Original Article

Orofacial Cancers: Pattern and Management in Ibadan, Nigeria

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ABSTRACT

Background: Orofacial cancers remain a significant health burden globally, especially in the developing countries where the incidence is higher and appears to be increasing. This study aims to document the pattern, management and survivorship of patients with orofacial cancers as seen at a tertiary healthcare facilityin Nigeria.

Materials and Methods: This is a retrospective study of patients who presented at our centre with orofacial cancers in the period between January 2010 and December. Patients' demographics, location of lesion, histopathological diagnosis, treatment given and follow-up events were extracted from the records. Patient with insufficient data for analysis were excluded. Data was analysed using IBM SPSS version 21.

Results: 21,090 patients were seen during the study period and 228 of the 1,029 biopsies done were malignant. The study included 213 patients (121 males and 92 females. mean age 48.2 years) with orofacial cancers. The commonest sites were the jaws (48.8%), palate (13.1%) and the tongue (7.5%).Carcinomas constituted 71.8% and were the commonest malignancies. All patients presented in stages III (34.6%) or IV (65.4%). 39.4% of patients had no treatment instituted and surgery alone (21.9%) was the commonest treatment provided. The mean interval between treatment and recurrence was 3.0 months while mean expiration period was 13.5 months.

Conclusion: Treatment conferred a higher probability of survival. Patients treated with surgery (and radiotherapy/chemotherapy) survived better than those treated non-aggressively. In general, about a third (30.8%) of orofacial cancer patients were alive at 5 years post presentation and about 50% of these survivors were living with the disease.

INTRODUCTION

Orofacial cancers are a group of diverse malignancies that affect the soft and hard tissues of the maxillofacial region. These cancers remain a health burden as their incidence ranks sixth globally amongst all cancers.[] Numerous reports have been published onorofacial cancers, especially squamous cell carcinomas (SCC). Reports on the prevalence, aetiological factors and patterns of presentation of orofacial cancers are replete in literature. However, publications on management of orofacial cancers and survival of orofacial cancers other than SCC are less common. Moreso, reports on the outcome of management of orofacial cancers are rare especially from developing countries. This study aims to document the pattern, multidisciplinary approach to management and survival of patients with orofacial cancers, from a tertiary hospital in southwestern Nigeria.

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Keywords: *Orofacial cancer; outcome; survival; Nigeria.*

MATERIALS AND METHODS

All patients diagnosed with orofacial cancers between January 2010 and December 2016 were included in the study. Information on biodata, primary site of the lesion and histological type of cancerwas obtained from clinic and laboratory records of the Departments of Oral and Maxillofacial Surgery and Pathology, while information on treatment, time of recurrence (duration in time before clinical evidence of disease was seen after intervention), time last seen or expiration (death) was retrieved from the case notes. Patients' follow up was from the time of presentation to the time of this study. Phone calls were also made to contact the patient or patients' relatives for follow-up information in cases where patient had defaulted in clinic attendance. Site of lesion was categorized a supper or lower maxillofacial regions with the occlusal plane being the dividing line to ease survival analysis. Treatment was categorized into three groups; aggressive treatment (surgical ablation of disease involving en-bloc resection with or without postoperative chemo-radiation), non-aggressive treatment (chemo-radiation) and no intervention at all.

Data was analysed with IBM SPSS software version 20. Univariate analysis was used to generate tables and figures. Means were compared using Independent T-test and Chi square for categorical variable. Kaplan-Meier curve was generated for survival according to disease site and treatment protocol. Statistical significance was set at $p<0.05$. Ethical approval was obtained from the Ethics review board of the University of Ibadan/University College Hospital Ibadan.

RESULTS

A total of 21,090 patients were seen at the facility during the seven-year study period and 1,029 of these patients had biopsies done, 228 (22.2% of biopsies) of these were malignant. This gave a hospital prevalence of 1.1% of all cases seen during the study period. Data for 213 cases(93.4% of the identified cancer cases) was retrieved from clinic and laboratory records. There were 121 males and 92 females (M:F = 1.3:1) with a mean age of 48.2 (SD ± 21.0) years, their ages range from 3 to 92 years. Seventy-nine (37.1%) were below the age of 40 years. The age distribution according to type of cancer is as shown on Table 1. The differences in age were significant with a p-value = 0.0001. Carcinomas (71.8%) were the commonest orofacial cancer in this study with SCC having the highest occurrence (38.0%) followed by adenocarcinomas(13.1%),which incidentally occurred more frequently in females, although this was not statistically significant (p=0.489) (Table 1). The commonest sites were the jaws (48.8%) followed by the palate and the tongue 13.1% and 7.5% respectively (Table 2).

