CLINICAL FEATURES AND TYPES OF PAEDIATRIC OROFACIAL MALIGNANT NEOPLASMS AT TWO HOSPITALS IN NAIROBI, KENYA

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DECLARATION

This thesis is my original work and has not been presented for a degree in any other university.

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DEDICATION

To my loving wife, Judith O. Okutoyi, and my lovely daughter, Monicah A. Sanya, for all the support, patience and understanding.

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ABBREVIATIONS

BDS Bachelor of Dental Surgery

UoN University of Nairobi

UNDH University of Nairobi Dental Hospital

KNH Kenyatta National Hospital

ENT Ear, Nose and Throat

RMS Rhabdomyosarcoma

FS Fibrosarcoma

SCC Squamous cell carcinoma

BL Burkitt's lymphoma

NPC Nasopharyngeal carcinoma

RTB Retinoblastoma

KS Kaposi's sarcoma

NB-NHL Non-Burkitt's non-Hodgkin's lymphoma

OS Osteosarcoma

DEFINITION OF TERMS

Malignant neoplasm	Dysmorphic proliferations of tissues with the capacity for continuous autonomous growth
Carcinoma	Malignancy involving cells of epithelial origin
Sarcoma	Malignancy involving cells of mesenchymal origin
Lymphoma	Malignancy involving cells of lymphoreticular origin
Rhabdomyosarcoma	Malignant mesenchymal tumour arising from cells committed to form striated muscle
Fibrosarcoma	Malignant mesenchymal tumour arising from fibrous tissue cells
Oral squamous cell carcinoma	Malignant epithelial tumour arising from oral keratinocytes
Burkitt's lymphoma	Malignant form of non- Hodgkin's lymphoma arising from B cells
Retinoblastoma	Malignant tumour arising from retinal cells
Kaposi's sarcoma	Malignant mesenchymal tumour arising from vascular endothelial cells
Osteosarcoma	Malignant mesenchymal tumour arising from bone cells
Leucocoria	White papillary reflex or cat's eye reflex
Eye injection	Eye redness

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ABSTRACT

Background: Orofacial malignant neoplasms are the sixth commonest malignancies in the world and together with cancer of the pharynx, they are the third most common malignancies in developing countries. While a few reports exist in the English literature, published studies specific on paediatric orofacial malignant neoplasms are scarce. In addition, most of these studies have been retrospective in nature and there is scanty information on the clinical features of these neoplasms at presentation.

Objective: To describe the clinical presentation and histopathologic types of orofacial malignant neoplasms in children.

Materials and Methods: A hospital-based cross-sectional study with a convenient sample of paediatric patients aged 15 years and below. A questionnaire and clinical examination form were used to record the data. The data were then coded and major trends described using the Statistical Package for Social Sciences (SPSS) 12.0 programme. Descriptive statistics included measures of central tendency and dispersion for continuous variables and proportions for categorical variables. Differences among dependent variables and independent variables were analysed using Pearson's chi square test and/or Fisher's exact test. A P- value of <0.05 was considered significant.

Results: The study included 65 children among whom 44(67.7%) were male and 21(32.3%) female. The age ranged from 0.25 years to 14 years with a mean of 5.3 years (± 3.4 SD). The main complaint was swelling 61(93.8%) followed by visual disturbance

29(44.6%). Overall, the mean duration of presenting symptoms ranged between 0.17- 36 months. Notably, and with the exception of retinoblastoma, the presentation of patients with sarcomas was relatively earlier than for carcinomas and lymphomas. The most frequent signs associated with the neoplasms were leucocoria 23(35.5%), proptosis 19(29.2%) and loss of vision 15(23.1%). The most common site was eye/orbit 30(46.2%), followed by the maxilla 11(16.9%) and other sites on the face 10(15.4%). A majority of the neoplasms were retinoblastoma (RTB) 26 (40%), followed by 14(21.5%) cases of Burkitt's lymphoma (BL), 9(13.8%) of rhabdomyosarcoma (RMS), 6(9.2%) of non- Burkitt's non- Hodgkin's lymphoma (NB-NHL), 3(4.6%) of osteosarcoma (OS), 3(4.6%) of Kaposi's sarcoma (KS), 2(3.1%) of squamous cell carcinoma (SCC), 1(1.5%) of fibrosarcoma (FS) and 1(1.5%) of nasopharyngeal carcinoma (NPC). Most neoplasms occurred in patients aged less than 5 years (40 cases) followed by 19 cases in children aged between 5 and 10 years. Only 2 infants were diagnosed with neoplasms.

Conclusions: Paediatric orofacial malignancies were more common in males than females except for RTB which was more common among female patients. Most of the malignancies were observed in the age group of 1-5 years. The clinical features of most paediatric orofacial malignant neoplasms depended mainly on the site of primary involvement with swelling having been the most common presenting complaint irrespective of tumour type. The most common sign was visual disturbance including leucocoria, loss of vision and proptosis. The commonest site of presentation was the orbital region and most neoplasms were advanced at the time of diagnosis. RTB

accounted for the majority of paediatric orofacial malignancies, followed by BL and RMS.

Recommendations: It is necessary to conduct population based studies targeting the different types of paediatric orofacial malignant neoplasms, especially RTB, to ascertain their exact incidence and prevalence in Kenya. There is also need to formulate strategies aimed at educating the public on the recognition of the clinical features of paediatric orofacial malignant neoplasms to ensure that early treatment is sought. In addition, research should be conducted to establish other reasons behind patient presentation with advanced disease to ensure prompt intervention so as to reduce morbidity and mortality.

CHAPTER 1

1. 1. Introduction and Literature review

Paediatric whole body malignancy is relatively rare. It is estimated that one child in 650 children may develop cancer before the age of 15 years. Available literature also indicates the occurrence of new whole body malignancies at the rate of 100 per one million children (Malpas, 1987). Orofacial malignant neoplasms are the sixth most common malignancies in the world and together with cancer of the pharynx, they are the third most common malignancies in developing countries (Parkin et al., 1993). They occur at any age without predilection for gender (Chidzonga, 2006; Chidzonga and Mahomva, 2006; Aregbesola et al., 2005; Parkin, 1993; Johnson, 1991).). There exist a number of reports on orofacial neoplasms in children worldwide. However, reports specific on paediatric orofacial malignant tumours are scarce in the literature (Aregbesola et al., 2005; Ajayi et al., 2004; Keszler et al., 1990; Chuong & Kaban, 1985; Blackwood, 1965; Bhaskar, 1963). Of all the head and neck neoplasms reported, only 3-5% has been found in children (Keszler et al., 1990; Bhaskar, 1963). In Japan, a retrospective study by Tanaka et al. (1999) reported 3 cases of malignant orofacial tumours out of 105 cases in children aged less than 15 years. This study reported an age range of 6 months to 15 years with no difference in occurrence between boys and girls. Two of the cases occurred in the mandibular gingiva and one in the tongue.

Oral carcinoma constitutes more than 50% of orofacial malignant neoplasms (Chidzonga, 2006; Johnson, 1991) and over 98% of the affected patients have been reported to have

been aged above 40 years (Barnes, 2005; Adekeye et al., 1985). Dimba et al. (2007) reported that about 10% of oral cancers occur in patients aged below 40 years and no statistical differences existed between the genders. However, for children below 10 years, only 2 (5.6%) out of 358 cases of orofacial squamous cell carcinoma (OSCC) occurred in this age group (Chidzonga and Mahomva, 2006). Onyango et al., (2004) in a retrospective descriptive study on oral cancer at KNH over a 20- year period, found that six patients aged between 0-9 years had oral cancer. OSCC tends to occur sporadically at a much higher incidence but closer examination of a subset of tumour patients has revealed familial clustering of oral squamous cell carcinoma suggestive of an autosomal dominant mode of inheritance (Ankathil et al., 1996). This may, in part, explain the occurrence of some of these neoplasms in the paediatric age groups.

