

# Predisposing Factors and Clinico-Pathological Presentation of Malignant Lesions Of the Oro-Facial region in Dar es Salaam, Tanzania

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## ABSTRACT

**Background:** The oro-facial region is made up of a complex anatomical relationship of structures which may be a source of development of malignant lesions. Majority patients who present at the oral and maxillofacial unit of MNH with a variety of malignant lesions are referred cases from upcountry district/regional hospitals and present with advanced stages of disease often with a wide range of complications. Of recent, there has been a dramatic change in the characteristics and demography of some of the common malignant lesions of the oro-facial region. Such changes might be attributed to predisposition or systemic changes following exposure to certain external factors.

**Objective:** To determine the predisposing factors and clinico-pathological presentation of malignant lesions of the oro-facial region among patients attending the Muhimbili National Hospital.

**Methodology:** This was a cross-sectional descriptive hospital-based study carried out in the

Department of Oral and Maxillofacial Surgery at the Muhimbili National Hospital. A sample of 186 patients with malignant tumours in the oro-facial region attended at MNH during the study period. For every patient, demographic details were recorded and history, clinical examination and laboratory investigations, including biopsy were done.

**Results:** A total of 186 patients, 104 (56.0%) males and 82 (44.0%) females with a ratio of 1.3:1 were included in the study. The age ranged from 3 to 83 years with a mean age of  $48.4 \pm 19.2$  SD years. Thirty-three percent of the patients were aged below 40 years. The commonest reported oral and maxillofacial malignant tumour was SCC with 96 (51.6%) patients followed by KS which had 17 (9.1%) patients and non-specific carcinoma 10 (5.4%) patients. Tobacco use was reported by 89 (47.8%) among whom 62 (69.6%) had used tobacco for more than 20 years. Ninety-six (51.6%) patients reported alcohol use among whom 49 (51.0%) reported to have used alcohol for more than 20 years. Thirty-three (17.7%) patients were HIV positive. All patients with KS were also HIV positive. MEP and PLGA were among very rare tumours occurring in the maxillofacial region that were encountered in this study.

**Key words:** Malignant lesions, maxillofacial region, Tanzania

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**Conclusion:** There was an increased frequency of malignant tumours in the oral and maxillofacial region among young patients. Tobacco use and HIV infection seemed to have influence on the occurrence of SCC and KS respectively. Majority of patients reported late with advanced disease and over 95% of patients with SCC presented with stages III or IV tumours.

## INTRODUCTION

Several studies have revealed an increase in number of oro-facial malignant tumours such as squamous cell carcinoma (SCC), adenoid cystic carcinoma, lymphomas and sarcomas<sup>1-7</sup>. The prevalence and predisposition of oral cancer have been reported to differ among different populations across the globe. According to the American Cancer Society, 39,440 new cases of oral cancer were expected in 2011<sup>8</sup>. In Canada, oral cancer was reported to account for 2.0% of all cancer cases while in the United Kingdom they accounted for 5.4% of all oral and maxillofacial specimens<sup>4,6</sup>. A study on oral and perioral cancers in Iran revealed that malignant lesions accounted for 6 percent of maxillofacial tumours<sup>9</sup>. In Indonesia and China, malignant tumors constituted 45.3% and 50% of oro-facial tumours respectively<sup>2,3</sup> and in Iran, the highest prevalence of about ninety percent was reported<sup>7</sup>.

The occurrence of oro-facial malignant lesions across Africa has shown variations in different countries with frequencies ranging between 18% and 75% reported in Nigeria, Zimbabwe, Tanzania and Uganda<sup>10-12</sup>. Malignant lesions occurring in the oro-facial region affect all age groups with frequencies generally increasing with advanced age<sup>13</sup>. A sex predilection has been reported with the oro-facial malignant tumours seen more commonly in males than in females. The male to female ratio has, however, been rapidly changing from 6:1 in the last few decades to 2:1 currently. In the extremes of old age, females have, however, shown to

predominate<sup>14</sup>. Kalyani et al.<sup>1</sup> reported a slightly higher female predominance on cancer profile in India.

