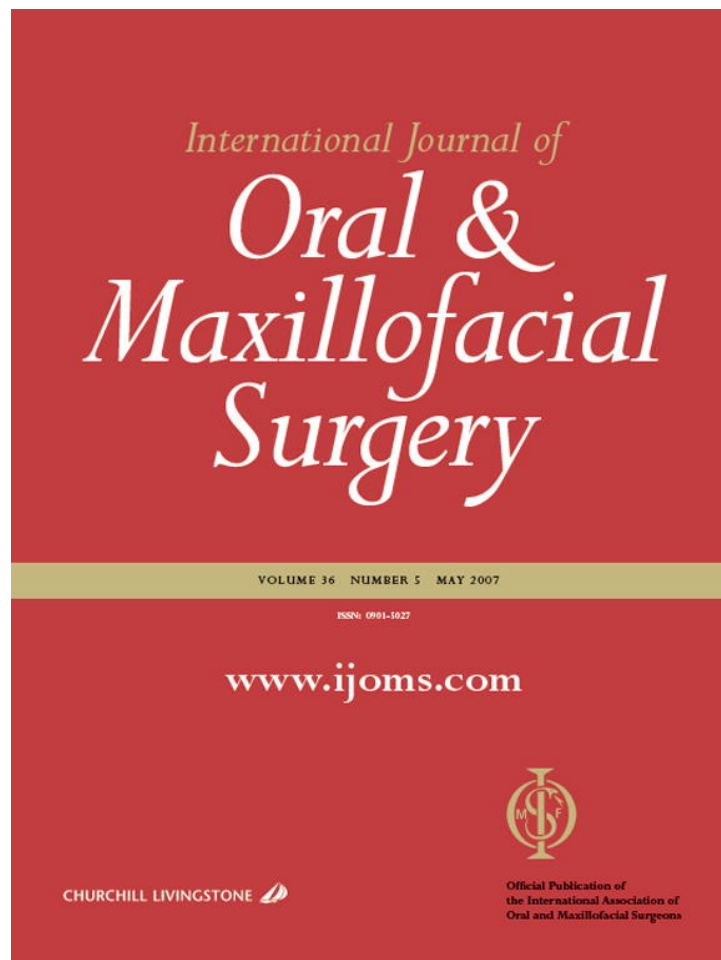


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Clinical Paper  
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# Primary malignant neoplasms of orofacial origin: a retrospective review of 256 cases in a Nigerian tertiary hospital

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**Abstract.** A retrospective review of cases histologically diagnosed as malignant lesions of the orofacial region in 1992–2003 from the records of the Department of Oral Pathology and Biology, Lagos University Teaching Hospital, Nigeria was carried out. All cases were subjected to analysis of age, gender, site distribution and histologic types. Malignant tumours constituted 18% of all the biopsies of orofacial lesions seen within the period. The mean age of patients was  $42.2 \pm 21.5$  years (range: 2.5–85). There were 177 (69%) epithelial tumours of which squamous cell carcinoma was predominant, 47 (18%) sarcomas and 32 (13%) lymphomas. Squamous cell carcinoma (44%) was the most common malignant orofacial tumour. Osteosarcoma (32%) and Burkitt's lymphoma (56%) was the predominant sarcoma and lymphoma, respectively. Patients with a histologic diagnosis of carcinoma were older than those with sarcomas and lymphomas ( $P < 0.01$ ), and those with a histologic diagnosis of malignant lymphoma were significantly younger than those with sarcomas ( $P < 0.01$ ). Almost 25% of patients with carcinomas were below the age of 40 years. Malignant orofacial tumours are not uncommon in the studied environment, with a sizable proportion of carcinomas occurring before the age of 40 years.

Key words: malignant neoplasms; orofacial region; retrospective study.

