Original Article

Locally Advanced Orofacial Malignancy: Synopsis of Inoperable Lesions at an Urban Tertiary Health Facility in Nigeria

CE Anyanechi[1,2], OD Osunde[1,2], BD Saheeb[3,4]

[1]Department of Oral and Maxillofacial Surgery, University of Calabar Teaching Hospital, Calabar, [2]Department of Oral and Maxillofacial Surgery, University of Calabar, Calabar, [3]Department of Oral and Maxillofacial Surgery, University of Benin Teaching Hospital, Benin-City, [4]Department of Oral and Maxillofacial Surgery, University of Benin, Benin-City, Nigeria

Received: 06-Nov-2019;
Revision: 02-Dec-2019;
Accepted: 24-Jan-2020;
Published: 04-May-2020.

ABSTRACT

Background: Locally advanced inoperable orofacial malignancies do present clinically, and constitute a significant public health burden worldwide. **Objective:** To determine the prevalence and clinical characteristics of Stage IV locally advanced inoperable orofacial malignancies for consecutive patients. **Materials and Methods:** A 24-year retrospective study was undertaken, and data obtained from hospital register, case files, and histopathological reports of patients were recorded in a proforma. The variables studied were age, sex, type of lesion and site, duration of lesion, tobacco/alcohol use, and socioeconomic status of the patients and clinical features of the lesions. **Results:** Twenty-six patients presented, giving a prevalence of 11.2%. The most common lesion was adenoid cystic carcinoma, 23.1%. Males accounted for 18 (69.2%) cases and females, 8 (30.8%) giving a male to female ratio of 2.3:1. The ages ranged from 21 to 65 years, mean (SD) 48.6 (7.3) years. The gender distribution was clinically and statistically significant in favor of the males (P = 0.001). The patients were in the low socioeconomic class and 20 (76.9%) indulged in chronic use of tobacco and alcohol. The duration of the lesions ranged from 1.8 to 3.1 years. The maxilla/facial skin was the commonest site (46.2%). Clinically and statistically, the relativity of site distribution of lesions was significant (P = 0. 002). The clinical features occurred in combination resulting in an average of 10 symptoms and signs in each patient. **Conclusion:** The synopsis of these lesions shows that all have undergone metastasis; salivary gland malignancies were most common with maxilla as the commonest site.

KEYWORDS: *Inoperable, locally advanced, malignancy, orofacial, synopsis*

INTRODUCTION

Like in other parts of the body, advanced inoperable malignant lesions do present clinically in the orofacial region as documented by Wadhwan *et al*.[1] and Kumar *et al*.[2] Locally advanced orofacial malignancies in patients are of clinical importance because of their site of occurrence, spread to contiguous structures, high morbidity and mortality rates coupled with late presentation for clinical evaluation and treatment due to ignorance, traditional belief in alternative therapy, and low socioeconomic status of most of the patients.[3-6] In addition, the occurrences of some of the lesions in relatively obscure sites in the orofacial region like the retromolar trigone contribute to inoperable advanced disease on presentation as stated by Vishak *et al*.[7] and Seoane-Romero *et al*.[8] These lesions present with facial disfigurement, functional impairment, and psychosocial problems constituting a significant public health burden worldwide.[9-11] Lakshmaiah *et al*.,[12] Braimah *et al*.,[13] and Parkins *et al*.[14] noted that the dearth of trained healthcare providers and limited health services centers in certain rural areas particularly in sub-Saharan Africa leads to delay in diagnosis and treatment of the lesions and consequently advanced stage on presentation.

Access this article online

Quick Response Code:

Website: www.njcponline.com

DOI: 10.4103/njcp.njcp_607_19

Address for correspondence: Dr. CE Anyanechi, Department of Oral and Maxillofacial Surgery, University of Calabar Teaching Hospital, Calabar, Nigeria. E-mail: ceanyanechi@gmail.com

How to cite this article: Anyanechi CE, Osunde OD, Saheeb BD. Locally advanced orofacial malignancy: Synopsis of inoperable lesions at an urban tertiary health facility in Nigeria. Niger J Clin Pract 2020;23:691-6.