The advent of the human immunodeficiency virus (HIV) infection has influenced changing patterns of occurrence of some disease conditions including malignant lesions. Oral Kaposi's Sarcoma (KS) has been reported to be the commonest oral malignant lesion among HIV/AIDS patients<sup>15,16</sup>. Malignant lymphoma (ML) mostly sub-classified as non-Hodgkin (NHL) [including Burkitt's lymphoma (BL)] and Hodgkin's lymphoma (HL) are associated with the human herpesvirus type 8 (HHV-8)/Kaposi's sarcoma-associated herpesvirus (KSHV)<sup>15</sup>.

In Tanzania and Kenya, KS, NHL, and SCC were the commonest oro-facial malignant lesions found in HIV/AIDS patients<sup>15,16</sup>. Similarly, Chidzonga reported a higher prevalence of KS and NHL among other oro-facial lesions in Zimbabwean patients<sup>17</sup>.

African studies have reported that the majority of oro-facial malignant lesions presented in late stages (III and IV), contrary to studies elsewhere in which the majority presented in early stages (I and II)<sup>17,18</sup>.

Several studies have strongly implicated some predisposing factors in certain types of oral cancers<sup>1,19-22</sup>. The implicated aetiological factors of oro-facial malignancies, however, differ in different environments in different countries. Infection by certain viruses and bacteria has been associated with some malignant conditions, for example, HKSV has been strongly associated with KS. HIV infection is associated with KS and oral squamous cell carcinoma (OSCC) at young ages. Epstein Barr virus (EBV) is associated with BL while Syphilis in the oral cavity has for a long time been associated with predisposition to the development of OSCC<sup>15,21,23</sup>.

Behavioural and environmental factors such as use of tobacco and alcohol consumption, poor oral

hygiene, trauma, chronic irritation, nutritional deficiencies, exposure to sunlight, and certain carcinogenic dyes have been seen to have varying degrees of association with certain types of oro-facial malignancies<sup>19,24-27</sup>. Other factors that have been associated with the occurrence of oro-facial malignancies include radiation, exposure to some carcinogenic dyes, herbicides or certain metals and trauma from sharp edges of grossly carious teeth and/or ill-fitting dentures, thermal or acid burns and in the vicinity of plastic or metal implants<sup>28-29</sup>.

There is a paucity of information on the possible aetiologies of oral and maxillofacial malignant tumours in Tanzania. Therefore, the aim of this study was to determine the predisposing factors and clinical-pathological presentation of malignant lesions of the oro-facial region among patients attending the Muhimbili National Hospital.

## **MATERIAL AND METHODS**

### **Study settings**

This descriptive prospective cross-sectional study was conducted at the Muhimbili National Hospital in 2011. It included 186 patients with histologically confirmed malignant lesions who presented during the study period.

### **Data collection**

After getting an informed consent each patient was interviewed using a specially designed questionnaire. The questionnaire consisted of sociodemographic data and patient's main complaint (ulcer, pain, swelling, bleeding, difficulty in chewing, difficulty in opening the mouth, nasal congestion, tooth/teeth mobility, numbness/paresthesia and difficulty in breathing). Occupation of the patient, tobacco use, alcohol consumption and betel/areca use were recorded. Inquiry on tobacco use included the type or form (dipping, chewing, snuffing and smoking),

frequency per day and duration in years. Also, for alcohol consumption, the type (beer, local brew, spirits or local spirits), frequency and duration in years were recorded.

### **Clinical examination**

Clinical examination was done to determine the presence of swelling, induration, ulcer, discolouration or a combination of these. Location of the lesion in the oro-facial region, size of the primary tumour at the greatest diameter measured in centimeters, involvement and/or destruction of local tissues and lymph node status (size, consistency and, whether fixed or not) were recorded.

### **Laboratory investigations**

Haematological and histological investigations were done. Haematological investigations included full blood picture, erythrocytes sedimentation rate, ELISA and VDRL.

### **Radiological investigations**

Conventional x-rays, ultrasound and CT scan were accordingly done. Incisional biopsy was done and submitted to the pathologist.

