

Histopathological Trends of Orofacial Squamous Cell Carcinoma in a Tanzanian Cohort of 465 Patients

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Abstract

Orofacial squamous cell carcinoma (OfSCC) represents a significant proportion of malignant head and neck lesions, with an estimated incidence of up to 90%. This study investigated the histopathological traits of OfSCC in Tanzanian patients, focusing on factors such as patient age, gender, and tumor location. The study analyzed cases diagnosed between 2016 and 2021 at the Oral and Maxillofacial Surgery Department, Muhimbili National Hospital. The data collected included patient demographics, tumor sites, and histological grading. The results showed an average patient age of 55.85 years, with a slightly higher incidence in males (male-to-female ratio 1.4:1). The majority of patients were in the age group of 60 years and above, accounting for 45.2% of cases. Intraoral tumors were the most common (87.6%), with the tongue and gingiva/alveolar ridge being the most affected sites (34.5% and 25.6%, respectively). For extra-oral cases, the midfacial region was the most frequently involved (68.5%). Histological analysis showed that 72% of the cases were classified as grade I. The findings indicated a predominance of older male patients, with the tongue, gingiva, and buccal mucosa being the primary intraoral sites and the midface the predominant extra-oral location.

Keywords: Orofacial, Squamous cell carcinoma, Histopathology, Tanzania

Introduction

Orofacial cancers, particularly squamous cell carcinoma (SCC), are a major concern in global oncology, accounting for a significant portion of head and neck malignancies. OfSCC, a subset of SCC, originates from the mucosal epithelium of the oral cavity, pharynx, and sinuses, or the epidermal keratinocytes in the skin. These tumors contribute substantially to the morbidity and mortality associated with oral cancers, particularly in sub-Saharan Africa [1-5].

OfSCC exhibits a higher incidence in men compared to women, with a notable peak in diagnosis around the sixth decade of life. However, recent studies indicate a concerning rise in younger individuals diagnosed with the disease. In terms of anatomical sites, the most frequent occurrences of OfSCC are found on the tongue, lips, and floor of the mouth, though other regions of the orofacial area can also be involved [6-8].

The development of OfSCC follows a multi-stage process, beginning with cellular changes such as hyperplasia, followed by dysplasia in varying degrees, and culminating in carcinoma. The histopathological classification of OfSCC is based on the differentiation of the tumor cells, ranging from well-differentiated forms that resemble normal tissue to poorly differentiated, more aggressive forms [9-14].

In Tanzania, there is limited research on the epidemiological and histopathological patterns of OfSCC, despite the increasing incidence of oral cancers

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in the region. Understanding the characteristics of OfSCC in the Tanzanian context is essential to improving early detection, diagnosis, and management of this disease. This study seeks to provide critical insights into the age, gender, and anatomical distribution of OfSCC cases, contributing to a more detailed understanding of this malignancy in Tanzania.

Materials And Methods

This research was conducted as a retrospective review at the Muhimbili University of Health and Allied Sciences (MUHAS), specifically within the Department of Oral and Maxillofacial Surgery (OMFS) in Dar es Salaam, Tanzania. The study focused on histopathological reports of malignant orofacial lesions from the period between January 2, 2016, and December 31, 2021. Data was sourced from the department's archive, including all documented cases of squamous cell carcinoma diagnosed in the orofacial region. Reports that were inconclusive or lacked a definitive diagnosis were excluded from the analysis.

The data extraction process involved reviewing the histopathological reports to gather key information, including patient demographics (age and gender), tumor site, histological grade, and corresponding identification numbers. In cases where a patient had multiple biopsies (pre-operative and post-operative), the final post-surgical result was used for analysis.

For statistical analysis, we utilized SPSS version 26 (IBM Corp., Armonk, NY). Descriptive statistics were calculated, with continuous data presented as medians and categorical data expressed as percentages. Age categories were classified into four groups: pediatric (< 18 years), young adults (18–39 years), middle-aged adults (40–59 years), and elderly (≥ 60 years). Tumor locations were categorized into intra-oral (e.g., tongue, gingiva, palate) and extra-oral (e.g., facial skin, salivary glands). For the extra-oral sites, further subdivision into upper, mid, and lower facial regions was made.

To assess data distribution, the Shapiro-Wilk test for normality was applied, with a significance threshold set at $P < 0.05$. The relationship between sociodemographic factors and tumor characteristics (location and grading) was analyzed using One-Way ANOVA and chi-square tests. Univariate and multivariate regression models were employed to identify potential correlations between patient characteristics and tumor location.

