Original Research Article

SQUAMOUS CELL CARCINOMA OF THE ORAL AND MAXILLOFACIAL REGION: A 12-YEAR ANALYSIS AT A TERTIARY HEALTHCARE FACILITY FROM NORTH-WESTERN NIGERIA

ABSTRACT

Background

Orofacial cancers remain a serious burden in developing countries largely due to scarcity of resources in both diagnosis and treatment. This study aimed to present the pattern of clinical presentation and management of squamous cell carcinoma (SCC) of the oral and maxillofacial region at a tertiary health care facility, Northwestern Nigeria.

Materials and method: This study was a retrospective analysis of cases of squamous cell carcinoma of the oral and maxillofacial regionseen in the past 12 years (January 2012 to January 2023). After obtaining ethical approval from the research and ethics committee of the institution, patients' demographic characteristics, risk factors, sites, stage, histologic diagnosis, and treatment status were extracted from the patient's record. The data were analyzed using IBM SPSS version 25 software.

Results: A total of 233 cases(114 (76.8%) males and 54 (23.2%) females) were analyzedin the age range of 20-80 years with a mean±SD of 52.98±16.08years. Most of the patients 174(74.7%) were farmers. The onset ranged from 6 weeks to 2 years. The main complaint of the patients were pain and swelling (132 (56.7%)). Extensive or multiplesites (72 (30.9%)) constitute the majority of the SCC. Well-differentiated SCC(133 (57.1%)) was the predominant diagnosis and, the majority (86 (36.9%)) were Stage IV lesions. The male patients were found to have more advanced disease compared to females with a statistically significant difference(p= 0.000). Surgery+ referral for chemotherapy/radiotherapy (125(57.1)) was the main treatment modality.

Conclusion: The well-differentiated SCC was thecommonest histologic subtype. Surgery and chemoradiation therapy were treatment modalities offered the patients especially with the early lesions and prompt initiation of treatment.

Keywords: Cancer, Orofacial, Squamous cell carcinoma, Chemotherapy,Radiotherapy

INTRODUCTION

Squamous cell carcinoma (SCC) of the oral and maxillofacial region is a potentially life-threatening malignancy due to its invasiveness into the orofacial and neck vital structures.[1] Oral SCC is the most common carcinoma of the oral cavity and has been ranked the 12th most common cancer worldwide. The incidence and mortality associated with cancers in the maxillofacial region varies across different part of the world and higher in developing countries. [2] Most epidemiological studies revealed heavy smoking and alcohol intake to be the most important risk factors for the development of SCC. [ref]Other etiological agents such as irradiation, viruses, chronic irritation and genetics have been implicated. [3]

The common clinical features of SCC include ulcerated lesions with rolled margins usually containing a central necrotic area. [4] These lesions can be seen in all parts of the orofacial region lined by squamous epithelium. [4, 5] The common sites are the buccal mucosa, tongue, floor of the mouth, palate, and lip. [6] The diagnosis of SCC is through history, examination (visual and tactile inspection of the accessible oral structures) together with histopathological examination. [7] Imaging modalities such as computed tomography (CT) and magnetic resonance imaging (MRI) are helpful in staging and identification of the extent of the tumors including metastasis. [8] For most of the cancers of the oral and maxillofacial region, surgery is the initial treatment of choice especially for stages I and II. Radiation or chemoradiation is added postoperatively if the disease is more advanced or has high-risk histologic features including nodal involvement.

The diagnosis and treatment of squamous cell carcinoma of the oral and maxillofacial region remainsa great challenge in our clime. This has been due to multifactorial factors

such as lack of sufficient access to oral healthcare, limited awareness, serious cultural barriers, late presentation and lack of fundamental infrastructure. There is also insufficient report as it regards to etiological factors, pattern of presentation, available approaches to the management and their outcome. [9] Hence, this retrospective study aimed to present the pattern of clinical presentation and management of squamous cell carcinoma (SCC) of the oral and maxillofacial region in a resource-limited environment.