### **Consistency**

To ensure consistency, all examinations were done by the same examiner. The histopathologic specimens were reviewed by one experienced consultant pathologist.

### **Data handling and analysis**

Data was entered and managed in a personal computer on the same day of collection. Data management included: daily data quality checks for inconsistencies and wrong entries. The data was analyzed using SPSS software for Windows. Statistical significance testing was done using the chi-square test; p-value of less than 0.05 was considered statistically significant.

**Ethical clearance**

Ethical clearance was obtained from the Research and Publication committee of the Muhimbili University of Health and Allied Sciences and permission to conduct the study was granted by the Muhimbili National Hospital administration.

**RESULTS**

**Demographic features**

The study group consisted of 104 (56%) males and 82 (44%) females, with a male to female ratio of 1.3:1. The age at the time of diagnosis ranged from 3 to 83 years with mean age of 48.4 years and 19.2 SD. The peak age was at 50-59 years (19.9%) followed by 30-39 (16.1%) (Table1). Patients aged below 40 years accounted for about 33%.

**Frequency of occurrence of oral maxillofacial malignant tumors**

Ninety-six (51.6%) patients had squamous cell carcinoma, 17 (9.1%) had Kaposi's sarcoma, 10 (5.4%) had non-specific carcinoma and 7 (3.8%) had adenoid cystic carcinoma. Burkitt's lymphoma, adenocarcinoma, and mucoepidermoid carcinoma were diagnosed in 5 (2.7%) patients and osteosarcoma and basal cell carcinoma in 4 (2.2%) patients each. Basal cell adenocarcinoma, diffuse large cells lymphoma, acinic cell carcinoma, Hodgkin's lymphoma, malignant melanoma, diffuse lymphocytic lymphoma, PLGA, nasopharyngeal carcinoma, verrucous carcinoma, eccrine poroma, leiomyosarcoma were seen in one (0.5%) patient each.

**Table 1. Distribution of patients by age and sex**

Age group (years)	Sex				Total	
	Male		Female		n	%
	n	%	n	%		
0-9	3	1.6	2	1.1	5	2.7
10-19	3	1.6	9	4.8	12	6.5
20-29	6	3.2	8	4.3	14	7.5
30-39	17	9.1	13	7.0	30	16.1
40-49	15	8.1	13	7.0	28	15.1
50-59	19	10.2	18	9.7	37	19.9
60-69	20	10.8	9	4.8	29	15.6
70-79	14	7.5	10	5.4	24	12.9
80+	7	3.8	0	0.00	7	3.8
	104	55.9	82	44.1	186	100.0

**Duration of lesion**

Generally, 133 (71.4%) patients reported a duration of between 2 and 12 months, among this 58.6 % were males and 41.4% were females (p=0.47). Only 9 (4.8%) patients reported duration of ≤1 month while 24 (13%) reported duration of >24 months.

**Predisposing factors**

Tobacco use was reported by 89 (47.8%) patients, 69 (37.1%) males and 20 (10.8%) females. Ninety-six (51.6%) patients, 67 (36.0%) males and 29 (15.6%) females reported alcohol use. Among tobacco users, 62 (69.6%) reported having used tobacco for more than 20 years while 49 (51.0%) alcohol users reported to have used it for more than 20 years. Only 1 (0.5%) male patient reported use of betel/areca. Statistically, tobacco and alcohol use was

significantly more in males than females ( $p=0.000$  and  $p=0.000$  respectively).

Among squamous cell carcinoma patients, 62 (64.6%) used tobacco of one form or another and 60 (64.5%) used alcohol (Table 2). Forty-four (71.0%) of tobacco users were smokers while 11.3% were tobacco dippers, 4.8% snuffers and 3.2% tobacco chewers.