These cancers, due to their locally advanced nature and huge size, spread to contiguous and distant sites, and present management challenges. It was reported that the patients afflicted by the lesions are sometimes treated with nonsurgical methods like radical radiotherapy, palliative radiation, induction chemotherapy, concurrent chemoradiation, and supportive care.[15-17] These treatment modalities have been effective in down staging the cancer and sometimes enabling radical resection, thereafter with resultant improved quality of life of the patient as documented by Patil *et al*.[17]

Presently, no study in our community has evaluated the prevalence of inoperable locally advanced orofacial tumors with a view to determining an increase in their occurrence over a certain period. In addition, the specific clinicodemographic variables and histopathological pattern of the tumors have not been determined. This study therefore determines the prevalence and clinical characteristics of Stage IV locally advanced inoperable orofacial malignancies for consecutive patients, who presented in a tertiary health facility over a 24-year period.

Materials and Methods

This study aimed to retrospectively determine the prevalence rate and clinical characteristics of Stage IV[18,19] locally advanced inoperable lesions for consecutive patients who presented with orofacial malignancies. Using the eight edition of TNM (Tumor, Lymph Nodes, Metastasis) classification[18] to determine the clinical stage of the lesions on presentation, Type IV orofacial malignancies in the patients were defined as locally advanced and inoperable, and were studied. The TNM criteria used for the classification of carcinomas, bone and soft tissue sarcomas was based on the eight editions of TNM classification as documented by Lydiatt *et al*.,[18] and Amin *et al*.[19] The TNM staging was done after including histological grading of the tumors to the TNM classification of soft tissue sarcomas. The patients that presented to the Oral and Maxillofacial Surgery Clinic of the study institution between January 1995 and December 2018 were studied. Cases with complete records were included in the study, whereas those with incomplete records were excluded. In addition, cases diagnosed as Hodgkin and non-Hodgkin's lymphomas were also excluded. Approval from Health Research Ethics Committee of the institution was obtained, dated 04/12/2018.

Information obtained from the hospital register, case files, and histopathological reports were age, sex, type of lesion, site; duration of lesion, tobacco/alcohol use, socioeconomic status of the patients and clinical features which were recorded in a proforma designed for the study. The extents of the lesions were determined by clinical examination and radiological evaluation, which include the use of plain radiographs and sometimes ultrasound and computed tomography scans. In addition to the parameters listed above, the socioeconomic status of the patients was also determined, and this was based on Adedeji's classification.[20]

The data obtained were analyzed using SPSS Version 13, Chicago, IL, USA. The results were presented as frequencies, percentages, means, and standard deviations (SD). Inferential statistics were done using Fisher's exact test where appropriate, and statistical significance was set at $P < 0.05$.

Results

Twenty-six (26) patients out of 232 with orofacial malignancies seen over the period of study had locally advanced and inoperable lesions, giving a prevalence of 11.2%. All the patients that were seen during this period had complete record and were included in the study. Male accounted for 18 (69.2%) cases and female, 8 (30.8%) giving a male to female ratio of 2.3:1. The ages ranged from 21 to 65 years, mean (SD) 48.6 (7.3) years. The

Table 1: Age distribution of malignant inoperable orofacial lesions (*n*=26)

Lesion	21-30	31-40	41-50	51-60	61-70	Total
Adenoid cystic carcinoma	0	0	2	4	0	6
Mucoepidermoid carcinoma	0	0	0	0	4	4
Osteogenic sarcoma	2	2	0	0	0	4
Chondrosarcoma	0	2	2	0	0	4
Squamous cell carcinoma	0	0	0	0	4	4
Rhabdomyosarcoma	2	0	0	0	0	2
Malignant fibrous histiocytoma	0	2	0	0	0	2
Total	4	6	4	4	8	26