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Malignant lesions of the orofacial region are not uncommon<sup>9</sup>. They constitute the main life-threatening disease apart from maxillofacial trauma that may be encountered in dental practice. In most parts of

Europe and America, oral cancers account for 2–4% of all cancers<sup>23,40</sup>, but in India and Sri Lanka they are reported to account for up to 40% of all cancers<sup>9,40</sup>. Oral carcinoma is the most common malignant

tumour of the orofacial region constituting over 50% of these lesions<sup>1,17</sup>.

Oral carcinoma is an age-related disease, and about 90–95% of patients are reported to be over the age of 40 years<sup>22,38</sup>.

The overall incidence in the population is only about 1 in 20,000; this rises to 1 in 1100 in males of 75 years and above<sup>9</sup>. Squamous cell carcinoma (SCC) is the most common carcinoma of the orofacial region<sup>9,23,26,29</sup>. Sarcomas of the orofacial region are reported to be less common than carcinomas<sup>9,32</sup>. They account for less than 1% of all malignant neoplasms occurring in the head and neck in adults<sup>35</sup>. These tumours exhibit variable growth and degrees of aggressiveness that are primarily dependent on histologic grade. They tend to affect a considerably younger age group than carcinomas<sup>9,32</sup>. Lymphomas are malignant lesions that can arise from any type of lymphocyte, but most frequently from B-cells<sup>9</sup>. They comprise Hodgkin's and the more common non-Hodgkin's lymphoma. Lymphomas frequently involve the cervical lymph nodes but are rare in the mouth<sup>9</sup>.

There have been few reports published on malignant lesions of the orofacial region in an African environment<sup>4,13,17</sup>. The present study reviews 256 consecutive cases of orofacial malignant lesions seen over a 12-year period (1992–2003) at the Lagos University Teaching Hospital, Nigeria, with a view to highlighting age, gender, site distribution and histologic variants.

## Material and methods

A retrospective review of cases that were histologically diagnosed as malignant lesions of the orofacial region from January 1992 to December 2003 from the records of the Department of Oral Pathology and Biology of the Lagos University Teaching Hospital, Nigeria was carried out. The slides were reevaluated with a view to classifying the lesions. All cases were subjected to analysis of age, gender, site distribution and histologic types.

Data were analyzed using the software SPSS for Windows (version 12.0: SPSS, Chicago, IL, USA). Simple frequency charts, descriptive statistics and a test of significance were used (Chi-square and *t*-test). A level of  $P < 0.05$  was considered to be statistically significant.

## Results

A total of 256 malignant lesions of the orofacial region were diagnosed during the given time period. This represented 18% (256 out of 1431) of all the biopsies of lesions seen within this period. The age of patients ranged from 2.5 to 85 years (mean 42.2 years, SD 21.5 years). Fifty-one (20%) of these patients were  $\leq 20$  years. Patients