Table 1: *Age distribution according to type of cancer*

Type of cancer	Male	Female	Total Number of cases	Mean age in years* (SD)	Median age in years
Carcinomas					53.0
Squamous cell Ca	48	33	81	53.9 (SD ±18.9) Range: 4 – 92 years	
Adenocarcinomas**	11	17	28		
Others	25	19	44		
			153		
Sarcomas					31.0
Osteosarcoma	11	5	16	30.5* (±15.068) Range: 3 – 60 years	
Rhabdosarcoma	4	2	6		
Others	8	4	12		
			34*		
Lymphomas	14	12	26	35.4 (±22.991) Range: 6 - 75 years	35.0
Total			213*	48.2 (±21.030) Range: 3 – 92 years	49.0

P=0.000, *Age was not documented for 3 cases.

**Adenocacinoma (NOS)

Table 2: ***Site distribution of cancer by histological type***

Site	Carcinomas			Sarcomas			Lymphoma	Total
	SCC	Adenocarcinoma	Others	Osteosarcoma	Rhabdomyosarcoma	Others		
Maxilla	20	11	10	2	2	2	4	51
Mandible	14	4	8	14	2	5	6	53
Palate	10	6	7	0	0	1	4	28
Tongue	14	0	0	0	0	1	1	16
Cheek	3	1	3	0	0	2	0	9
FOM	2	2	1	0	0	0	0	5
Parotid	0	2	4	0	0	0	0	6
Submandibular	1	1	2	0	0	0	0	4
Face	5	0	2	0	0	0	4	11
Sublingual	0	0	1	0	0	0	0	1
Lower lip	4	1	0	0	0	0	0	5
Upper lip	2	0	2	0	0	0	0	4
Lip NOS	1	0	1	0	0	0	0	2
Oropharynx	1	0	1	0	0	0	2	4
Total	77	28	42	16	4	11	21	199*

*Site was not specified for 14 cases.

The medical records of137 (64.3%) patients had adequate information for further analysis. All patients presented in stages III (34.6%) or IV (65.4%). Seven cases of metastasis were recorded; 5 to the lungs and 2 to the spine. This included 5 cases of squamous cell carcinoma, and 1 case each of lymphoma and adenoid cystic carcinoma.

Over a third (39.4%) of the patients had no intervention while surgical intervention as only mode of treatment was instituted in 21.9% of patients (Figure 1).Follow up was documentedin83 cases and the range was 5 to 93 months. Mean follow up period was 49.6 months (±27.0), median 46.0 months. Recurrence was recorded in 20 cases (35.1%) and ninety percent of recurrence occurred in the first year. The mean interval between treatment and recurrence was 3.0(SD±1.4) months. Time of expiration (death) was available for 55 cases: mean expiration period was 13.5 (± 11.1), median was 10.0 months, ranging from 1 month to 48 months from presentation in clinic. The differences in the follow up periods according to gender, site of cancer, type of cancer and treatment provided were not statistically significant. Also, the differences in survival according to gender, type of cancer and site of cancer were not statistically significant (Table 3). However, there was a significant difference in the number of cases that recurred according to gender and the number of cases that survived according to the type of treatment (Table 3). Treatment conferred a higher probability of survival (Figure 2) and those treated aggressively survived better than those treated non-aggressively (Figure 3). In general, about a third (30.8%) of orofacial cancer cases were alive at 5 years post presentation and about 50% of these survivors were living with the cancers (Figure 4).

Figure 1: *Treatment provided*

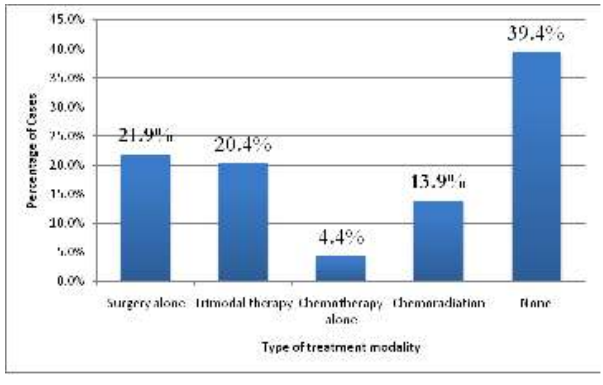
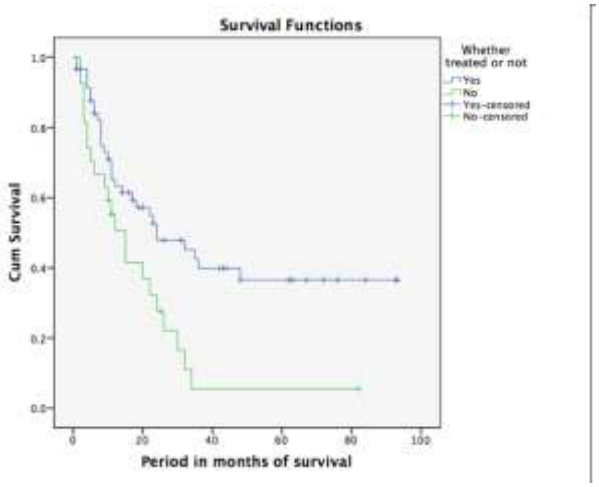