Sarcomas of the orofacial region have been described as being less common than carcinomas and they tend to affect younger patients compared to carcinomas (Ogunlewe et al., 2006; Barnes et al., 2005). Lymphomas, in contrast to carcinomas and sarcomas, are malignant lesions that can arise from any type of lymphocyte, but most frequently from B-cells. They comprise the Hodgkin's (HL) and the more common non-Hodgkin's lymphoma (NHL) (Barnes et al., 2005). Getachew (2001) in a retrospective study on malignant lymphoma in Western Ethiopia over a 10- year period, reported eight cases of NHL in children aged between 1-10 years. In this category of NHL, Burkitt's lymphoma (BL) was the most common childhood tumour in tropical Africa (Hesseling et al., 2003). It is predominantly extra- nodal and is unusual in that its onset is in childhood with the jaw as the single most common initial site (Barnes et al., 2005). Mwanda (1999) found

BL to have been the commonest childhood tumour in Kenya followed by nephroblastoma, HL, acute lymphoblastic leukemia (ALL) and retinoblastoma (RTB) in reducing order of frequency. This neoplasm has been described to present as a rapidly growing jaw swelling in 51.6% (916 cases) of children aged 14 years and below. It is more common in boys than girls with a ratio of 1.5:1 (Mwanda, 2004).

A clinicopathologic study of orofacial malignant neoplasmms in children and adolescents in a Nigerian tertiary hospital by Oluseyi et al. (2007) reported 13.3% cases of orofacial malignant neoplasms. The age range was 2.5- 19 years and the male to female ratio was 2.9:1. BL (38.3%) was the most frequent malignant tumour with 72% of them having been recorded in the first decade of life. Lymphomas accounted for 53.2% of the malignancies followed by sarcomas (36.2%) and carcinomas (10.6%). Carcinomas exclusively affected patients in the second decade of life and were predominantly glandular carcinomas. Osteosarcoma (OS) and rhabdomyosarcoma (RMS) were the most common sarcomas. The most common site of occurrence was the maxilla/maxillary antrum (38.3%), followed by the mandible (29.8%). However, the clinical presentation of these tumours was not described in this retrospective study. Similar earlier studies in Nigeria by other workers have, however, reported 14.4% and 8% occurrences of these tumours (Johnson, 1991; Keszler et al., 1990). Bhaskar (1963) examined 293 cases of orofacial tumours among American children and found that only 9% were malignant. The occurrence of paediatric orofacial Kaposi's sarcoma (OKS) is not well documented in Kenya. Butt et al. (2007) in an evaluation of oral manifestations of HIV/AIDS in a

Kenyan provincial hospital documented 13% cases of OKS in 61 patients aged 16 years and above.

Histopathologically, orofacial malignant neoplasms can be divided into carcinomas, sarcomas and lymphomas (Oluseyi et al., 2007). They may be odontogenic or non-odontogenic. Carcinomas include squamous cell carcinoma, adenocarcinoma, adenoid cystic carcinoma and mucoepidermoid carcinoma. Sarcomas include OS, chondrosarcoma, fibrosarcoma (FS), Ewing's sarcoma, myxosarcoma, RMS, leiomyosarcoma and malignant fibrous histiocytoma. However, the international classification of childhood cancer (ICCC) divides these neoplasms into diagnostic groups I to XII (Steliarova- Foucher et al., 2005).

RMS is the most common soft tissue sarcoma in the first 2 decades of life (Raney et al., 2001), a third of which occur in the head and neck region and of these, approximately two thirds are of the embryonal RMS variety (Hicks and Flaitz, 2002). Neoplasms of the salivary glands are rare in children, representing fewer than 10% of all pediatric head and neck tumours (Callender et al., 1992). Approximately 80% of salivary gland tumours are considered benign with pleomorphic adenoma being the most common type (Chidzonga et al., 1994). Mucoepidermoid carcinomas account for 50% of malignant salivary gland tumours in children (Byers et al., 1984). Of all the 50 cases of primary orofacial leiomyosarcomas reported in the English literature since 1980, only 3 cases have been found in patients aged less than 15 years. There are no obvious gender differences and the sites of presentation include the maxillary and mandibular alveolar ridges and submandibular region (Georgios et al., 2005).

OS is the most common primary neoplasm of bone, typically affecting the metaphysis of the femur or tibia of a child. It is the third most common malignancy in adolescents. In the head and neck region OS represents about 7% of all neoplasms involving mainly the jaws (Wanebo, 1992). Chindia et al. (1998) in a report of 14 cases of OS of the maxillofacial bones among Kenyans found 3 cases in patients aged less than 15 years. All the 3 cases were in the mandible and presented with pain, swelling and ulceration.

From the foregoing literature, it will be noted that most studies on orofacial malignant neoplasms have been retrospective in design and have scanty information on the clinical features of these neoplasms at presentation. There is hardly any published data available regarding the occurrence, incidence and prevalence of these neoplasms in terms of clinical presentation and histopathologic types in the paediatric age group in a Kenyan population. This is a special age group as it presents various challenges both in diagnosis and management of these neoplasms when they occur. Therefore, there is need for basic research in this area for better understanding of these neoplasms with regard to prompt intervention. The information is certainly of great value for clinicians who may manage paediatric patients. The aim of this study, therefore, was to determine the clinical presentation, histopathologic types and relative frequency of the various types of orofacial malignant neoplasms among paediatric patients at the Kenyatta National Hospital (KNH) and University of Nairobi Dental Hospital (UNDH). The results from this study may help advance the knowledge about the clinical presentation and histopathologic variants of paediatric orofacial malignant neoplasms at two Kenyan urban referral centres. They also act as baseline data that will help in the setting up of follow-up

studies in addition to being used by health planners for resource planning in the management of paediatric orofacial malignant neoplasms.

1. 2. RESEARCH PROBLEM AND JUSTIFICATION

1. 2. 1. Statement of the problem and Justification

Orofacial malignant neoplasms present in a variety of ways with regard to the histopathologic types, site and size. The clinical features guide in the diagnosis and overall management of the patient. These clinical features may be due to local and systemic effects of the neoplasm on host tissues. In terms of treatment costs and the time lost in the course of management, these neoplasms may be considered to be a major health issue and, therefore, early recognition is vital in reducing the morbidity and mortality associated with late diagnosis. Besides, even if disease control is achieved, it is normally at the expense of substantial functional loss and disfigurement and, therefore, adversely influences the quality of life of affected patients. Awareness of the occurrence and clinical features of these neoplasms may help health care institutions and policy makers in improving the overall care of this special group of patients.

Paediatric orofacial malignant neoplasms have been described as rare in other parts of the world and most of these studies have focused on retrospective reviews of patients' records. As a result, data on clinical features at presentation may be incomplete. There is scanty information in Kenya regarding orofacial malignant neoplasms in the paediatric age group. Therefore, this could be the first such study focusing on the clinical presentation and histopathologic features of paediatric orofacial malignant neoplasms.

Correct and early diagnosis is important in reducing costs incurred during their management. This study certainly yields important data for oral and maxillofacial surgeons as well as other health professionals from related disciplines involved in the care of paediatric patients.

1. 3. Objectives of the study

1. 3. 1. Main Objective

To describe the clinical presentation and histopathologic types of paediatric orofacial malignant neoplasms.