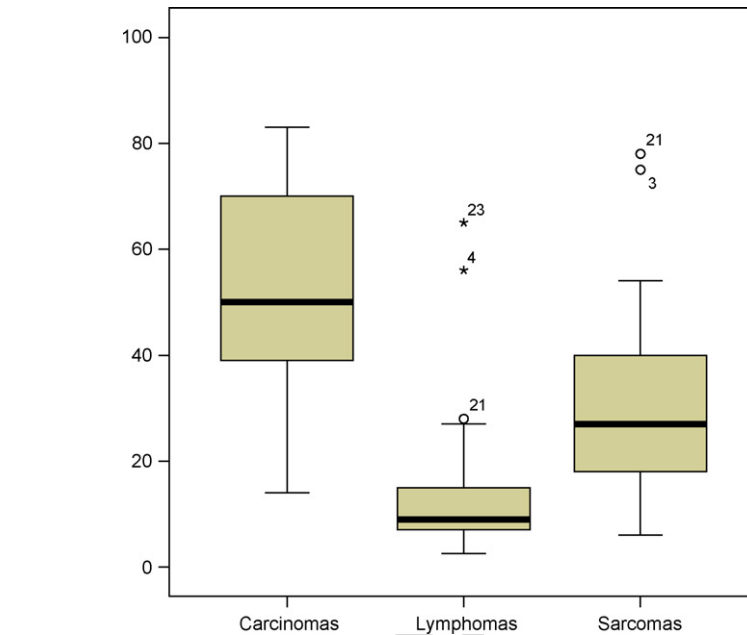


Fig. 1. Comparative analysis of age of patients with carcinomas, sarcomas and lymphomas ( $P < 0.05$ ). Medians and quartiles are displayed in the box plot, and the extreme values are represented by the horizontal lines outside the box. (Asterisks and circles outside boxes = outliers.)

with a histologic diagnosis of carcinoma were older than those with sarcomas and lymphomas ( $P < 0.01$ ), and those with a histologic diagnosis of malignant lymphoma were significantly younger than those with sarcomas ( $P < 0.01$ ) (Fig. 1). The male ( $n = 171$ ) to female ( $n = 85$ ) ratio was 2:1. Malignant non-odontogenic tumours were seen in 251 (98%) cases and malignant odontogenic tumours in 5 (2%). Epithelial tumours, mainly carcinomas, constituted 177 (69%) of the cases seen, followed by sarcoma, 47 (18%), and lymphoma, 32 (13%). SCC (44%) was the most common malignant orofacial tumour.

### Epithelial tumours

Epithelial malignant neoplasms constituted 12% (177 of 1431) of all the biopsies seen within the period. Mean age  $\pm$  SD of patients at presentation was  $51 \pm 17$  years (range 11–85 years). The majority (75%) of the patients were 40 years or above. The peak age of incidence was found to be in the 5th–8th decade of life. Table 1 shows age distribution of epithelial tumours. There were 118 males and 59 females at a ratio of 2:1. SCC was the most common lesion (63%), followed by adenocarcinoma (15%) and adenocystic carcinoma (9%) (Table 2). A case of malignant melanoma involving mandibular gingiva was seen in a 42-year-old woman. Common sites of occurrence were maxillary antrum (33%), mandible gingival/alveolus

(22%), palate (15%) and tongue (7%) (Table 2).

### Sarcomas

Sarcomas constituted 3% (47 of 1431) of all the biopsies seen within the period. The age of patients with a diagnosis of sarcoma ranged from 5 to 78 years (mean age  $\pm$  SD,  $29.2 \pm 17.2$  years). The peak age of incidence was in the 2nd and 3rd decades of life (Table 3). Male-to-female ratio was 1.6:1 (male, 29; female, 18), and 60% of patients were  $\leq 28$  years of age. The mandible was equally affected as the maxilla with a ratio of 1:1 (Table 4). Osteogenic sarcoma (32%) was the most common tumour, followed by fibrosarcoma (15%) and rhabdomyosarcoma (15%). Three (6%) cases of malignant fibrous histiocytoma (MFH) were also histologically diagnosed. Table 4 shows the distribution of sarcomas according to site of occurrence.

### Lymphomas

Lymphomas constituted 2% (32 of 1431) of all the biopsies seen within the period. Non-Hodgkin's lymphomas were diagnosed in 28 (88%) cases and Hodgkin's lymphomas in 4 (13%) cases. Mean age  $\pm$  SD of patients was  $14.7 \pm 14.1$  years (range 2.5–65 years). The peak age of incidence was in the first decade of life. Table 5 shows age distribution of