Results and Discussion

Demographic Data

This retrospective analysis reviewed histological data for 778 patients diagnosed with malignant lesions, of which 465 (59.8%) were found to have orofacial squamous cell carcinoma (SCC). The ages of the patients ranged from 5 to 100 years, with an average age of 55.85 years (SEM = 0.77). The largest proportion of patients (45.2%, $n = 210$) were aged 60 years and above. Males comprised 57.6% ($n = 268$) of the total patient population, giving a male-to-female ratio of 1.4:1 (see **Table 1**). The average age of male patients was 54.16 years (SEM = 0.99), while the average age of female patients was 58.16 years (SEM = 1.18). The difference in the average age between males and females was statistically significant ($P = 0.009$).

Table 1. Patient distribution by demographics, tumor location, and histopathological grade

Category	Frequency (n = 465) N (%)
Age groups (years)	
< 18	9 (1.9%)
18 to 39	60 (12.9%)
40 to 59	186 (40.0%)
≥ 60	210 (45.2%)
Gender	
Male	268 (57.6%)
Female	197 (42.4%)
Tumor location	
Not specified	28 (6.0%)
Intra-oral	383 (82.4%)
Extra-oral	54 (11.6%)
Histological grade	
Grade I	334 (71.8%)
Grade II	73 (15.7%)
Grade III	23 (4.9%)
Not specified	35 (7.5%)

Lesion sites and histological classification

In 437 (94%) of the cases, the location of the orofacial lesions was documented. A predominant number of these lesions, 87.6% ($n = 383$), were found in intraoral areas. Regarding the histological grading, 430 (92.5%) of the cases provided this information. The majority of these were classified as grade I squamous cell carcinoma, accounting for 77.7% ($n = 334$) of the cases (refer to **Table 1**).

Histopathological images are presented in **Figure 1**.

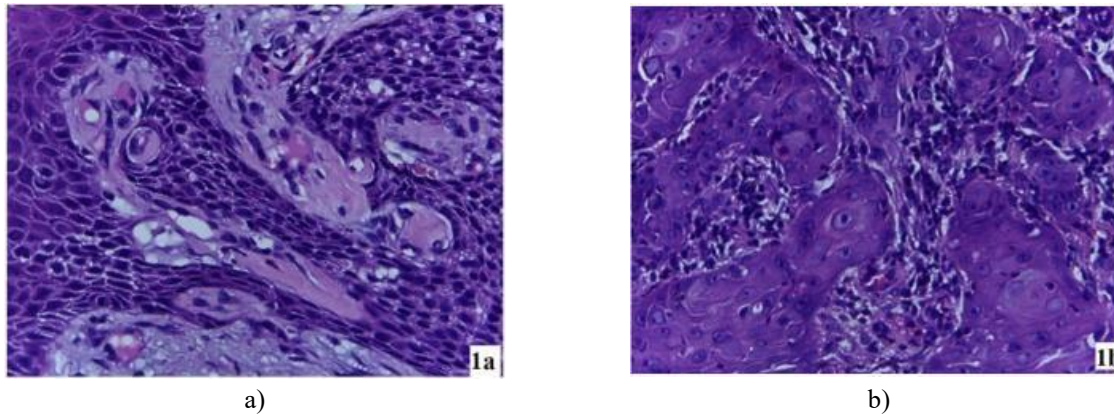


Figure 1. Histopathological images: a) the histopathological examination reveals pleomorphic, hyperchromatic, polygonal cells with abundant eosinophilic cytoplasm; intracellular bridges, keratinization, and dyskeratosis are present, which are typical for grade I squamous cell carcinoma (magnification x400); b) this section displays moderately pleomorphic, hyperchromatic cells, with abundant eosinophilic cytoplasm; the nuclei are characterized by open chromatin and prominent nucleoli. Intracellular bridges are present, but keratin formation is absent, and abnormal mitotic figures are observed, indicative of grade II squamous cell carcinoma (magnification x400).

Squamous cell carcinoma in extra-oral locations

Among the 54 (12.4%) reports of squamous cell carcinoma occurring in extra-oral regions, 30 (55.6%) were males, resulting in a male-to-female ratio of 1.25:1. The age of these patients ranged from 5 to 86 years, with an average age of 45.54 years (SEM = 2.41). The age group most affected was 40-59 years (42.6%, n = 23). The mean age of males was 46.1 years (SEM = 3.71), while for females, it was 44.83 years (SEM = 2.89), and

this difference was not statistically significant ($P = 0.797$).