Fisher's Exact Test: χ^2=8.726; P=0.105

Table 2: Gender distribution of inoperable orofacial malignancies (*n*=26)

Lesion	Male	Female	Total (%)
Adenoid cystic carcinoma	2	4	6 (23.1)
Mucoepidermoid carcinoma	2	2	4 (15.4)
Osteogenic sarcoma	4	0	4 (15.4)
Chondrosarcoma	4	0	4 (15.4)
Squamous cell carcinoma	2	2	4 (15.4)
Rhabdomyosarcoma	2	0	2 (7.7)
Malignant fibrous histiocytoma	2	0	2 (7.7)
Total	18	8	26 (100.1)

Fisher's Exact Test: χ^2=40.097; P=0.001

Table 3: Site distribution of inoperable malignant lesions (*n*=26)

Lesion	Maxilla	Mandible	Floor of the mouth	Total
Adenoid cystic carcinoma	4	2	0	6
Mucoepidermoid carcinoma	0	2	2	4
Osteogenic sarcoma	4	0	0	4
Chondrosarcoma	2	2	0	4
Squamous cell carcinoma	2	2	0	4
Rhabdomyosarcoma	0	0	2	2
Malignant fibrous 30 histiocytoma	0	0	2	2
Total	12	8	6	26

Likelihood Ratio: χ^2=30.737; df=12; *P*=0.002

Table 4: Clinical features of the 26 inoperable malignant lesions

Clinical feature	Frequency
Weight loss	26
Pain	26
Swelling	26
Metastasis	26
Cervical lymphadenopathy	26
Ulceration	24
Toothache	22
Bleeding per oral	22
Numbness	20
Missing tooth/teeth	18
Epistaxis	8
Nasal discharge	6
Blurred vision	4
Total	254

distribution of the lesions according to age and gender are shown in Tables 1 and 2, respectively. The age distribution of the patients was insignificant (P = 0.105). However, the gender distribution was clinically and statistically significant in favor of the males (P = 0.001). The patients were in the low socioeconomic category; Class IV, 6 (23.1%) and class V, 20 (76.9%). Those who indulged in chronic use of tobacco and alcohol were 20 (76.9%) while the remaining 6 (23.1%) patients did not use these substances. The duration of the lesions ranged from 1.8 to 3.1 years (mean 2.4 ± 0.7 years). Tables 3 and 4 respectively show the site distribution and clinical features of the malignancies that presented. The maxilla/facial skin accounted for 46.2% of the sites, whereas the mandible/facial skin, 30.8% and floor of the mouth, 23.1% were the other sites the lesions developed [Figures 1 and 2]. The lesions affected simultaneously the hard and soft tissues and facial skin at sites where they presented. Both clinically and statistically, the relativity of site distribution of the lesions that presented was significant (P = 0. 002). Lesions like adenoid cystic carcinoma, osteogenic sarcoma, rhabdomyosarcoma, and malignant fibrous histiocytosis were site specific. While adenoid cystic

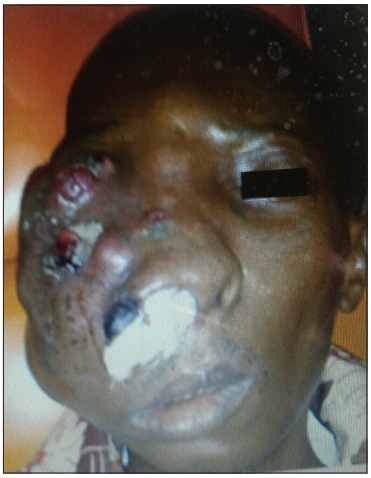

Figure 1: Extraoral view of adenoid cystic carcinoma of the minor salivary gland affecting the upper jaw in a 41-year-old male patient who presented 1.3 years after the lesion was first noticed