Table 1. Age distribution of orofacial epithelial malignant tumours

Histologic types	Age range (years)									Total (%)
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	
Squamous cell carcinoma	0	1	4	14	25	20	22	22	4	112 (63)
Adenocarcinoma	0	2	3	5	3	2	5	5	1	26 (15)
Adenocystic carcinoma	0	1	1	5	2	2	3	1	1	16 (9)
Mucoepidermoid carcinoma	0	1	0	4	4	0	2	0	0	11 (6)
Basal cell carcinoma	0	0	0	0	2	0	0	1	0	3 (2)
Carcinoma in pleomorphic	0	0	0	0	3	0	0	0	0	3 (2)
Ameloblastic carcinoma	0	0	0	0	0	0	2	0	0	2 (1)
Malignant ameloblastoma	0	0	1	0	0	0	0	0	0	1 (<1)
Malignant melanoma	0	0	0	0	1	0	0	0	0	1 (<1)
Odontogenic carcinoma	0	0	1	0	0	0	0	0	0	1 (<1)
Verrucous carcinoma	0	0	0	0	0	0	1	0	0	1 (<1)
Total (%)	0	5	10	28	40	24	35	29	6	177 (100)

Table 2. Distribution of epithelial malignant neoplasms according to site

Histologic types	Site of occurrence											Total
	Cheek	Fom	Lip	Man	Max	Subman	Palate	Parotid	Retro	Ton	Ns	
Squamous cell carcinoma	3	6	2	31	32	2	13	1	2	10	10	112
Adenocarcinoma	1	0	0	2	10	1	8	2	0	1	1	26
Adenocystic carcinoma	0	0	0	0	9	1	3	2	0	0	1	16
Mucoepidermoid carcinoma	0	1	0	1	4	1	1	2	0	1	0	11
Basal cell carcinoma	0	0	0	0	3	0	0	0	0	0	0	3
Carcinoma in pleomorphic	0	0	0	0	0	1	1	1	0	0	0	3
Ameloblastic carcinoma	0	0	0	1	0	0	0	0	0	0	1	2
Malignant ameloblastoma	0	0	0	1	0	0	0	0	0	0	0	1
Malignant melanoma	0	0	0	1	0	0	0	0	0	0	0	1
Odontogenic carcinoma	0	0	0	1	0	0	0	0	0	0	0	1
Verrucous carcinoma	0	0	1	0	0	0	0	0	0	0	0	1
Total	4	7	3	38	58	6	26	8	2	12	13	177

Fom, floor of the mouth; Man, mandible gingiva/alveolus; Max, maxillary antrum; Subman, submandibular; Retro, retromolar region; Ton, tongue; Ns, not specified.

Table 3. Age distribution of orofacial sarcomas

Histologic types	Age range (years)									Total (%)
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	
Osteosarcoma	0	4	4	4	2	0	0	0	0	14 (30)
Fibrosarcoma	0	3	4	0	0	0	0	0	0	7 (15)
Rhabdomyosarcoma	2	2	1	0	0	1	0	1	0	7 (15)
Chondrosarcoma	0	0	1	3	1	0	0	0	0	5 (11)
Neurofibrosarcoma	0	0	0	0	1	1	0	1	0	3 (6)
Ewing's sarcoma	1	2	0	0	0	0	0	0	0	3 (6)
Myxosarcoma	0	1	0	0	0	1	0	0	0	2 (4)
Liposarcoma	0	0	0	0	1	0	0	0	0	1 (2)
Spindle cell sarcoma	0	0	0	0	0	1	0	0	0	1 (2)
Odontogenic sarcoma	0	0	1	0	0	0	0	0	0	1 (2)
Malignant fibrous histiocytoma	0	2	0	0	1	0	0	0	0	3 (6)
Total (%)	3	14	11	7	6	4	0	2	0	47 (100)

the lymphomas. Male-to-female ratio was 3:1. Over 78% of these patients were below 20 years (Table 5). Lesions were commonly found in the maxilla (44%) and mandible (16%). Involvement of both the maxillary and mandibular bones was seen in 8 (25%) patients (Table 6).