MATERIALS AND METHOD

This research was a retrospective study conducted at the dental and maxillofacial surgery clinic of UsmanuDanfodiyo University Teaching Hospital Sokoto over a period of 12 years (January 2012 to January 2023). All case notes of patients seen and managed with squamous cell carcinoma of the oral and maxillofacial region were retrieved after obtaining ethical approval from the research and ethics committee of the institution. Included in the study were case records with complete relevant information and histological diagnosis. Case records of patients with nasopharyngeal carcinoma, metastatic carcinomas to the oral and maxillofacial region, or those who absconded at first presentation were excluded from the study. Patients' demographic characteristics such as age, sex, level of education and occupation were recorded. The Patients recorded main complaints, tobacco using habit, site, stage, histological diagnosis, and treatment status were also extracted. The data obtained were analyzed using IBM SPSS version 25. The age variable was expressed using range, mean and standard deviation, categorical variables were expressed as frequencies and percentages and all tests of associations were done using chi square. A p-value less than 0.05 was taken as statistically significant.

RESULTS

A total of 233 cases of histologically diagnosed squamous cell carcinoma were seen during the study period. There were 179 (76.8%) males and 54 (23.2%) females in the age range of 20-80 years with a mean±SD of 52.98±16.08 years. Majority (78(33.5%) of the cases were in the 6^{th} decade of life and most of the patients(174(74.7%)) were male farmers who had no formal education compared to female with a statistically significant difference. Table 1 shows the analysis of socio-demographics of the study patients.

The record of predisposing factors to squamous cell carcinoma of the oral and maxillofacial region showed that only 15 (6.4%) of the patients were tobacco users (Figure 1). No statistically significant differencein the tobacco history among the males and females' patients ($\chi 2$ value df=3, P-value= 0.768) Table 2.The period range of onset before presentation to the oral and maxillofacial surgery clinic was 6 weeks to 2 years.

The main complaint of the patients was pain and swelling (132 (56.7%)) and the least were others such as difficulty in breathing, chewing and, nasal blockage (11(4.7%)) (Figure 2).

The lower lip (53 (22.7%)) was the commonest sites of occurrence of the squamous cell carcinoma, followed by the buccal mucosa (37(15.9) and the least was cheek and tongue + floor of the mouth with 3 (1.3%) cases respectively (Table 3).The analysis of the site of the lesion and the histological diagnosis revealed no statistically significant difference ($\chi 2=23.467$, df= 24 p= 0.492) Table 3.

The distribution of diagnosis according to histology was well-differentiated squamous cell carcinoma (WDSCC) 122 (52.4%), moderately differentiated squamous cell carcinoma (MDSCC) 64 (27.5%) and, poorly differentiated squamous cell carcinoma (PDSCC)47 (20.2%) (Table 4).

Stage IV lesions constitute the majority (86 (36.9%)), followed by Stage III (58 (24.9%)0, Stage II (56 (24.0%)), and, the least was Stage I (33 (14.2%)) (Table 2). The male patients were found to have more advanced disease compared to females with a statistically significant difference ($\chi 2=31.28$ df= 3 p= 0.000) (Table 2). The treatment status of patients in this study includes Surgery+referral for chemotherapy/ radiotherapy (125(57.1%)), referral for chemotherapy/radiotherapy (62 (26.6%)), referral for chemotherapy/radiotherapy+ surgery (14 (6.0%)) and no treatment in 32 (13.7%) cases. There was poor follow up record as only 78 (38.8%) patients out of the 201 patients treated was retrieved. The survival rate of the patients treated in one year follow up period was 92.3%.

Table 1: Distribution of sociodemographic variables of the study subjects.