The midfacial region had the highest number of extra-oral lesions, with 68.5% (n = 37) of cases located there, followed by the upper face (16.7%, n = 9) and lower face (14.8%, n = 8) (see Figure 2a). Out of the 41 (75.9%) reports that included histological grading, 68.3% (n = 28) were classified as grade I squamous cell carcinoma (refer to **Table 2**).

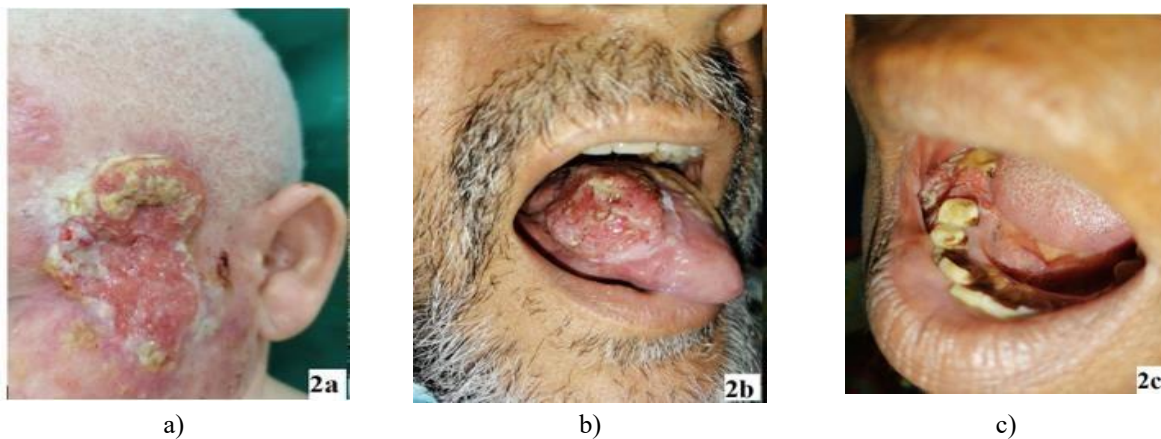


Figure 2. Clinical pictures of orofacial squamous cell carcinoma: a) an ulcerative lesion in the extra oral site (temporo-zygomatic region) in a patient with albinism, b) an ulcerative lesion on the lateral border of the tongue, and c) an ulcerative lesion on the gingiva around the region of lower right molars.

Table 2. Comparison of patient demographics and tumor characteristics for extra-oral vs intra-oral squamous cell carcinoma

Variable	Extra-oral (n = 54)	Intra-oral (n = 383)	P-value
Age group (years)			
< 40	15 (27.8%)	42 (11.0%)	0.001

≥ 40	39 (72.2%)	341 (89.0%)	
Sex			0.630
Male	30 (55.6%)	226 (59.0%)	
Female	24 (44.4%)	157 (41.0%)	
Lesion location			
Upper face	9 (16.7%)	N/A	N/A
Mid face	37 (68.5%)	N/A	
Lower face	8 (14.8%)	N/A	
Labial mucosa	N/A	34 (8.9%)	
Tongue	N/A	132 (34.5%)	
Buccal mucosa	N/A	59 (15.4%)	
Gingiva/Alveolar ridge	N/A	98 (25.6%)	
Floor of mouth	N/A	23 (6.0%)	
Retromolar trigone	N/A	5 (1.3%)	
Hard palate	N/A	32 (8.4%)	
Tumor grade			0.239
Grade I	28 (51.9%)	289 (75.4%)	
Grade II	11 (20.4%)	60 (15.7%)	
Grade III	2 (3.7%)	20 (5.2%)	
Not indicated	13 (24.1%)	14 (3.7%)	

Note: Eight reports lacked both tumor location and grading.

Intra-Oral squamous cell carcinoma analysis

For the 383 cases of intra-oral squamous cell carcinoma, 226 (59%) were male, with a male-to-female ratio of 1.44:1. Ages ranged from 8 to 100 years, with a mean age of 57.31 years (SEM = 0.814). Nearly half (48.8%, n = 187) of cases were found in patients aged 60 and above. The mean age for males was 54.84 years (SEM = 1.03), and for females, it was 60.86 years (SEM = 1.28), showing a significant difference between the genders ($P < 0.000$).

Common intra-oral sites included the tongue (34.5%, n = 132), gingiva/alveolar ridge (25.6%, n = 98), and buccal mucosa (15.4%, n = 59), as depicted in Figures 2b and 2c. Histological grading was recorded for 368 cases, with the majority (75.5%, n = 289) classified as grade I squamous cell carcinoma (**Table 2**).