**Table 2. Habits of patients with squamous cell carcinoma**

Habit		Sex				Total		P-value
		Male		Female				
		n	%	n	%	n	%	
Tobacco	Yes	46	48.4	17	17.9	63	66.3	0.001
	No	12	12.6	20	21.1	32	33.7	
Alcohol	Yes	43	45.3	16	16.8	59	62.1	0.002
	No	15	15.8	21	22.1	36	37.9	
Betel/areca	Yes	1	1.1	0	0	1	1.1	-
	No	57	60.0	37	38.9	94	99.9	

**Anatomical location of tumors**

Twenty-seven percent (27.1%) of squamous cell carcinoma was located on the tongue, 18.8% were on the gingivae, 12.5% on the skin, 8.3% on the oropharynx and floor of mouth each. About 6% of the tumors were located on the maxillary sinus, 5% on the palatal mucosa, 4% on the buccal vestibule while the lips and sinonasal were locations in 3.1% each.

Kaposi's sarcoma was most (29.4%) commonly located on palatal mucosa, followed by oropharynx (23.5%) and tongue (17.6%) while the gingivae and skin were locations in 11.8% each.

Verrucous carcinoma was located on the mandibular gingivae in one patient while in the other was on the palatal mucosa. Malignant melanoma was exclusively located on the palate.

**Distant metastasis**

In one HIV positive case with CD4+ count of 53 cells/ $\mu$ l, who did not use any form of tobacco or alcohol with a well-differentiated squamous cell carcinoma of the tongue there was distant metastasis to the lungs. The lesion had a duration of between 12 and 18 months.

**Clinical stage of the tumor**

Ninety (93.8%) patients, 58(60.4%) males and 32 (33.3%) females with squamous cell carcinoma, had stage IV tumour ( $p=0.154$ ). Only 6 (6.2%) patients had stage II and III tumours.

**Histological features**

Epithelial tumours were the most common, found in 142 (76.3%) patients, 84 (59.2%) males and 58 (40.8%) females, with male to female ratio of 1.4:1 ( $p=0.020$ ). The age at the time of diagnosis ranged from 6 to 83 years with a mean age of  $53.3 \pm 17.2$  SD years. Majority 121 (86%) of patients with epithelial tumours were aged between 30 and 79 years while only 13 (9.2%) patients were below 30 years. Ninety-six (67.6 %) of epithelial tumours were SCC.

Twenty-five (13.4%) patients, 8 (32.0%) males and 17 (68.0%) females, with female to male ratio of 2.1:1 were found to have various types of soft tissue mesenchymal tumours. The age at the time of diagnosis ranged from 16 to 75 years with a mean age of  $35.2 \pm 14.2$  SD years. Kaposi's sarcoma which was the commonest soft tissue mesenchymal tumour was seen in 17 (68.0%) patients.

Hard tissue mesenchymal tumours were found in 5 (3.3%) patients, 3 (60.0%) males and 2 (40.0%)

females in this study ( $p=0.261$ ). Osteosarcoma was the commonest hard tissue mesenchymal tumour found in 4 (2.2%) patients in this study. Burkitt's lymphoma was the predominant lymphoma.

### **Histological grade of SCC**

Histological review of SCC revealed that 53 (55.2%) were well-differentiated (G1), 32 (33.3%) moderately differentiated (G2), and 11 (11.5%) were poorly differentiated (G3).

### **Histological grade of SCC in relation to age**

Well-differentiated tumours were found in 75 (52%) of SCC patients aged 40 years and above. However, there was no statistical significance between the histological grade of SCC and age ( $p=0.299$ ).

### **Histological grade of SCC in relation to clinical stage of SCC**

Ninety-four (94.3%) of well-differentiated SCC were clinical stage IV while poorly differentiated tumour was in clinical stage II. However, no statistical significance was established between this relationship ( $p=0.885$ ).

### **General features.**

About 80% of the patients presented with different levels of anaemia (i.e.  $Hb < 10g/dl$ ). Regarding HIV serology, 33(17.7%) patients tested positive, 152 (81.7%) negative, and 1 (0.5%) refused to be tested. Majority (81.8%) of HIV positive patients were aged between 20 and 49 years, out of which 77.2% were females.