Sex n (%)	**M n (%)**	**F n (%)**	**Total n (%)**	**Test statistics**	**Level of significance**
Age categories					
0-10	0 (0)	0 (0)	0 (0)		
11-20	12 (5.2)	0 (0)	12 (5.2)		
21-30	8 (3.4)	0 (0)	8 (3.4)		
31-40	35 (15)	0 (0)	35 (15)	$\chi2$=49.305, df= 6	P= 0.000*
41-50	18 (7.7)	24 (10.3)	42 (18)		
51-60	59 (25)	19 (8.2)	78 (33.5)		
61-70	17 (7.3)	0 (0)	17 (7.3)		
71-80	30 (12.9)	11 (4.7)	41 (17.6)		
Total	179 (76.8)	54 (23.2)	233 (100)		
Level of education					
Primary	44 (18.9)	0 (0)	44 (18.9)		
Secondary	17 (7.3)	0 (0)	17 (7.3)	$\chi2$=30.186, df= 3	P= 0.000*
Tertiary	9 (3.9)	0 (0)	9 (3.9)		
Others	109 (46.8)	54	163 (69.9)		
Total	(23.2)		233 (100)		
	179 (76.8)	54			
	(23.2)				
Occupation					
Farming	128 (96.2)	46	174 (74.7)		
Business	(19.7)		33 (14.2)		
Civil	25 (10.7)	8 (3.4)	18 (7.7)	$\chi2$=8.904, df= 3	P=0.031*
servant	18 (7.7)	0 (0)	8 (3.4)		
Others	8 (3.4)	0 (0)	233 (100)		
Total	179 (76.8)	54			
	(23.2)				

P* indicate significant when less than 0.05

Table 2: Distribution of tobacco habit among the study subjects

Tobacco habit	Male (n=179) (%)	Female (n=54) (%)	Total	χ^2 value(df=3)	P value
No tobacco Smokeless Smoking Smokeless + Smoking	168 (72.1) 1 (0.4) 9 (3.9) 1 (0.4)	50 (21.5) 1 (0.4) 3 (1.3) 0 (0)	218 (93.6) 2 (0.8) 12 (5.2) 1 (0.4)	1.139	0.768
Total	179 (76.8)	54 (23.2)	233 (100)		

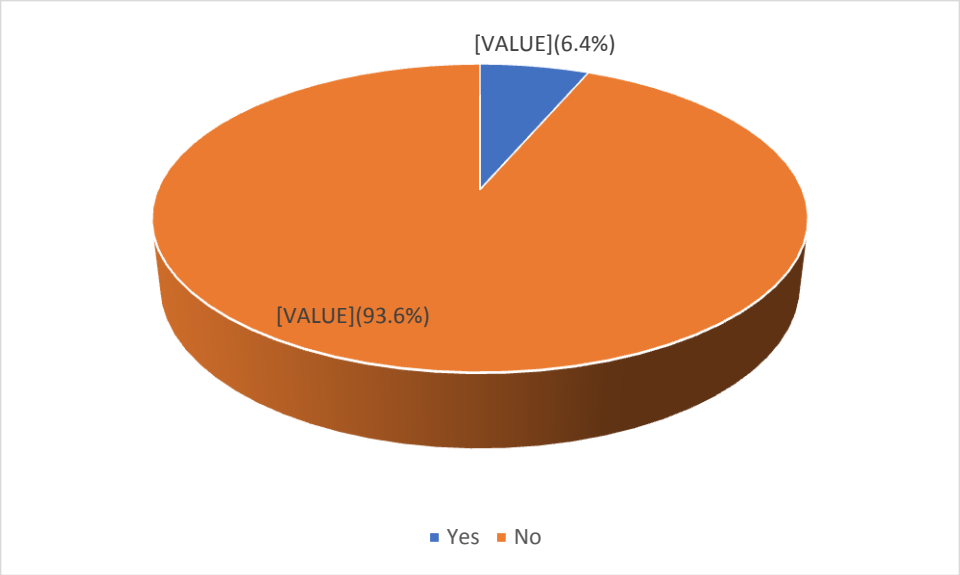

Figure 1: The distribution of tobacco and non-tobacco users among the study patients.