1. 3. 2. Specific Objectives

1. To describe the demographic pattern of paediatric orofacial malignant neoplasms.
2. To describe the clinical presentation of paediatric orofacial malignant neoplasms.
3. To describe the histopathologic types of paediatric orofacial malignant neoplasms.

1.4 Hypothesis

Burkitt's lymphoma shall be the most common paediatric orofacial malignant neoplasm.

CHAPTER 2

2. 0. Materials and Methods

2. 1. Study design

Descriptive cross-sectional hospital-based study.

2. 2. Study area

The study was conducted at KNH and UNDH. KNH is the largest national referral, teaching and research hospital in Kenya. Patients are admitted with orofacial diseases to various wards including ENT, ophthalmology, paediatric oncology and oral and maxillofacial surgical wards.

2. 3. Study population

The study involved paediatric out-patients and in-patients aged 15 years and below visiting the Oral and Maxillofacial Surgical ward at the UNDH and paediatric in-patients at KNH in the Paediatric, Oral and Maxillofacial Surgery, ENT, Ophthalmology and Paediatric Oncology wards. The study was conducted from July, 2008 to December, 2008.

2. 4. Variables

Variable	Description	Scale of measure
Socio-demographic variables		
• Age	Age of patient in years	Interval
• Gender	Male or female	Nominal
• Nationality	Country of origin/birth	Nominal
• Residence	Where the patient lives (District/Province)	Nominal
Independent variables		
Clinical presentation		
• Site		Nominal
• Size (known anatomic landmarks)		Interval
• Duration		
• Pain		Interval
• Swelling/deformity/facial asymmetry		Nominal
• Bleeding		Nominal
• Disordered sensation		Nominal
• Constitutional symptoms (anorexia, weight loss, pallor)		Nominal
• Family history of similar illness		Nominal
• Nasal symptoms (discharge, obstruction, epistaxis)		Nominal
• Eye symptoms (visual disturbances, excessive tearing)		Nominal
Dependent variables		
• Histopathologic diagnosis		Nominal

2. 5. Sampling procedure

The sampling unit was the paediatric in- patient and out- patient with orofacial malignant neoplasm. Convenience sampling was used and included all paediatric patients with the histopathological diagnoses of orofacial malignant neoplasms who met the inclusion criteria. The orofacial region was defined by the following boundaries: inferiorly- the sublingual and submandibular triangles bilaterally, posteriorly- external acoustic meatus and superiorly- anterior part of the scalp including the temporal regions (Fig. 1). Tumours arising within the confines of the dura were excluded.

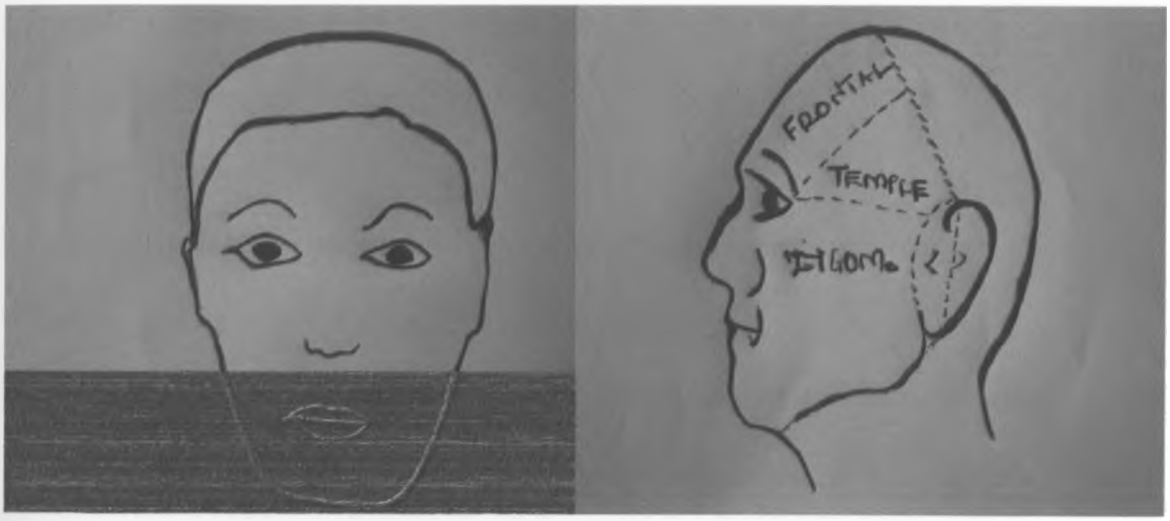

Fig. 1. Orofacial region description.

2. 5. 1. Sample size determination

The sample size was determined using Epi info™ version 6 statististical programme for calculating sample size for descriptive studies. With a power of 80, 95% confidence level and least expected frequency of 8% and worst expected frequency of 14.4% (Johnson,

1991 ;Keszler et al., 1990) the sample size required was 40. However, all the patients (65) who fulfilled the criteria during the study period were included in the data analysis.

2. 6. Inclusion criteria

1. Paediatric patients aged 15 years or less with confirmed histopathological diagnosis of orofacial malignant neoplasms.

2. Paediatric patients whose parents or legal guardians consented to the study.

3. Paediatric patients who gave assent to the study.

2. 7. Exclusion criteria

1. Paediatric patients with no confirmed histopathological diagnosis of orofacial malignant neoplasms.

2. Paediatric patients whose parents or legal guardians did not consent (except infants).

3. Paediatric patients who did not assent to the study.

4. Paediatric patients without clinical evidence of tumour on physical examination.

5. Paediatric patients with unverifiable neoplastic lesions.

2. 8. Data collection and analysis

An interviewer-administered questionnaire and clinical examination form were used to record data obtained from the interviews, clinical examination and laboratory histopathology reports (Appendix 1). The data collected included demographic details, clinical features and histopathologic diagnosis as reported by histopathology laboratories

at the KNH and the UNDH. Size was described using clearly defined anatomical landmarks.

2. 8. 1. Validity and reliability of the data

Prior to data collection, the principal investigator was calibrated by one of the supervisors to measure the intra-examiner reliability. A repeat examination on every tenth case was done to enhance reliability. A kappa value of 1 was obtained. Reliability was further enhanced by ensuring that only histopathological reports from two laboratories, the KNH and UNDH, were used for the purpose of this study.

2. 8. 2. Data analysis and presentation

Data were coded and major trends described using the Statistical Package for Social Sciences (SPSS) 12.0 programme. Descriptive statistics included measures of central tendency and dispersion for continuous variables and proportions for categorical variables. Differences between dependent variables and independent variables were analysed using Pearson's chi square test and/or Fisher's exact test. A P- value of <0.05 was considered significant. The results were presented in the form of tables, pie-charts and bar graphs.

2. 9 Ethical considerations

Ethical clearance to carry out the study was sought and granted by the KNH and the University of Nairobi (UoN) ethics, research and standards committee for approval (Approval No. P97/05/2008). The purpose of the study, expected risks and benefits were

explained to the patients and their parents/legal guardians. Assent from patients/written informed consent by parents/legal guardians to participate in the study and publish the results was then sought (Appendix 3).

CHAPTER 3

3. 0. RESULTS

3. 1. Socio- demographic characteristics

The study included 65 children among whom 44(67.7%) were male and 21(32.3%) female (Fig. 2) accounting for a male to female ratio of 2.1:1. The age ranged from 0.25 years to 14 years (Fig. 3) with a mean of 5.3 years (± 3.4 SD). On average the female participants were slightly younger (mean 4.2 years ± 3.3 SD) than male participants (mean 5.8 years ± 3.4 SD). However, the difference was not statistically significant (t=1.81, P=0.078). As shown in Table 1, most patients came from Western province followed by Coast province and Nyanza in reducing order.