Relationship between lesion location, age, and sex

There was no significant association between the lesion site (extra-oral vs intra-oral) and the patient's sex. However, a significant correlation was found between the lesion site and age group ($P = 0.001$). Patients under 40 years old were three times more likely to develop squamous cell carcinoma at extra-oral sites compared to

those aged 40 years and older (OR = 3.1, 95% CI = 1.59–6.14).

Conversely, individuals aged 40 years and above had a threefold higher likelihood of developing squamous cell carcinoma in intra-oral locations compared to those younger than 40 years (OR = 2.8, 95% CI = 1.41–5.79).

Location and its relationship to sex and age groups

There was no significant association between the sex of the patients and the location of the lesion ($P \geq 0.05$) for both intra-oral and extra-oral lesions. Regarding the patient's age, no correlation was found for intra-oral sites ($P \geq 0.05$). However, for extra-oral sites, a significant relationship was observed only in the mid-face area ($P = 0.004$). Patients under 40 years of age were three times more likely to have squamous cell carcinoma in the mid-face than those aged 40 years and above (OR = 3.2, 95% CI = 1.51–7.02).

Average age and histological classification based on lesion location

Table 3 shows the average age of patients and the histological classification of their squamous cell carcinoma based on the location of the lesion.

Table 3. Average age and histological grade of squamous cell carcinoma by location

Lesion location	Average age ($\pm$ SEM)	Histological grade
Extra-oral locations		
Upper-face	33.00 $\pm$ 6.08	Grade I: 7 (77.8%) Grade II: 2 (22.2%)
Mid-face	45.84 $\pm$ 2.60	Grade I: 19 (73.1%)

Lower-face	58.25 ± 6.33	Grade II: 5 (19.2%) Grade III: 2 (7.7%) Grade I: 2 (33.3%) Grade II: 4 (66.7%)
Intra-oral locations		
Labial mucosa	55.74 ± 3.50	Grade I: 29 (85.3%) Grade II: 3 (8.8%) Grade III: 2 (5.9%)
Tongue	54.90 ± 1.12	Grade I: 101 (80.8%) Grade II: 18 (14.1%) Grade III: 6 (4.8%)
Buccal mucosa	59.46 ± 2.21	Grade I: 47 (82.5%) Grade II: 8 (14%) Grade III: 2 (3.5%)
Gingiva/Alveolar ridge	58.74 ± 1.85	Grade I: 68 (73.1%) Grade II: 22 (23.7%) Grade III: 3 (3.2%)
Floor of mouth	55.52 ± 3.09	Grade I: 16 (69.6%) Grade II: 3 (13%) Grade III: 4 (17.4%)
Retromolar trigone	59.00 ± 1.92	Grade I: 4 (80%) Grade II: 1 (20%)
Hard palate	59.44 ± 13.84	Grade I: 24 (75%) Grade II: 5 (15.6%) Grade III: 3 (9.4%)

Note: The table does not include data from 27 cases where histological grading was missing.

Orofacial squamous cell carcinoma (OfSCC) overview

Orofacial malignancies involve cancers that affect the oral cavity, adjacent regions such as paranasal sinuses, and salivary glands. Squamous cell carcinoma (SCC) makes up a significant portion of these cancers, with estimates ranging from 50% to 90%. The present study reported that OfSCC accounts for roughly 60% of orofacial malignancies, consistent with findings from other studies, including those in Tanzania. This high occurrence is largely due to squamous cell carcinoma's origin from epithelial cells, which are widespread in the orofacial region. Since the area is frequently exposed to carcinogens that enter through various pathways like the mouth, nose, and ears, it is more vulnerable to developing squamous cell carcinoma.

Gender and age distribution in OfSCC

Numerous global studies on orofacial squamous cell carcinoma (OfSCC) report that males are more frequently affected than females, with male-to-female ratios ranging from 1:3:1 to 20.3:1 [2, 12, 14-17]. Similarly, this study showed a slight male predominance. The link between orofacial cancer and risky behaviors, such as smoking and alcohol consumption, is well-established, and these behaviors tend to be more

prevalent among males [18]. However, the observed male predominance cannot be solely attributed to risky behavior exposure, as a variety of factors, including infections (e.g., HPV) and genetic predispositions, also play a role.