Eighteen (64%) of the 28 cases of non-Hodgkin's lymphoma were Burkitt's lymphomas (BL) (Table 6). BL was only seen in the first and second decades of life (Table 5). Mean age (SD) of patients with

diagnosis of BL was  $8.0 \pm 2.6$  years (range 2.5-13 years). Males were eight times more affected than females (M:F ratio of 8:1), and the majority (56%) of cases involved the maxilla (Table 6).

## Discussion

Oral cancer is a growing health problem and is common in several regions of the world. Oral malignant neoplasms are the sixth most common malignancy in the

world, and when malignancy of the pharynx is included they account for the third most common malignancy in the developing world<sup>13,34</sup>. Global epidemiology shows that head and neck cancers constitute between 5% and 50% of all cancers, and the orofacial region has been reported to be a common site<sup>4,20</sup>. Many studies have shown that the wide variation in incidence of oral malignant neoplasia across the world can be partly explained by the difference in prevalence of the

Table 4. Site distribution of sarcomatous lesions

Histologic types	Site of occurrence							Total (%)
	Mandible	Maxilla	Lip	Cheek	Parotid	Zygoma	Ns	
Osteosarcoma	5	7	0	0	0	0	2	14 (30)
Fibrosarcoma	4	2	0	0	0	0	1	7 (15)
Rhabdomyosarcoma	3	3	1	0	0	0	0	7 (15)
Chondrosarcoma	3	1	0	0	0	1	0	5 (11)
Neurofibrosarcoma	3	0	0	0	0	0	0	3 (6)
Ewing's sarcoma	0	2	0	1	0	0	0	3 (6)
Myxosarcoma	1	1	0	0	0	0	0	2 (4)
Liposarcoma	0	1	0	0	0	0	0	1 (2)
Spindle cell sarcoma	1	0	0	0	0	0	0	1 (2)
Odontogenic sarcoma	0	1	0	0	0	0	0	1 (2)
Malignant fibrous histiocytoma	0	2	0	0	1	0	0	3 (6)
Total (%)	20	20	1	1	1	1	3	47 (100)

Table 5. Age distribution of orofacial lymphomas

Histologic types	Age range (years)									Total (%)
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	
Burkitt's lymphoma	14	4	0	0	0	0	0	0	0	18 (56)
Non-Hodgkin's lymphoma	3	3	3	0	0	1	0	0	0	10 (31)
Hodgkin's lymphoma	0	1	1	1	0	0	1	0	0	4 (13)
Total (%)	17	8	4	1	0	1	1	0	0	32 (100)

major risk factors in different geographic areas and also between genders<sup>8,23,36,40</sup>. Various known predisposing/aetiological factors that have been implicated are tobacco use, alcohol ingestion and smoked foods, very hot foods, viruses and industrial pollution<sup>23,25,39</sup>.

Orofacial malignancies are not uncommon at the centre studied, constituting 18% of all biopsies over a period of 12 years. CHIDZONGA<sup>13</sup> in a similar study from Zimbabwe reported that oral malignant neoplasms constituted 25% of all biopsies seen. In the present study, epithelial malignant neoplasms constituted 69% of malignant neoplasms seen. This is in agreement with reports in the literature<sup>1,2,13,17,33</sup>. Epithelial tumours are con-

sidered the most common malignant tumours of the orofacial region constituting over 50% of these lesions<sup>1,13,17,33</sup>. In the present study, in agreement with several previous reports<sup>4,13,36</sup>, sarcomas (18%) were the second most common malignancies of the orofacial region, although OTOH et al.<sup>33</sup> reported more cases of lymphomas than sarcomas.

Patients with a histologic diagnosis of carcinoma were found to be significantly older than those with sarcomas and lymphomas. In addition, patients with a diagnosis of sarcoma were found to be significantly older than those with lymphomas. Sarcomas and lymphomas have been reported to affect a considerably younger age group than carcinomas<sup>9,13,32,36</sup>. In

agreement with previous studies<sup>2,4,13</sup>, males were predominantly affected by the tumours in the present study.