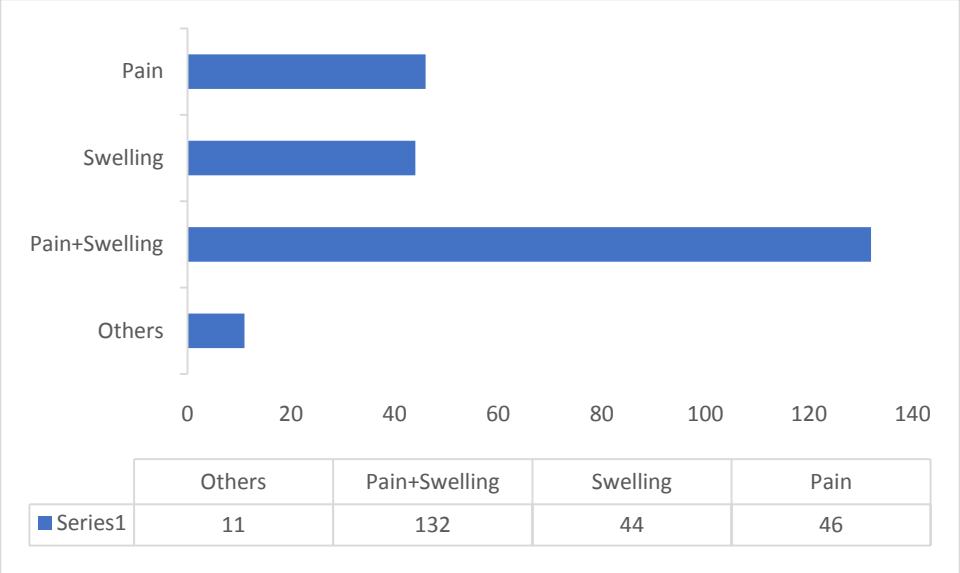

Figure 2: Distribution of patients' main complaints.

Table 3: Distribution of the site of the lesion with the histological diagnosis

Site	Histological diagnosis			Total
	WDSCC	MDSCC	PDSCC	
Floor of the mouth	14 (6.0)	5 (2.1)	3 (1.3)	22 (9.4)
Palate	11 (4.7)	5 (2.1)	1 (0.4)	17 (7.3)
Buccal mucosa	19 (8.2)	13 (5.6)	5 (2.1)	37 (15.9)
Tongue	8 (3.4)	9 (3.9)	4 (1.7)	21 (9.0)
Lower lip	24 (10.3)	15 (6.4)	14 (6.0)	53 (22.7)
Maxilla + maxillary antrum	16 (6.9)	5 (2.1)	5 (2.1)	26 (11.2)
Lip + Cheek	4 (1.7)	1 (0.4)	2 (0.8)	7 (3.0)
Tongue + Floor of the mouth	2 (0.8)	0 (0)	1 (0.4)	3 (1.3)
Mandible + Floor of the mouth	5 (2.1)	2 (0.8)	4 (1.7)	11 (4.7)
Lip + Mandible	8 (3.4)	5 (2.1)	4 (1.7)	17 (7.3)
Parotid	2 (0.8)	0 (0)	3 (1.3)	5 (2.1)
Upper lip	6 (2.6)	4 (1.7)	1 (0.4)	11 (4.7)
Cheek	3 (1.3)	0 (0)	0 (0)	3 (1.3)
Total	122 (52.4)	64 (27.5)	47 (20.2)	233 (100)

$\chi 2=23.467$, df= 24 P= 0.492

Table 4 : Analysis of gender and SCC staging among the study cases

SCC staging	Gender		Total
	Male, n (%)	Female, n (%)	
Stage I	27 (11.6)	6 (2.6)	33 (14.2)
Stage II	50 (21.5)	6 (2.6)	56 (24.0)
Stage III	53 (22.7)	5(2.1)	58 (24.9)
Stage IV	49 (21.0)	37 (15.9)	86 (36.9)
Total	179 (76.8)	54 (23.2)	233 (100)
Chi square ($\chi 2$) =31.28; degree of freedom (df)= 3; p-value= 0.000; n = total number of cases per category			