Table 1. Distribution of patients according to place of residence.

Province	**Number of patients**
Western	15
Coast	13
Nyanza	12
Eastern	11
Central	9
Rift Valley	3
North Eastern	1
Nairobi	1
Total	**65**

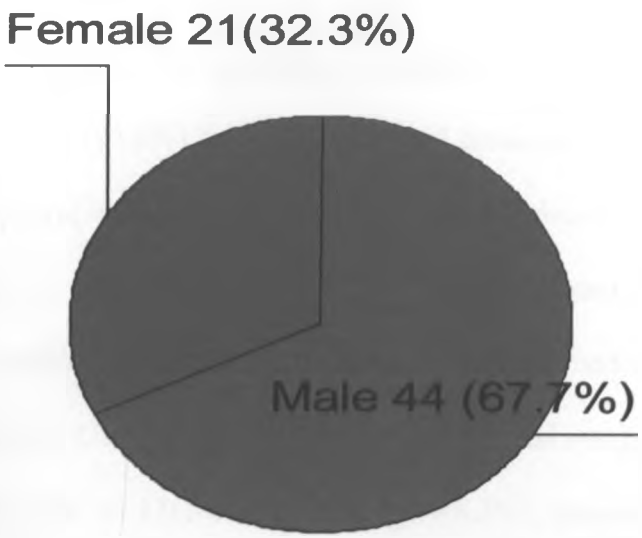

Fig.2. Distribution of patients according to gender.

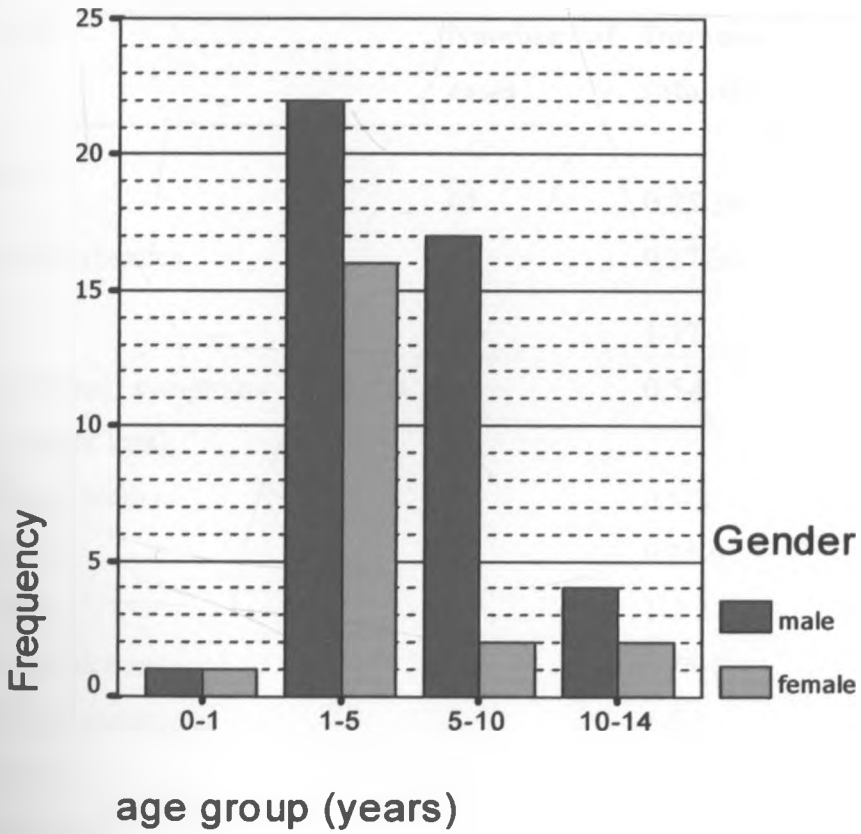

Fig.3. Distribution of patients according to age.

3. 2. Symptoms

Table 2 shows the presenting complaints of the patients. The main complaint was swelling 61(93.8%) followed by visual disturbance 29(44.6%). A higher proportion of females 16(76.2%) complained of visual disturbance compared to males 13(29.5%). This difference was statistically significant (Fisher's exact test = 0.001). Seventeen (26.2%) of the patients complained of pain, 11(16.9%) had mobile teeth and 8(12.3%) had ulceration. Other complaints were constitutional symptoms including anorexia, fever and weight loss in 11(16.9%), bleeding 4(6.2%), dysaesthesia/paraesthesia 4(6.2%), nasal obstruction 4(6.2%), epistaxis 3(4.6%) and proptosis 1(1.5%).

Table 2. Presenting complaints.

Symptom	Number of cases	Duration (Months)	Percentage (N=65)
Swelling	61	0.25-36	93.8%
Visual disturbances	29	0.17-30	44.6%
Pain	17	1-12	26.2%
Constitutional symptoms (anorexia, fever, weight loss)	11	0.5-8	16.9%
Mobility of teeth	11	0.5-3	16.9%
Ulceration	8	0.25-9	12.3%
Bleeding	4	1-3	6.2%
Nasal obstruction	4	0.75-6	6.2%
Disordered sensations	4	1-2	6.2%
Epistaxis	3	0.5-2	4.6%
Eye proptosis	1	1	1.5%

Overall, the mean duration of the presenting symptoms (Table 2) ranged between 0.17-36 months. Patients with epistaxis, ulceration, bleeding and dysaesthesia/paraesthesia seemed to present earlier than patients with pain and swelling. However, patients with FS, nasopharyngeal carcinoma (NPC), Kaposi's sarcoma (KS) and non- Burkitt's/non-Hodgkin's lymphoma (NB-NHL) presented earlier with dysaesthesia/paraesthesia, visual disturbances, swelling and mobility of teeth respectively. Notably, and with the exception of RTB, the presentation of patients with sarcomas was relatively earlier than for carcinomas and lymphomas.

Table 3. Mean duration of symptoms of orofacial malignant neoplasms (months).

Symptom	RMS	FS	SCC	BL	NPC	RTB	KS	NB-NHL	OS
Bleeding	1	2	2.5	-	-	-	-	-	-
Ulceration	2	2	5.5	0.4	-	0.5	-	-	1
Pain	5.1	3	7.5	5	-	6.3	-	-	1.7
Swelling	7.9	4	2	2.6	1	14.7	5.3	6.5	1.8
Disordered sensations	1.5	1	-	-	-	-	-	-	1
Epistaxis	2	-	-	0.7	-	-	-	-	-
Visual disturbances	3.9	-	-	-	0.25	11.3	-	-	-
Mobility of Teeth	3	-	-	1.5	-	-	-	1	-
Constitutional symptoms	4	2	3.3	2	3	0.5	8	-	-

3. 3 Signs

On physical examination, the most frequent signs associated with the neoplasms were leucocoria 23(35.5%), proptosis 19(29.2%) and loss of vision 15(23.1%) (Fig.4). The patients with leucocoria comprised 10(22.7%) males and 13(61.9%) females. This difference was found to have been statistically significant (Fisher's exact test = 0.005). Patients with loss of vision comprised 6(13.6%) males and 9(42.8%) females and this difference in gender was also found to have been statistically significant (Fisher's exact test = 0.01). Other frequent signs were ulceration 11(16.9%), regional lymphadenopathy 9(13.8%) and tooth mobility 8(12.3%). The least common signs were discolouration (4), eye injection (2), exposure keratitis (2), surface necrosis (1), albinism (1), loss of tactile sensations (1), cortical bone expansion (1), trismus (1), splenomegaly (3), pus discharge (3), bleeding (2) and tenderness (2).