Table 3: *Follow up, recurrence and survival in months according to gender, site of cancer, type of cancer and type of treatment.*

			Number of cases	–	Median	p-values
Gender	Male	Follow up	43	48.5 (±29.639)	44.0	Follow up = 0.706 Recurrence = 0.025* Survival = 0.235
		Recurrence	11	2.5 (±0.688)	2.0	
		Survival period	43	21.2 (±21.704)	15.0	
	Female	Follow up	40	50.8 (±26.4)	47.0	
		Recurrence	9	3.78 (±1.641)	3.0	
		Survival period	40	27.7 (±28.054)	16.0	
Site of cancer	Upper maxillofacial region	Follow up	37	57.4 (±26.609)	63.0	Follow up = 0.058 Recurrence = 0.802 Survival = 0.083
		Recurrence	11	3.0 (±1.414)	3.0	
		Survival period	37	29.2 (±27.726)	20.0	
	Lower maxillofacial region	Follow up	31	44.6 (±27.886)	40.0	
		Recurrence	6	2.8 (±0.983)	2.5	
		Survival period	31	18.7 (±20.115)	10.0	
Type of cancer	Carcinomas	Follow up	59	50.8 (±26.962)	48.0	Follow up = 0.084 Recurrence = 0.480 Survival = 0.168
		Recurrence	14	3.3 (±1.490)	3.0	
		Survival period	59	27.5 (±26.233)	18.0	
	Sarcomas	Follow up	17	54.6 (±32.018)	68.0	
		Recurrence	5	2.4 (±0.894)	2.0	
		Survival period	17	18.7 (±23.33)	8.0	
	Lymphomas	Follow up	7	27.7 (±16.889)	27.0	
		Recurrence	1	3.0 (single case)	3.0	
		Survival period	7	11.7 (±9.196)	10.0	
Treatment	Treated aggressively	Follow up	48	50.0 (±29.103)	48.0	Follow up = 0.894 Survival = 0.024*
		Recurrence	18	3.2 (±1.383)	3.0	
		Survival period	48	30.7 (±28.047)	21.0	
	Not treated aggressively	Follow up	8	53.0 (±31.433)	54.0	
		Recurrence	NA	NA	NA	
		Survival period	14.5	14.5 (±19.849)	7.0	
	Not treated	Follow up	27	47.9 (±25.7433)	43.0	
		Recurrence	NA	NA	NA	
		Survival period	27	16.0 (±16.468)	11.0	

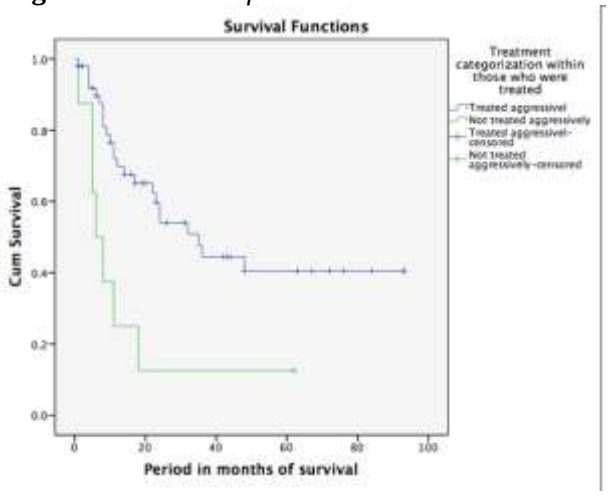
**Significant.*

Figure 2: *Survival of those treated and not treated*



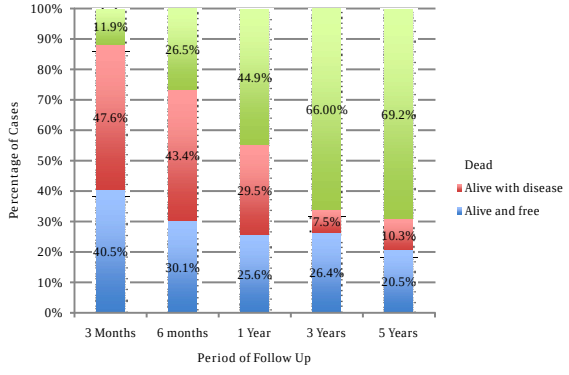
Kaplan-Meier Log Rank (Mantel-Cox) = 0.007