Age of diagnosis and cancer trends

In this study, the average age of diagnosis was 56 years, which aligns with findings from Kenya [2], Iran [16], and Taiwan [17] but is lower than that reported in Romania [8]. Cancer is typically viewed as an age-related disease, with incidence increasing as individuals age [19, 20]. The greater frequency of malignant conditions in older populations can be explained by the multi-stage model of carcinogenesis, which suggests that genetic changes accumulate over time, ultimately leading to cancer [21]. Additionally, some of the biological processes associated with aging may contribute to cancer development [19]. OfSCC is rarely seen in pediatric populations [2, 16], and this study found that less than 2% of patients were under 18. Most of these pediatric cases had underlying conditions, such as albinism or xeroderma pigmentosum.

Gender-Based age differences

Consistent with research from Germany [18], this study found that males were diagnosed with OfSCC at an

earlier average age than females, by about four years. This could be because males typically engage in risky behaviors earlier than females. Nonetheless, it's worth considering whether biological differences between the sexes might influence cancer development. Preston et al. [22] suggested that the higher rate of cell division in males might increase their susceptibility to developing cancer.

Age-Related trends in extra-oral and intra-oral sites

The study revealed that younger individuals (< 40 years) were more likely to develop extra-oral OfSCC compared to those aged ≥ 40 years. This may be due to younger people spending more time outdoors, increasing their exposure to ultraviolet radiation. Additionally, individuals with skin conditions like albinism and xeroderma pigmentosum are more likely to develop OfSCC at a younger age, particularly in this region. In contrast, older individuals had a higher likelihood of developing OfSCC in intra-oral sites, likely due to the cumulative effects of prolonged carcinogen exposure.

Lesion locations in extra-oral sites

In extra-oral locations, the majority of lesions were found in the midface, followed by the upper face. This can be attributed to the anatomical features of these regions, as the midface contains structures such as the paranasal sinuses, nasal cavities, and parotid glands, which are vulnerable to squamous cell carcinoma. In the upper face, most lesions were concentrated in the frontal region, particularly among patients with albinism. The forehead is directly exposed to sunlight, and individuals with albinism lack melanin, making them more susceptible to ultraviolet radiation-induced DNA damage that leads to OfSCC [23].

Common intra-oral sites for OfSCC

OfSCC can occur in various intra-oral locations. The current study found that the tongue, gingiva/alveolar ridge, and buccal mucosa were the most commonly affected sites, which is consistent with studies from around the world [12, 14, 17, 18, 24]. The tongue is a frequent site for oral cancer, and its development is believed to be influenced by multiple factors, including tobacco, alcohol, chronic trauma, and infection [25]. Locations like the ventral tongue and the floor of the mouth are particularly prone to cancer due to their thin

non-keratinized epithelium, which allows carcinogens to penetrate easily and reach the underlying cells [6]. Additionally, individuals with a history of areca nut or tobacco chewing often develop OfSCC in the buccal mucosa or floor of the mouth due to continuous exposure to carcinogens and chronic inflammation [26].

Grading of OfSCC and prognostic implications

Histological grading plays a critical role in predicting the behavior of cancer, including its aggressiveness and response to treatment [27]. In this study, most OfSCC cases were grade I, indicating well-differentiated lesions. Grade I tumors typically invade local tissues, including connective tissue, muscle, or bone, before spreading to regional lymph nodes. In contrast, grade III tumors are poorly differentiated, more aggressive, and spread to lymph nodes earlier in the disease [6]. While lower-grade OfSCCs are generally associated with better outcomes, the grading system used in this study, based on Broders' criteria, has limited prognostic value [9].

Study strengths and limitations

One of the strengths of this study is its setting at a well-established oral and maxillofacial surgery center in Tanzania, which treats a large number of patients from across the country. As a result, this study offers a comprehensive overview of OfSCC in Tanzania, reflecting the disease's prevalence and characteristics in this population.

Study limitations

There were some limitations in this study. One concern is that certain histological reports from patients who were treated at our center may have been overlooked, possibly due to missing or lost results. Another issue was the absence of details about the location and grading of OfSCC in some of the pathology reports. This problem with incomplete reporting is not unique and highlights the need for a standardized template for pathology reports that includes all key variables that influence prognosis [28]. Despite these limitations, the study offers valuable insights into the patterns of OfSCC in Tanzania, providing essential information for healthcare professionals. This can help dentists and general practitioners remain more cautious when diagnosing non-healing or indurated lesions in younger individuals [14].

Conclusion

Squamous cell carcinoma (OfSCC) is the most common form of cancer in the orofacial region. It primarily affects males, with the majority of cases occurring in older adults. The midface is the most common site for extra-oral lesions, while intra-orally, the tongue, gingiva, and buccal mucosa are the most frequently affected areas. Most OfSCC cases are classified as well-differentiated (grade I).

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