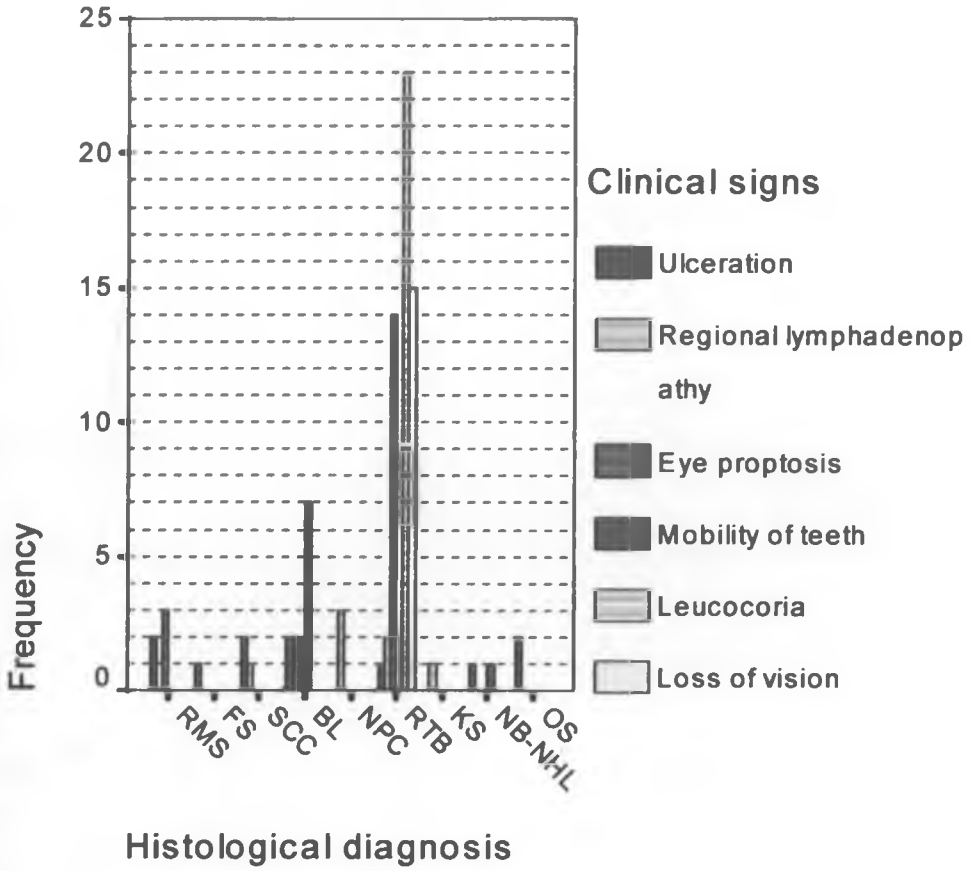

Fig.4. Common signs associated with orofacial malignant neoplasms.

3. 4. Site distribution of neoplasms

As depicted in Table 4, the most common site was the eye/orbit 30(46.2%), followed by the maxilla 11(16.9%) and other sites on the face 10(15.4%) which excluded all neoplasms located in the eye/orbit and parotid regions. The submandibular region constituted 6(9.2%) of the malignancies while the mandible accounted for 4(6.2%) of them. Only 2 of the tumours were located intra- orally and 1 in the parotid region. One patient presented with a neoplasm involving the maxilla, mandible and the face.

Table 4. Site distribution of orofacial malignant neoplasms.

Site	Frequency (N=65)
Eye/Orbit	30 (46.2%)
Maxilla	11 (16.9%)
Other sites on the face	10 (15.4%)
Submandibular region	6 (9.2%)
Mandible	4 (6.2%)
Intra-oral	2 (3.1%)
Maxilla, mandible and other sites on the face	1 (1.5%)
Parotid region	1 (1.5%)

3. 5 Histopathologic types of neoplasms

Nine histopathologic types of orofacial malignant neoplasms were encountered during the study (Fig. 5). A majority of the neoplasms were RTB which accounted for 40% (26) of the cases. These were followed by 21.5% (14) cases of BL, 13.8% (9) of RMS, 9.2% (6) of NB-NHL, 4.6% (3) of OS, 4.6% (3) of KS, 3.1% (2) of SCC, 1.5% (1) of FS and 1.5% (1) of NPC.

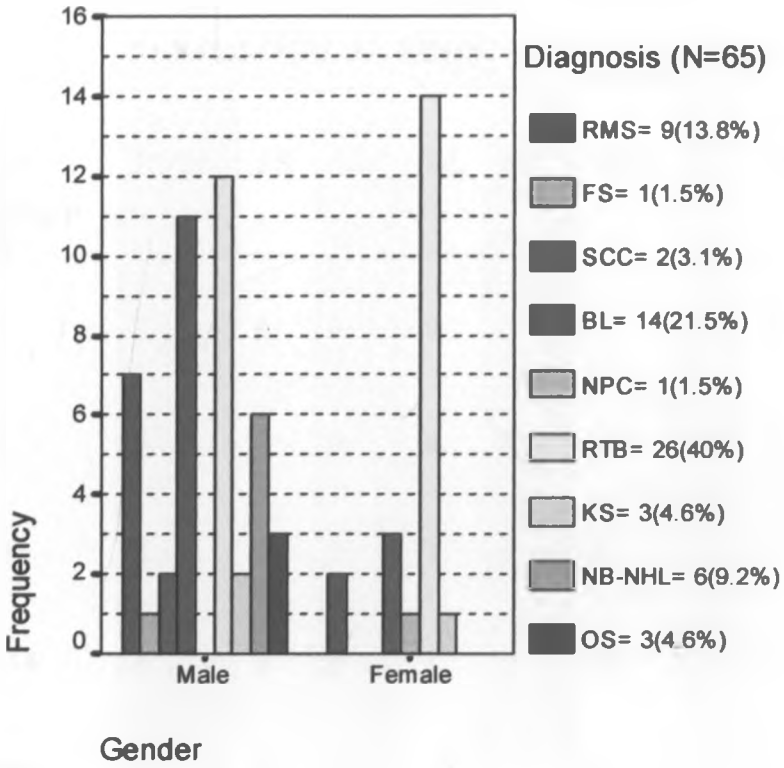

Fig. 5. Histological diagnosis of orofacial malignant neoplasms.

Most neoplasms occurred in patients aged less than 5 years (40 cases) followed by 19 cases in children aged between 5 and 10 years. Only 2 infants were diagnosed with malignant neoplasia (Table 5).

Table 5. Patient ages at diagnosis of orofacial malignant neoplasms.

AGE GROUP	HISTOLOGICAL FINDINGS									Total (%)
	RMS	FS	SCC	BL	NPC	RTB	KS	NB-NHL	OS	
0-1	1	0	0	0	0	1	0	0	0	2 (3.1)
1-5	4	1	0	6	0	23	1	2	1	38(58.5)
5-10	3	0	2	7	0	2	1	4	0	19(29.2)
10-14	1	0	0	1	1	0	1	0	2	6(9.2)
Total	9	1	2	14	1	26	3	6	3	65(100.0)

3. 5. 1. Squamous cell carcinoma (SCC)

Two cases of SCC were encountered during the study both cases having been males aged 5 and 10 years (Table 4). The 2 cases presented with constitutional symptoms including pain, bleeding and ulceration. The duration of symptoms was 6 to 9 months with a mean of 7.5 months. The neoplasms were located both intra- and extra- orally and were associated with regional lymphadenopathy and splenomegaly. One of the cases had albinism.