Figure 3: *Survival of treated cases*



Kaplan-Meier Log Rank (Mantel-Cox) = 0.005

Figure 4: *Frequency of survival of MXF in time*



DISCUSSION

The incidence of oral cancers varies according to geographical location, race and gender.[2,3] The South Asian region has the highest incidence in the world; while European region has the least incidence.[2,4] Community incidence reports in African countries is plagued by incomplete data and therefore not commonly reported. However, hospital-based prevalence reports are more common. Relative frequencies have been reported such as 2.1% in Zaire[5] and this is similar to the 1.1% observed in this study. Community base study on incidence of oral and maxillofacial malignancy will be helpful in accessing the burden of disease in our environment.

Oral cancer is reported more commonly in the male gender with varying male to female ratios.[6,7] The male female ratio for oral cancer in Nigeria appears to be reducing, a trend that was enunciated in a previous study in this centre.[8] The decline was observed as 1.7:1 in 1975, 1.6:1 in 1985, 1.5:1 in 1995 and 1.4:1 in 2007[8-11],the gender gap is even narrower in the present study at 1.3:1. This increasing incidence of orofacial malignancies in females was also observed in a study of head and neck cancer, in Lagos.[12] It has been suggested that increased participation of females in habits that predispose to oral cancers like tobacco use and alcohol intake may contribute to the higher incidence being observed in them. However, reason(s) for the increasing incidence of oral cancer in females needs to be further investigated.

Generally, oral cancer is associated with advanced age. However, the mean age in this part of the world was younger than that observed in the developed world. A mean age of 48.2 years seen in this study was similar to the reports of 42.2years from Lagos[13] and 42.3 years from Zaire.[5] On the contrary, a mean age of 61.7years was reported from a study in the United Kingdom by Jerjes in 2010.[6] Some authors have suggested that shorter life expectancy and/or early exposure risk factors to in Africans may explain the lower mean age compared to those USA and UK.[14]

Patients presenting late with very large lesions is a common scenario in our environment. Adekeyeet al, 1985, Otoh, 2004 and Oji, 2006 reported 137 cases, 54 cases and 81cases of oral cancers respectively, none of the cases presented early.[4,15,16] All cases observed in this study presented in stages III or IV only, similar to a previous report by Oji.[16] Lack of awareness on the nature of oral cancer, financial incapacitation, lack of access to specialized health care services and faith in traditional healers are possible reasons that have been proposed for these late presentations.[15] However, studies are needed to identify the causes of these late presentations and how to mitigate it.

The tongue and floor of mouth are the most commonly affected sites in the Caucasian population.[6,7,17] A predominant gingival site has previously been reported with the mandibular gingiva slightly higher than the maxillary gingiva, as noted in this study.[18-20] The jaw was the predominant site in this study, this may reflect initial affectation of the gingivae with subsequent involvement of the jawbone as the tumour increased in size with late presentation. The second commonest site was the palate, which has been reported to be the commonest site in many African studies.[5-8] Although some Nigerian studies have documented tongue as the most common site of occurrence.[21]

Squamous cell carcinoma was the most common orofacial cancer in this study; the relative frequency of 38.0% seen in this study was less than previous reports of 42.8% to 90.0% of all cancers reported in literature.[5,22,23] Squamous cell carcinoma has been the most common type of oral carcinoma followed by adenocarcinomas.[8,15,23,24] Among the sarcomas, osteogenic sarcoma was the commonest histological type, which has been similarly reported by other authors.[13,23]

The majority of the metastatic cases was to the lungs and was most frequently thesquamous cell carcinoma, this may be because squamous cell carcinoma was the most common type of oral cancers observed.

Publications on oral cancer from developing countries are more commonly focused on clinical presentations, pathologic characteristics and less commonly quality of life after treatment.[12, 13, 28, 29, 14, 16, 22-27] Even less common are reports on management and outcome of management of orofacial cancers. There are few reports of management and management outcome that were descriptive in nature without statistical analysis[15,16,30] These reports at best can only imply but cannot be used to evaluate the impact of treatment.

