places where malaria is holoendemic.<sup>26</sup> Three clinical variants have been described: endemic, sporadic and immunodeficiency-associated.<sup>27</sup> The cases seen in this dataset will nearly all be the endemic variant since this is the variant associated with geographical places where malaria is endemic like Nigeria and in fact most of sub-Saharan Africa.<sup>28</sup> Burkitt lymphoma has been reported to account for nearly 90% of pediatric lymphomas and half of all pediatric cancer cases in these high risk areas.<sup>28</sup>

However result from this study disagreed slightly from this report; Burkitt lymphoma only accounted for about a third of all pediatric cancers in this study though it made up 86% of all lymphomas cases seen. The reduced incidence

of Burkitt lymphoma in this study might be due to improvement in the living conditions and better control of malaria.<sup>29</sup> Burkitt lymphoma is twice as common in boys than girls<sup>28</sup> a similar trend was observed in this study with M:F ratio of 1.9:1. The peak of incidence in this study was in the 6-10 years age bracket which is similar to what has been previously reported.<sup>28</sup>

Rhabdomyosarcoma is a regularly seen neoplasm in the pediatric age group; it is the commonest form of soft tissue sarcoma in children<sup>30</sup> and among the most common neoplastic lesions in this age group.<sup>31</sup> Reviews of childhood tumors from different centers in Nigeria listed soft tissue sarcoma among the top five common neoplasm's encountered in children.<sup>29,32-35</sup> Male gender preponderance has been reported in childhood rhabdomyosarcoma<sup>30,36,37</sup> this is similar to the result in this study which showed a male to female ratio of 2:1. Unlike a previous report which showed majority of pediatric rhabdomyosarcoma occurring in children <5years<sup>38</sup> we found that majority of the cases were seen in children aged 6-18 years. The difference may be due to the anatomical restriction of our data to the head and neck region unlike studies which encompassed all anatomical regions.

Neural malignancies carry a poor risk in developing countries; dissemination of the disease is a common cause of death in these countries.<sup>39</sup> Retinoblastoma is a developmental cancer arising from the retina; 80% of the estimated 8,000 annual cases are seen in developing countries.<sup>39,40</sup> The average age of diagnosis of unilateral cases have been stated to be 2years<sup>41</sup> this conforms with our results which shows most of the cases in this study were diagnosed between 2nd-5th year of life. Retinoblastoma is highly curable however several factors such as late diagnosis and poor treatment compliance have contributed to dismal survival rates from developing countries.<sup>39</sup> Since 90% of the diagnoses seen in the study population were in children less than 5 years, policy modifications to grant free access to healthcare to these group of children may improve significantly the outcome of retinoblastoma.<sup>42</sup>

In conclusion, the pattern of head and neck malignancies in children in sub-Saharan Africa is changing, the dominance of infectious disease related cancers such as Burkitt lymphoma is now waning. Multiple factors are responsible for the changing trend however public health policies that guarantee free provision of health care for children will improve the rate of diagnosis and ensure treatment compliance by affected families.



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