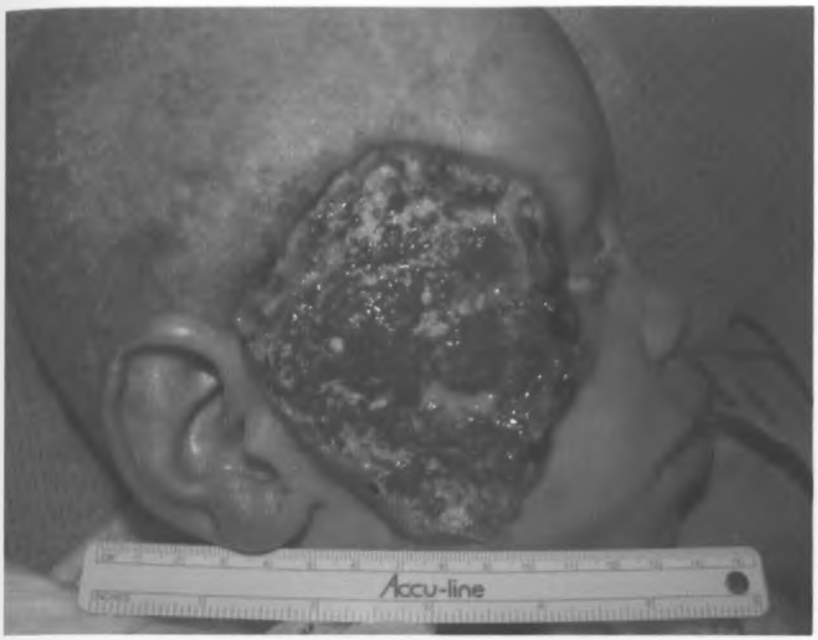

Fig.4. Presentation of SCC of the temple in a 5- year- old male.

3. 5. 2. Non-Hodgkin's lymphoma (NHL)

NHL accounted for 30.5% (20) of all the neoplasms with BL (14 cases) forming a majority of these cases. There was a male preponderance in the occurrence of BL with a male to female ratio of 3.7:1. However, this difference was not statistically significant ($P>0.05$). A majority of these neoplasms were diagnosed in children aged between 1 and 10 years (Table 5). There was no associated positive family history. The commonest sites of occurrence were the jaws (maxilla and mandible) for BL and in the submandibular region for the other types of NHL. Most patients with BL complained of swelling and mobility of teeth of duration ranging from 0.25 to 5 months. Clinically, most lesions were associated with mobility of teeth, ulceration and regional lymphadenopathy.

3. 5. 3. Retinoblastoma (RTB)

There were 26 cases (40%) of RTB with a male to female ratio of 1: 1.2. This difference was found to have been statistically significant ($P<0.05$). A majority of the cases (23 out of 26) were found in patients aged between 1 and 5 years with 1 case occurring in an infant (Table 5). All cases involved the eyes and most presented with visual disturbance and swelling ranging from 0.5 to 30 months in duration. One case was associated with a positive family history in a sibling. The commonest clinical findings were leucocoria, proptosis and loss of vision.

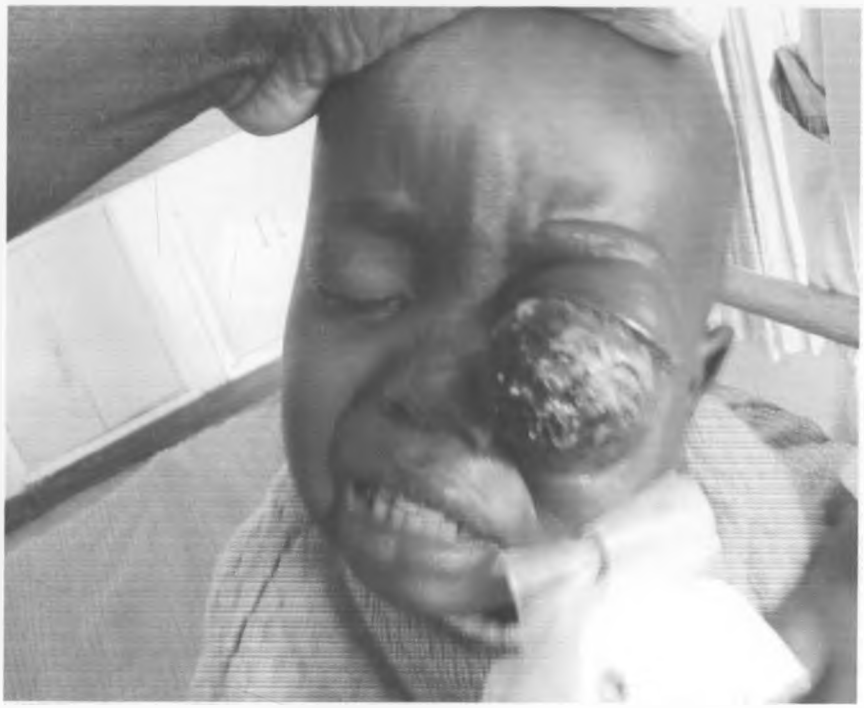

Fig. . Clinical apppearance of retinoblastoma in a 3- year- old male.

3. 5. 4. Rhabdomyosarcoma (RMS)

Nine cases of RMS were diagnosed in 7 male and 2 female patients giving a ratio of 3.5:1 respectively. This difference was not statistically significant ($P>0.05$). All the cases (8)

except one occurred in the first decade of life and involved mainly the facial and eye/orbital regions. The main presenting symptoms were swelling, pain and visual disturbances of about 0.17 to 24 months in duration. The principal findings on clinical examination were proptosis and ulceration

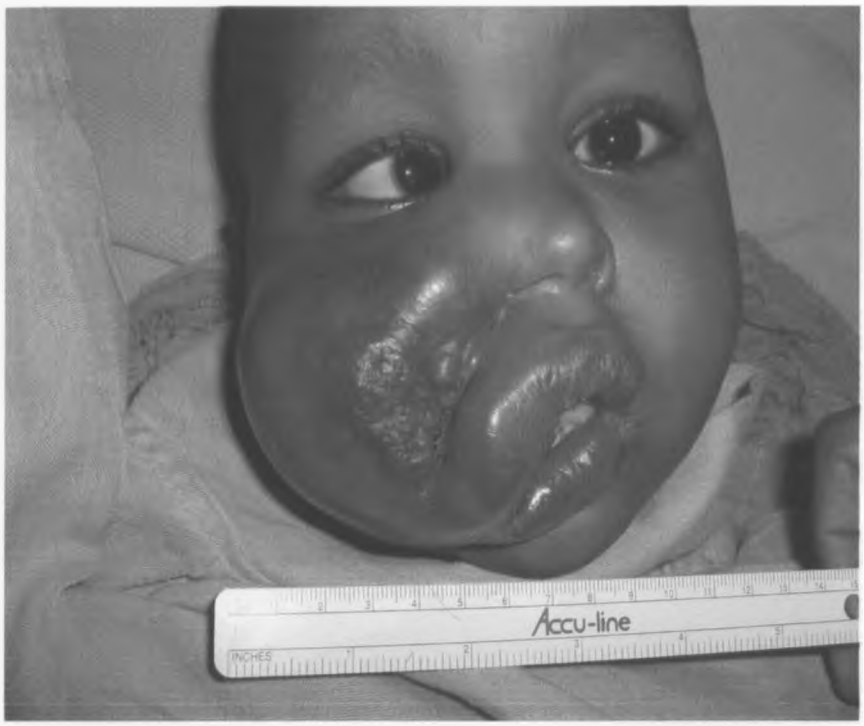

Fig. 8. Clinical presentation of RMS in the right labiobuccal tissues in a 3- year- old male.