Malignant odontogenic tumours constituted 2% of all tumours in comparison to malignant non-odontogenic tumours (98%). Malignant odontogenic tumours are rare<sup>27,28</sup>. They are reported to constitute less than 1% of all odontogenic tumours in America<sup>16</sup>, although higher incidences are reported from Africa and Asia<sup>27,30</sup>.

SCC was the most frequent histologic type of carcinoma in the present study. This is a common finding in other studies<sup>1,2,4,13,17,33,36</sup>. SCC constituted 44% of all the orofacial malignancies and 63% of all epithelial malignant tumours. This is in marked contrast to other reports<sup>8,38</sup>. CANTO & DEVESA<sup>8</sup> reported that SCC constituted 83% of oral and pharyngeal malignant tumours in the United States. In a recent study, SARGERAN et al.<sup>38</sup> reported that SCC constituted 87% of malignant lesions of the oral cavity in Iran. Whereas, maxillary antrum, mandibular gingiva/alveolus and palate were the most common sites of SCC in the present study, others<sup>8,12,13,15,26</sup> have reported mandibular gingiva, floor of the mouth and tongue as the most common. In sharp contrast to previous studies from the US which reported that the floor of the mouth and the tongue are the most frequent sites<sup>8,12,26</sup>, only 5% and 9% of SCC in the present series were found in the floor of the mouth and tongue, respectively. The frequent involvement of mandibular gingivae, floor of mouth and tongue in

Table 6. Characteristics of patients with a histologic diagnosis of lymphoma

	Histologic types			
	NHL*	HL	BL	Total (all lymphomas)
Age (years)				
Mean (SD)	11.9 ± 10.6	34.3 ± 21.5	8.0 ± 2.6	14.7 ± 14.1
Range (years)	2.5-56	19-65	2.5-13	2.5-65
Sex (%)				
Male	21 (75)	3 (75)	16 (89)	24 (75)
Female	7 (25)	1 (25)	2 (11)	8 (25)
Site of occurrence (%)				
Maxilla	14	0	10	14 (43)
Mandible	3	2	2	5 (16)
Mandible-maxilla	8	0	6	8 (25)
Neck	1	2	0	3 (9)
Palate	1	0	0	1 (3)
Submandibular gland	1	0	0	1 (3)

NHL, non-Hodgkin's lymphoma; HL, Hodgkin's lymphoma; BL, Burkitt's lymphoma.

\*NHL includes BL.

previous studies has been explained by the fact that carcinogens in either tobacco or alcohol, or dietary substances dissolved in saliva tend to pool and accumulate in gravity-dependent areas of the mouth<sup>12,26</sup>. In most series the hard palate is one of the sites of lowest risk<sup>23,26</sup>. The frequent involvement of the palate and maxillary antrum in the present study could point to some other aetiological factor apart from the traditional tobacco and alcohol. In addition, previous studies from India<sup>40</sup>, Zimbabwe<sup>15</sup> and Nigeria<sup>5,31</sup> have reported a high prevalence at these sites. In India, reverse smoking has been implicated, although the extent of this practice has not been investigated in Nigeria.

In the present study, carcinoma was found to be common in the 5th–8th decades of life. Oral carcinoma is an age-related disease, and about 90–95% of patients are reported to be over the age of 40 years<sup>22,38</sup>. Almost 25% of patients in this series were below the age of 40 years, and this frequency is higher than reported in Caucasians<sup>23,29</sup> but similar to other reports from Africa<sup>4,13,15</sup>. This may be due to a shorter life expectancy in Africans and/or early exposure to risk factors<sup>4</sup>. Nigeria is a country of about 131.8 million people with life expectancy (total population) at birth of 47.08 years (male = 46.52 years, female = 47.66 years)<sup>10</sup>. The percentage of people <40 years is much higher and life expectancy much lower in the general population than in the US<sup>10,11</sup>. This may be the reason for the higher frequency of carcinomas in patients below 40 years in the present study. It has also been reported in the UK and US that oral malignant neoplasia, in particular SCC, is now on the increase in a relatively young age group<sup>12,26</sup>.