All 17 (100%) patients with Kaposi's sarcoma tested positive for HIV while all patients with BL were HIV negative. Two (66.7%) of patients with diffuse large cells lymphoma were also HIV positive.

## **DISCUSSION**

In this study, over 60% of the patients were above 40 years of age. This is in concurrence with several

other African studies which also showed that malignant lesions of the oral and maxillofacial region more commonly occurred among patients above 40 years<sup>10,11,26</sup>. The slight male preponderance encountered in this study is in agreement with what was reported in other African studies<sup>10,30</sup>. Males tend to have a higher exposure to the commonly known predisposing factors to malignancies.

Squamous cell carcinoma (51.6%) was the most commonly seen malignant tumour in the oral and maxillofacial region with a peak incidence in the 6<sup>th</sup> decade of life. This is in concurrence with available literature from Africa and elsewhere<sup>9-11,31</sup>.

The frequency of occurrence of lymphomas was seen to be low compared to a previous Tanzanian study as well as other studies in Africa<sup>10-12</sup>.

A remarkable fact from this study is the presence of some malignant tumours which are rarely reported in the oral and maxillofacial region. A case of malignant eccrine poroma was encountered in a 48 years old male peasant who presented with a painful swelling on the right cheek for 2 years. Malignant eccrine poroma (eccrine porocarcinoma, EPC) is an extremely rare type of skin tumor arising from the intraepidermal portion of eccrine sweat glands or acrosyringium<sup>32</sup>. Little is available in both African and European literature regarding malignant eccrine poroma in the head and neck region<sup>32,33</sup>. Another rare finding in this study was a 60 years old HIV negative male, diagnosed with Castleman's disease which progressed into non-Hodgkin's lymphoma. Castleman's disease is a nonclonal lymphoproliferative disorder that can affect a single lymph node station or can be generalized. Castleman's disease has been reported to progress into either KS or NHL in HIV positive patients<sup>34</sup>. KSHV; also known as HHV8 is the causative agent of multicentric Castleman's disease (MCD) in HIV patients<sup>34,35</sup>. Since this patient was HIV negative this might mean that there are other unexplained factors

that are associated with this condition. Nevertheless, this must be interpreted with caution since this was only a single case.

Tobacco (47.8%) and alcohol (51.6%) use were high among males (over 70%). This conforms to reports from elsewhere<sup>10,36</sup>. The use of both alcohol and tobacco increases the possibility of developing cancer than using either of them<sup>10,20,24</sup>.

Betel use was reported by only one (1%) patient. This is very low compared to studies among Asians and some migrant communities in Africa, Europe, and North America<sup>108-111</sup>. Studies in Asia have proved that betel quid chewers are also heavy smokers and that there was an independent risk from betel quid chewing per se on oral cancer, over and above the risk from smoking<sup>37,38</sup>.

Although one-tenth of the patients in this study reported having one or more family member/relative who had suffered from some type of malignancy, the effect of genetics on cancers in the oral and maxillofacial region has to be further investigated.

In this study majority (71.0%) of squamous cell carcinoma, patients used tobacco in form of smoking. Tobacco smoking was ten-fold greater among males than females. This is in agreement with other African and Asian studies where tobacco smoking is a common practice among males<sup>10,36</sup>. On the other hand, dipping, snuffing and chewing together were nineteen-fold greater among females than males.

This is reflected in the finding of the sites of occurrence of SCC in the oral cavity whereby in females, the location was mostly on the gingivae. In South Africa and India tobacco dipping was common among males than it was for females<sup>38,39</sup>.

Most patients with SCC presented with stage IV disease. Pain, swelling, ulceration and aesthetics were the main reasons for reporting for medical care.

A higher frequency (18.9%) of young people with SCC was reported in this study compared to the previous study done in Tanzania<sup>12</sup>. This concurs with other African as well as western studies<sup>10,14,40</sup>. Such increasing frequencies of SCC among young adults could be attributable to several emerging risk factors such as viral infections especially HIV and HPV, family history of cancer, and dietary factors. Human Papilloma Virus (HPV) is an emerging risk factor associated with oral cancer, with high-risk strains like HPV 16/18 implicated with high malignant potential<sup>23</sup>.