3. 5. 5. Kaposi's sarcoma (KS)

There were 3 cases of KS among whom 2 were male (8 and 12 years old respectively) and 1 female (2 years old). The sites of presentation were the face, parotid and submandibular regions. The presenting symptoms included swelling and constitutional symptoms lasting about 4-8 months in duration. The most notable feature on clinical examination was the presence of regional lymphadenopathy.

3. 5. 6. Osteosarcoma (OS)

There were 3 cases of osteosarcoma all occurring in males aged 5, 11 and 13 years respectively. The lesions were found in the mandible and maxilla. The presenting complaints included pain, swelling, ulceration and dysaesthesia/paraesthesia lasting from 1 to 3 months in duration. Clinical examination confirmed the presence of ulceration, cortical bone expansion and loss of tactile sensation.

3. 5. 7. Fibrosarcoma (FS)

There was one case of FS in a male aged 4.5 years and presented in the face with ulceration, pain, bleeding and dysaesthesia. The individual symptoms ranged from 1 to 4 months in terms of duration with swelling and pain having been the initial symptoms. There was evidence of bleeding, ulceration and surface necrosis on clinical examination.

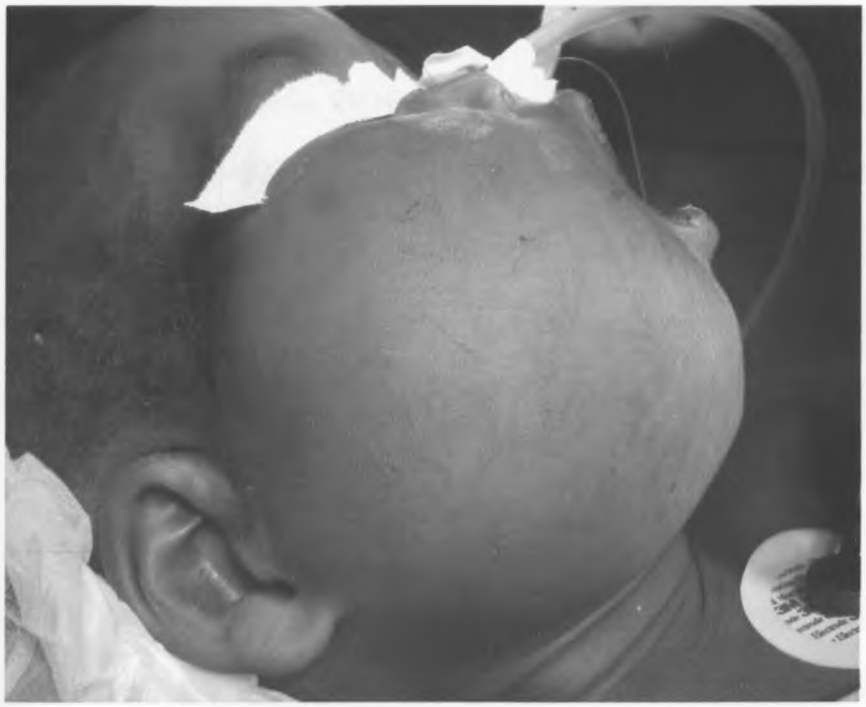

Fig. 9. Clinical presentation of FS involving the entire right side of the lower and mid- face in a 4.5- year- old male.

CHAPTER 4

4. 1. DISCUSSION

In general, the presenting signs and symptoms of the paediatric orofacial malignant neoplasms diagnosed in this study were closely correlated to the anatomic structures primarily affected and immediately contiguous to the malignancies. A majority of the tumours were found to involve the eye/orbital region followed by the other sites in the face, maxilla, submandibular region, mandible, intra- oral sites and the parotid area in reducing order of distribution. All were noted to have been primary tumours and most had no obvious clinical evidence of distant metastasis. Age differences were noted with most neoplasms having been more prevalent among children aged less than 10 years. BL was more prevalent in boys than girls and mainly extra- nodal with jaw swelling and tooth displacement. These findings were comparable to those in other similar studies done in Kenya (Mwanda, 2004; Mwanda, 1999), the rest of Africa (Otmani et al. 2008; Ugboko et al. 2004; Dubey et al. 1998; Hesseling et al. 1989) and the United States of America (Patton et al. 1990). Generally, and in agreement with some studies, sarcomas affected younger patients more than carcinomas save for RTB (Chidzonga, 2006; Aregbesola et al. 2005; Parkin et al. 1993; Johnson, 1991).

In terms of duration of symptoms, patients with RMS, BL, NPC and RTB were more likely to have sought treatment earlier than those with NB-NHL, OS, FS, KS and SCC. In addition, the general observation in this study was that patients with neoplasms associated with bleeding, ulceration, epistaxis and dysaesthesia sought treatment earlier even if pain and swelling had been the initial symptoms. Therefore, it may be speculated

that certain symptoms associated with malignancies may reflect the treatment seeking behaviour of the patients. However, caution should be exercised in the interpretation of these results because very young patients, especially those below 5 years of age including infants, are unlikely to complain of pain.

As a whole, RTB was the commonest malignant neoplasm (40%) followed by BL (21.5%) and RMS (13.8%). This compares well with other reports where RTB has been shown to be the most common primary eye cancer in children less than 15 years of age, habitually occurring in infancy, even in utero, but also being diagnosed in older children and young adults (Balmer et al. 2006). The higher proportion of girls seen among the RTB group was statistically significant ($P<0.05$) when compared with the overall group of cancer patients studied. This is in contrast to reports in the literature which show that RTB does not have an obvious predilection for gender (Balmer et al. 2006). Broader multi- centre studies are needed to confirm whether these data reflect the trend in our population. The finding of only one case of RTB with a positive family history may confirm the findings by Balmer et al. (2006) that a majority of RTB are sporadic in nature (60%) compared to heritable cases (40%) (Balmer et al. 2006). Abramson et al. (1998) in a retrospective chart review of 1265 patients with RTB over a 30- year period, found that 6.8% (86) of the patients had a positive family history. Eighty- three (96.5%) percent of those patients presenting with a family history did so before the age of 24 months. Given the current high rates of morbidity and mortality associated with RTB in Kenya (Mwanda, 1999), close follow- up of family members of RTB patients is recommended. The commonest presenting signs observed in this study could be as a result of the higher

proportion of RTB. This is in agreement with other reports that describe leucocoria, strabismus and poor vision as the commonest clinical features of RTB at presentation (Abramson et al. 1998).

OS of the jaws had a similar presentation of pain, swelling and paraesthesia as reported in other studies (Chindia, 2001; Shafer et al. 1983). RMS occurred with a higher proportion in males than females (male to female ratio of 3.5:1). This compares well with findings by Agarwala (2006) who reported a male to female ratio of RMS as 1.3-1.4:1 with a peak between 2-6 years. For most of the other neoplasms, the socio-demographic characteristics could not be compared well due to differences in the study methodologies, and also due to the relatively low occurrences of these tumours in paediatric patients.

4. 2. CONCLUSIONS

Paediatric orofacial malignancies were more common in males than females except for RTB which was more common among female patients. Most of the malignancies were observed in the age group of 1-5 years. The clinical features of most paediatric orofacial malignant neoplasms depended mainly on the site of primary involvement with swelling having been the most common presenting complaint irrespective of tumour type. The most common sign was visual disturbance including leucocoria, loss of vision and proptosis. The commonest site of presentation was the orbital region and most neoplasms were advanced at the time of diagnosis. RTB accounted for the majority of paediatric orofacial malignancies followed by BL and RMS.