Carcinomas arising from salivary glands (32%) were the second most common in the present study. This observation was also reported by others<sup>13,33</sup>. The majority (75%) of the glandular carcinomas arose from minor salivary glands. This is in agreement with several studies which reported a higher incidence of malignancy in minor salivary glands<sup>4,14,42</sup>.

A case of malignant melanoma involving mandibular gingiva was seen in a 42-year-old woman. This constituted <1% of oral epithelial malignancies and <1% of all oral malignancies seen in the present series. Mucosa melanoma of the oral cavity is rare<sup>13,43</sup>. It has been reported to account for <1% of all oral malignancies, and of all melanomas<sup>7,43</sup>. CHIDZONGA<sup>13</sup> in a recent study reported eight (2%) cases of malignant melanoma out of 428 oral malignant tumours. ATHEY et al.<sup>6</sup> recently

reported a rare case of malignant melanoma involving the maxillary antrum.

Sarcomas of the orofacial region are reported to be less common than carcinomas<sup>9,32</sup>. In the present study, they accounted for 18% of all malignant neoplasms of the orofacial region. As observed in the present series, they are reported to affect a considerably younger age group than carcinomas<sup>9,32</sup>. Osteosarcoma constituting 6% of all malignant tumours was the most frequently diagnosed sarcoma in the present study. This is a highly malignant tumour and is the most common primary malignant neoplasm of bone although rare in the maxillofacial region<sup>32</sup>. Three cases of malignant fibrous histiocytoma involving the maxilla (two patients) and parotid gland (one patient) were seen. Two of the three cases occurred in the 2nd decade of life (Table 3). MFH was first described in 1964 under the name malignant fibrous xanthoma. It is the most frequent soft-tissue sarcoma of adulthood<sup>18,39,44</sup>, although MFH of bone, first described by Feldman and Norman in 1972, may occur at any age<sup>16</sup>. Oral and maxillofacial sites are seldom involved<sup>18,39,44</sup>. In the head and neck, the nasal cavity and paranasal sinuses are the most commonly affected<sup>39,41,44</sup>.

Lymphomas constituted 13% of orofacial malignancies in the present series. This is higher than previous reports from Africa<sup>13,35</sup> and the Middle-east.<sup>36</sup> Non-Hodgkin's lymphomas constituted 88% of all lymphomas. Of these, BL (64%) was the predominant histologic variant. The age range of patients with BL was 2.5–13 years, with peak age of incidence in the 1st decade of life, predominantly affecting boys. BL is a common childhood malignancy in a number of African countries<sup>21,24</sup>. The Epstein–Barr virus is consistently found in tumour cells of BL<sup>3</sup>, which is endemic in East and Central Africa, where it is considered an aetiological factor with malaria also considered a pathogenic co-factor<sup>9,13,37</sup>. BL is predominantly extranodal, and is unusual in that its onset is in childhood and the jaw is the single most common initial site<sup>9</sup>. In the present series, BL constituted 7% of orofacial malignancies, and the majority were found in the maxilla. CHIDZONGA<sup>13</sup> in a recent study reported that BL constituted 5% of oral malignant neoplasia with male preponderance and occurred predominantly in the first decade of life.

Only four cases of Hodgkin's lymphoma constituting 13% of all lymphomas were recorded. Two cases each were found in the cervical lymph nodes and the mandible. Hodgkin's lymphoma is primarily a disease of lymph nodes and,

for this reason, seldom occurs as a disease primarily in the oral cavity<sup>37</sup>. A case of Hodgkin's lymphoma secondarily involving the mandible and the overlying alveolar mucosa has been previously reported<sup>19</sup>.

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