The most commonly affected site for SCC in this study was the tongue (Figure 1) which is also in concurrence with studies done within and outside the country<sup>30,31</sup>. Nevertheless, there was some variation from findings from Nigeria, Zimbabwe and India where the maxillary antrum, the mandibular gingivae and the buccal mucosa were reported to be the commonest sites<sup>10,14,39</sup>. Variation of anatomical sites has been postulated to be associated with aetiological factors involved in the geographical location<sup>36</sup>. Other sites in this study were gingivae, skin, oropharynx, maxillary antrum, lips, and floor of mouth (Figure 2).



**Figure 1: An ulcerative lesion on the dorsum of the tongue diagnosed as an advanced squamous cell carcinoma.**



**Figure 2: A young man with an advanced squamous cell carcinoma involving the maxillary sinus, the palate and the gingival mucosa.**



**Figure 3: A HIV +ve woman with Kaposi's sarcoma of the hard and soft palate, and the left cheek.**

In this study, majority (98%) of tumours were in advanced stages (III and IV). Similar results have been reported by other studies in the African continent and elsewhere<sup>18,21,40,41</sup>. Studies among Africans and black Americans reported that majority of tumours were diagnosed at an advanced stage, therefore, increasing the mortality rate of SCC patients. In this study therefore, the prognosis of majority of SCC patients was poor. This concurs with other studies showing late reporting of SCC

patients. Fifty-three (55.2%) out of all patients with SCC presented with tumours that were well differentiated. This finding is in agreement with other studies<sup>10</sup>. However, contrary to the reports from South America and Nigeria where majority of lesions were moderately and poorly differentiated respectively<sup>14,21</sup>. Majority (69.2%) of well-differentiated SCC were located on the tongue contrary to the mandibular gingivae as was reported in Zimbabwe<sup>10</sup>.

Verrucous carcinoma was encountered in 2 (1.1%) patients both of whom were males, one with the mandibular gingivae and the other palatal mucosa lesions. The frequency of verrucous carcinoma in this study was higher compared to previous studies in Tanzania, Uganda and Iran<sup>9,12</sup>. Verrucous carcinoma if delayed, as it was the case with most of our patients, could transform to invasive carcinoma.

Kaposi's sarcoma (Figure 3) was the second most common malignancy and was found among 17 (9.1%) patients in this study. This concurs with the previous study in Tanzania<sup>12</sup>. In contrast, in Uganda KS was reported as the commonest oral and maxillofacial malignant tumour<sup>12</sup>. Remarkably, all patients with Kaposi's sarcoma were HIV positive at the time of diagnosis. The male to female ratio in Kaposi's sarcoma in this study was 1:3.3. The female preponderance is in agreement with other studies<sup>16,42</sup>.

The frequency of lymphomas in this study was lower compared to what was reported from Nigeria<sup>11</sup>. However, some studies in Iran have reported lower frequencies compared to this study<sup>9,31</sup>. Contrary to other studies in East Africa where BL was the commonest NHL<sup>43</sup>, this study found that BL occurred at nearly the same frequency as other NHLs. This could be attributable to a smaller sample size in this study. A quarter (25%) of patients who were found to have lymphomas in this study were also HIV positive.



## CONCLUSION

The most common malignant tumour in the oral and maxillofacial region was SCC. The majority of patients with SCC had at various times in their lives used tobacco and/or alcohol. A rather young group of patients were found to have malignant lesions. Patients presented rather late with advanced tumours that mostly could only be managed by palliative therapy. All patients with KS were HIV positive.

## RECOMMENDATIONS

There is a need to educate the community on the predisposing factors and the importance of taking precautionary measures.

Raising awareness of the community on the importance of early reporting whenever they see development of suspicious signs.

Continuing education to non-dental health professionals on the importance of early detection and referral of suspected or diagnosed cases since they are the first to see the majority of the cases.

Strengthen the capacity of regional and district hospitals equipping them so that they can have the capacity to carry out histological diagnosis.

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