4. 3. RECOMMENDATIONS

1. It is necessary to conduct population based studies targeting the different types of paediatric orofacial malignant neoplasms, especially RTB, to ascertain their exact incidence and prevalence in Kenya.
2. There is need to formulate strategies aimed at educating the public on the recognition of the clinical features of paediatric orofacial malignant neoplasms to ensure that early treatment is sought.
3. Research should be conducted to establish other reasons behind patient presentation with advanced disease to ensure prompt intervention so as to reduce morbidity and mortality.

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4. 5. Appendices

4. 5. 1 Appendix 1: Questionnaire and data collection forms

Questionnaire

1. Patient number .....Ward/Clinic.....

2. Age of patient (yrs) .....

3. Gender of patient: Male Female = 1, 2

4. Nationality: Kenyan Non- Kenyan = 1, 2

5. Residence: Urban Rural = 1, 2

6. Presenting complaint (s): Tick as appropriate

Symptom	Yes	No	Duration (months)
Pain			
Ulceration			
Bleeding			
Disordered sensations			
Swelling/facial asymmetry			

Constitutional symptoms

(anorexia, pallor, weight loss)

Loose teeth

Nasal symptoms (discharge, obstruction, epistaxis)

Eye symptoms (visual disturbance, epiphora, photophobia)

---

7. Any family member with similar ailment: Yes No

If yes, state type of relationship: Father

Mother

Sibling

Other

(Specify).....

Laboratory Report

8. Histopathological diagnosis: Yes No

9. Reporting laboratory: KNH

UNDH

Other

(Specify).....

10. Histological finding.....

CLINICAL EXAMINATION FORM

Sign	Observation
Site	
Size of swelling (in mm or known anatomic landmarks)	
Bleeding	
Ulceration	
Discolouration	
Others	

4. 5. 2 Appendix 2: Consent form

CONSENT INFORMATION (ENGLISH VERSION)

Researcher greets and introduces himself to the patient and parent/legal guardian

Dear **Patient/Parent/Guardian,**

Purpose of study

I am conducting a research to find out the nature of disease your child is suffering from. I need to establish how this disease has affected him/her and how it has progressed since it was noticed.

Procedure

It involves clinical examination and answering some questions to ascertain that the patient has the condition under investigation. The questions asked will be on whether there is a history of similar illness in the family, on the medical and surgical history and history of the illness itself since it started.

Risks

There will be no risks involved because invasive procedures will not be performed and the entire clinical examination will be carried out under absolute hygienic measures. In cases where a biopsy will have to be taken, it will be done under aseptic techniques and adequate local anaesthesia.

Benefits

The study will help us in improving care of children who may have similar disease in our set-up. Information from the study and follow up studies will also help provide options for preventive measures and resource planning.

Participation

The participation is voluntary and you are free to ask any questions in relation to the study. Whatever decision you make, I thank you for your time and support.

Costs

The entire examination is free.

Confidentiality

The patient's identity and the results of the investigation shall be confidential.

I, **Dr. Sanya, B. O.**, confirm that I have explained the relevant parts of the study to the participant/parent or guardian.

Signed…….. Date…….

I, **the parent/guardian**, confirm that I have understood the relevant parts of the study and do hereby give consent to the participation of my child as explained to me by Dr Sanya, B. O.

This agreement is voluntary and without coercion and I further consent to the free use of this information and conclusion drawn among health professionals and any other persons involved in the improvement of human life.

I understand that while my child will be provided with optimum clinical care like all other patients in the hospital, he/she will not be provided with any form of compensation for the voluntary information I have given to the investigator.

Name.....

Signed..... Date.....

Contact of Investigator

Dr. Sanya B.O.

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School of Dental Sciences

University of Nairobi

Cellphone: = +254-722-313533

TAARIFA YA USHIRIKI (KISWAHILI VERSION)

Mtafiti anatoa salamu na kujitambulisha kwa mgonjwa na mzazi

Kwa **mgonjwa/mzazi mpendwa,**

Sababu ya utafiti

Ninafanya utafiti kupata kujua aina ya ugonjwa ambao mtoto wako anaugua. Ninahitaji kuthibitisha jinsi ugonjwa huu umemwathiri mtoto wako tangu ulipoanza hadi sasa.

Muundo msingi

Unahusu uchunguzi wa kidaktari na kujibu maswali fulani ili kuhakikisha kama mgonjwa anao ugonjwa unaochunguzwa. Maswala haswa ni kama kumekuwepo na ugonjwa kama huo kwa jamii na historia ya matibabu yoyote tangu ugonjwa ulipoanza.

Matatizo

Hakuna matatizo yoyote yanayotarajiwa kutokana na utafiti huu kwani utafanyika kwa hali ya usafi sanifu. Iwapo sehemu kidogo ya uvimbe itahitajika kutolewa, itafanyika kwa usafi sanifu na baada ya kupeana dawa ya kuzuia uchungu.

Mafanikio

Utafiti huu utatusaidia kuboresha utunzi wa watoto wengine ambao wanaweza kuwa na ugonjwa sawia. Matokeo pia yatachangia kufwatiliza mwelekeo wa chunguzi zingine baadaye ili kusaidia upatikanaji wa mbinu nyinginezo za kuzuia kuchipuka kwa maradhi kama hayo.

Kuhusishwa

Kuhusika ni kwa hiari. Unao uhuru wa kuuliza swali lolote kuhusu utafiti huu. Ninashukuru sana kwa uamuzi wowote utakaochukua pamoja na muda wako ambao umenipa.

Gharama

Utafiti wote utakuwa bila malipo

Kuwekwa siri

Majina na picha za wahusika zitawekwa siri

Mimi, **Daktari Sanya, B.O.**, nathibitisha ya kwamba nimwelezea mhusika/mzazi sehemu zote za umuhimu katika utafiti huu.

Sahihi..... Tarehe.....

Mimi, **Mzazi,** nathibitisha ya kwamba nimeelewa sehemu muhimu za utafiti huu, na ninatoa ruhusa kwa mtoto wangu kuhusishwa, kama nilivyoelezwa na Daktari Sanya, B.O.

Makubaliano haya ni ya hiari bila kusurutishwa. Pia ninatoa ruhusa kwa utumiaji wa matokeo ya utafiti huu kati ya madaktari na watu wengine ambao wanahusika katika kuboresha maisha ya binadamu.

Ninaelewa ya kwamba ingawa mtoto wangu atapata utunzi mahususi wa kidaktari kama wagonjwa wengine hospitalini, hatapewa malipo yoyote kwa kujitolewa kuhusika kwa utafiti huu.

Jina.....

Sahihi..... Tarehe.....

Anwani ya Mtafiti

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Ref: KNH-ERC/ 01/ 516

20th June 2008

Dr. Sanya Bernard Okumu
Dept. of Oral & Maxillofacial Surgery
School of Dental Sciences
University of Nairobi

Dear Dr. Okumu

RESEARCH PROPOSAL: "CLINICO-HISTOPATHOLOGIC VARIATIONS AND FEATURES OF PAEDIATRIC OROFACIAL MALIGNANT NEOPLASMS" (P97/05/2008)

This is to inform you that the Kenyatta National Hospital Ethics and Research Committee has reviewed and **approved** your above cited research proposal for the period 20th June 2008 – 19th June 2009.

You will be required to request for a renewal of the approval if you intend to continue with the study beyond the deadline given. Clearance for export of biological specimen must also be obtained from KNH-ERC for each batch.

On behalf of the Committee, I wish you fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of database that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Yours sincerely

PROF A N GUANTAI
SECRETARY, KNH-ERC

c.c. Prof. K.M.Bhatt, Chairperson, KNH-ERC
The Deputy Director CS, KNH
The Dean, School of Dental Sciences, UON
The Dean, Dept. of Oral & Maxillofacial Surgery, UON
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