Majority of the cases in this study did not receive treatment for reasons that were not documented. This lack of treatment was similarly documented for the majority of cases reported by a study in Jos, North Central Nigeria where 70.6% of the cases considered for treatment were not treated.[] The reasons for this lack of treatment need to be investigated in order to proffer possible solutions. However, out of pocket payment by patients for the management of orofacial cancers and late presentation with unresectable tumours may play important roles in the non-treatment of these patients.

Treatment of oral cancer in this part of the world, although far from optimal, appears to be improving. In the eighties, about two thirds of patients who presented with oral cancers in a tertiary Nigerian hospital did not receive any treatment.[15] This has reduced to just over a third of patients in this study.In addition, other treatment modalities like radiotherapy and chemotherapy are recently being used unlike surgical intervention alone that was previously the only available treatment modality.[15]

Trimodal treatment protocol involving surgery, chemotherapy and radiotherapy was employed as appropriate. Surgical intervention involved complete ablation of the disease with surgically safe margins, this was followed with radio-chemotherapy as necessary. However, lesions that were inoperable because of the extent of the lesion and or involvement of vital structures or extensive metastasis were offered palliative chemotherapy and radiotherapy only.

Despite the late presentation of these cases, intervention for those who were treated aggressively still had an impact on survival as these patients survived significantly longer than those who were not treated at all (Figure 1 and Table 3). This beneficial role of surgical treatment in advanced cancer cases has also been recognized in previous reports, especially when neoadjuvant chemotherapy was employed.[] However, it is noteworthy that lack of clinical evidence of a tumour does not translate to being cured of the disease. Therefore surgical interventions at stages III and IV although beneficial, may not be curative.

In this study males had significantly shorter recurrence period than females (Table 3). Masoudi et al similarly reported a two–fold higher risk of loco-regional recurrence in males and suggested the male gender is an indication for more frequent reviews.[32] In a study that estimated survival after initial treatment of oral cavity cancer, majority (66%) of patients who had recurrence were of the male gender.[33] The male gender has also been implicated for higher risk of competing cause of death such as cardiovascular disease, lung cancer and metachronous cancers.[34]

The global five-year survival rate from oral cancer has been documented to be about 50%.[2] Reports on survival of oral cancer in developing countries are limited in literature. In Brazil, one-year survival of oropharyngeal cancer is 32.6%, while the five-year survival from oral cancer in Chile ranged from 20% to 87.2%.[29] No report was found on the survival of Nigerian oral cancer patients. The five-year survival in this study (30.8%) is lower than the global report of about 50% but comparable to the report from Chileand Brazil (27%).[2,35] However, this differs appreciably from the 72.2% 5-year survival of oral squamous cell carcinoma in the United Kingdom.[6] Although the exact reasons for this disparity are not known, survival of oral cancer have been reported to depend on several factors such as the histological type and grade of the oral cancer, stage of the disease, site of occurrence, presence of lymph node involvement and/or distant metastasis, extent of surgical intervention, surgical margin, pre-treatment monocyte count, age and gender.[29,36,37] The influence of these factors on the survival of oral cancer in this study was difficult to assess as this was a retrospective study and all patients presented with late stage disease. It would be beneficial to investigate the reasons for the observed difference in survival rates using prospective studies. However, the late presentation observed in this study may account for the lower five-year survival rate.

Despite the general late presentation observed in the current study, treatment had significant impact on survival and those who were treated aggressively survived longer than those who were treated less aggressively (Table 3). It was also observed that those who did not have treatment at all survived longer than those who were treated with radio-chemotherapy alone (Figure 4). The reason for this could not be ascertained from available data in this study. It is opined that the effect of the palliative radio-chemotherapy on the background of the tumour burden allowed the patients to succumb earlier. This hypothesis however needs to be investigated.

This study has been able to document the hospital-based frequency of orofacial cancers and the impact of management on the survival of patients with these cancers in our environment. However, there were some limitations to this study. Most prominent amongst these challenges were follow up and missing data. The role of electronic data, ensured by data managers as well as use of standardized, structured proforma in which relevant questions are asked, as opposed to blank sheets for documenting cancer cases, should be explored to enhance adequate and more comprehensive data collection. The retrospective nature of this study did not allow the inclusion of some parameters such as the exact cause of death in the patients. This would have been informative, as some of the patients could have expired secondary to other causes, which were unrelated to the cancers. Additionally, among cases where the cause of death was related to the cancer, an appreciation of whether the death was related to primary site involvement or from metastatic site involvement would be informative. Also, of

importance would have been the type and pattern of complications of management. We recommend that a prospective longitudinal study investigating all these shortcomings will be useful in drafting treatment protocols for oral and orofacial cancers in our environment.

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