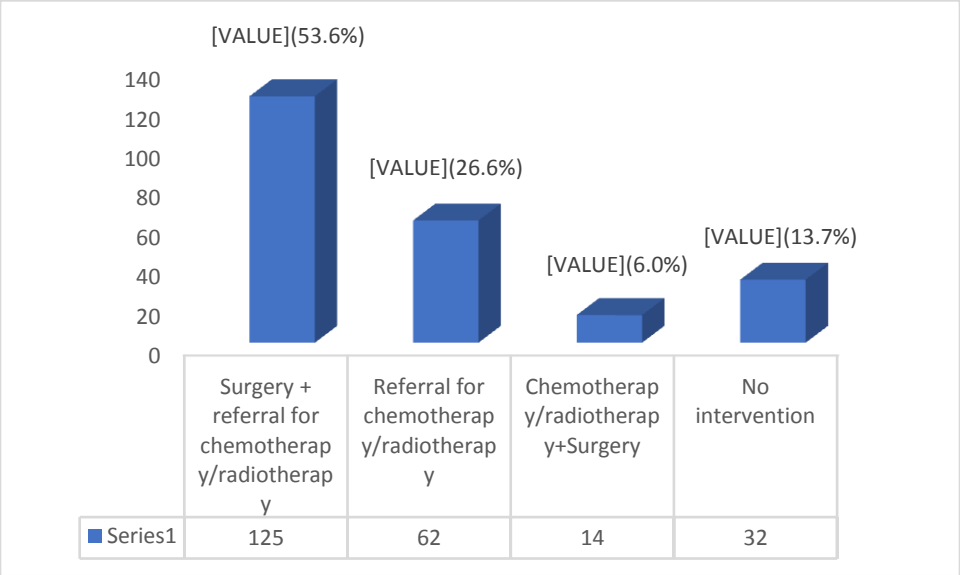

Figure 3: Treatment modalities of the study population

DISCUSSION

The oral and maxillofacial region, particularly the oral cavity, is a common site for squamous cell carcinoma. [10] Although it has predilection for specific sites such as buccal mucosa, tongue and floor of the mouth, sometimes its difficult to identify such specific sites due to the widespread secondary to patients' late presentation. [11, 12] This study revealed more male gender presenting with SCC of the oral and maxillofacial region, similar to several studies in the previous literature. [10, 13, 15] The vulnerability of the male gender to etiological risk factors such as smoking, tobacco and alcohol use, and ultraviolent rays among others were suggested by several authors. [12, 14, 16] Some authors observed decreasing male predilection in recent studies which was attributed to changes in social activities in women whereby they are likely to be equally exposed to risk factors. [17, 18] The results of gender analysis with age categories revealed more SCC in male patients in their 6^{th} decades of life with a statistically significant difference (p=0.000). This is similar to a study reported by Tadbir et al. [19] in an epidemiological analysis of 200 cases of oral squamous cell carcinoma in an Iranian population. Lawal et al. [20] in a retrospective study from the southwestern part of Nigeria reported more males at their 7^{th} decades of life. This means that squamous cell carcinoma of the oral and maxillofacial region is universally more common in males at above 50 years of age.

In this study, SCC was found to predominate in male farmers compared to females with a statistically significant difference(p=0.031). It was reported that the outdoor workers such as fishermen, farmers and gardeners, have a known high riskto the development of SCCof the oral and maxillofacial regionwhichwas attributed to exposure to the ultraviolent radiation. [21] Also theconstant use of agrochemicals such as pesticides, herbicides, fungicides and fertilizers by farmers has been established as a high-risk factor. [16] Thesecould be the reasons why male farmers are more commonly affected in this study. The fact that farming is the major occupation of people leaving in the community where this study was carried out, could also support our finding. Lip cancer was commonly reported in association with sun exposure particularly due to nature of

the individuals' occupation. [22] This study also found lip SCC to be the commonest presentation and therefore buttress previous findings.

Several risk factors were highlighted as the etiological factors for oral and maxillofacial cancers. These risk factors include tobacco and alcohol consumption, human papilloma virus, irradiation, immunosuppressive disorders, viruses, and genetic syndrome. [22, 23] The use of tobacco in various forms including betel quid, beedi, and hookah was reported as a potential etiological factor in oral SCC development. [24, 25] The risk of SCC development was found to be higher in those who chew tobacco and smoke at the same time. In Nigeria, particularly the northern part, where this study was carried out, the main etiological agent for the development of SCC is not known. This study revealed only 6.5% of the patients having a record of tobacco use inform of cigarette smoking.Effiom et al. [26] also highlighted the absence of clear predisposing factors in a similar study from the southern part of Nigeria. Multifactorial factors such as diet, oncologic viruses like the human papilloma virus, malnutrition, the genetic predisposition may be responsible. Nevertheless, there is a need for more investigation to find out the prominent etiological factors in this our clime. The fact that the available record has shown farming as the main occupation of the population in our clime, it may extend our speculation to the chemical exposure from the fertilizers and pesticides used by farmers.

The SCC in the oral and maxillofacial region could occur in any part of the region as the report on the commonest site of occurrence is variable. Singh et al. [23] reported buccal mucosa, and Mahmood et al. [27] reported tongue as the commonest site. In this study, the lower lip was identified as the most common sites for the SCC of the oral and maxillofacial region. This could highlight the role of sunlight exposure or chemical exposure from fertilizers, and pesticides. We opined these chemical exposures could to be the main etiological agents affecting farmers in our region. Anecdotal finding revealed domestic use of empty containers from those chemicals by the local people which could also be a source of carcinogens. Other specific environmental factors such as compromised immunity due to poor balanced diet, insurgency and banditry, poverty,

and illegal mining of minerals that can cause environmental pollution could also be a possibility.

Although clinical features may give a strong suspicion to the diagnosis of SCC, histopathological examination has been the gold standard in the confirmation. Concerning the histologic grading, well-differentiated squamous cell carcinoma constitutes the most common subtype in this study and this was in agreement with several studies in literature [20, 26]. This was found more predominantly in the lower lip compared to other sites with no statistically significant difference (p=0.492). Advanced imaging such as Computed tomography (CT) and Magnetic resonance imaging (MRI) may be necessary in extensive cases to identify the tumor extent and association with vital structures. [7] In our low-resource setting with “out of pocket” healthcare system, plane radiographs are valuable options.Thesurgical excision with a safety margin has been the initial treatment of choice especially in those who presented early. Radiation or chemoradiation is being used as an adjuvant or neoadjuvant. [28, 29] In this study, surgery and adjuvant chemotherapy or radiotherapy was the main treatment given. The requirement for chemoradiation in most of the cases was due extensive nature of the lesions because of late presentation which is a common phenomenon in our clime. The neo-adjuvant chemoradiation is employed to down-stage the tumour, while adjuvant chemoradiation is to mop up any residual lesion. However, a significant number of cases were considered in-operable and hence referred to the oncology unit for chemo or radiation therapy.In this study,13.7% of the cases were not treated. Financial constraints and lack of health insurance coveragewerethe hindering factors to treatment. There was scarcity of data on prognosis because of loss to follow up likely because of the distance from which the patient travel to seek medical care. From the available record, follow up data was available in only 78 (38.8%) of the 201 patients with 1 year survival rate of 92.3%.

CONCLUSION

In the current study, male farmers constitute the majority and only 6.4% were found to be tobacco users. Lower lip was the most common site for SCC of the oral and

maxillofacial region in which well differentiated type predominates.. Surgery, chemotherapy and radiotherapy were the treatment modalities used.

TRANSPARENCY STATEMENT

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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