Figure 2: Extraoral view of mucoepidermoid carcinoma of the minor salivary gland affecting the lower jaw in a 65-year-old male patient who presented 1.6 years after the condition was first noticed

carcinoma occurs twice as much in maxila as in the mandible, osteogenic sarcoma was predominantly seen in the maxilla. On the other hand, rhabdomyosarcoma and malignant fibrous histiocytoma occurred predominantly in the floor of the mouth. The clinical features occurred in combination resulting in an average of 10 symptoms and signs presenting in each patient. The common sites

of metastasis of the lesions were lungs 14 (53.8%), thyroid 6 (23.1%), kidney 4 (15.4%), and prostate 2 (7.7%). The patients were referred to other centers for non-surgical treatment after histopathological diagnosis.

Discussion

This study shows that Stage IV locally advanced inoperable orofacial malignant lesions do occur in the study environment as shown by the 11.2% prevalence rate. The lesions were described as inoperable because of their extent of spread within the contiguous and distant tissues and size. It is difficult to compare this prevalence rate with those of earlier studies because of differences in study design. Some earlier studies were presented as case reports or both benign and malignant lesions lumped together and studied and in some, only one type of malignant lesion which was inoperable was the focus of the study. However, the result obtained is lower than those of Lakshmaiah *et al*.[12] and Rudresha *et al*.,[21] who recorded 58 and 80 cases respectively of inoperable oral cavity malignant neoplasm during a shorter period of study but higher than the reports of Wadhwan *et al*.[1] and Fomete and Ogbeifun.[22] From the data obtained in this study regarding the duration of the lesions before the patients presented in the hospital, it is obvious they did present late if the time they presented is compared with the clinical course of the lesions. The reasons given by the patients for late presentation include not believing that cancer can be treated by orthodox medicine, superstitious belief, economic, ignorance, and negligence of their health on their part. These reasons have been adduced in studies done earlier in sub-Saharan Africa.[6,13,22] The patients that presented were in the lower socioeconomic class and majority of them were chronic users of tobacco and alcohol. Conway *et al*.[23] noted in their study that oral cavity cancer affects people in the lower socioeconomic strata of the society due to a higher exposure to risk factors such as the use of tobacco. The concomitant use of alcohol and tobacco has been shown to significantly increase the risk of head and neck malignancy by Zygogianni *et al*.[24] It has been found that persons who smoke and drink are nearly 38 times more likely to develop head and neck cancers than individuals who do neither.[25] Amanda *et al*.[26] also reported that low socioeconomic status patients have higher levels of several modifiable cancer risk factors. Consequently, they opined that such patients are also 2.5 times more likely to be current smokers compared to higher socioeconomic status individuals, and report lower rates of screening for cancer. Similarly, Clegg *et al*.[5] reported that socioeconomic patterns in incidence vary for specific cancers and such patterns were mostly associated with lower socioeconomic status.

As documented by earlier researchers, the mean age obtained in this study supports the view that orofacial malignancies occur more often with increasing age.[4,6] The increased incidence of malignancies with advancing age may be partly due to the increase of free radicals with aging as noted by Vokes *et al*.[27] Also, the diminishing ability of the immune system to eliminate altered cells by causing reduction in the effectiveness of cancer surveillance by immune cells is increased with advancing age.[28,29]

In the present study, males were affected more frequently than females as reported earlier in other studies.[12,13] Although orofacial malignancies affect males more commonly than females, some studies have shown that the ratio is equalizing without much gender difference.[6,12] The reason for the disparity in gender is not known but some researchers attribute it to genetic inheritance and the demographic characteristics of the population studied rather than gender disposition.[26,27]

As earlier documented by other researchers, maxilla, mandible, and floor of the mouth including facial skin was affected in the present study.[13-16] On the contrary, other sites of common occurrence reported for locally advanced and unresectable orofacial malignancies are buccal mucosa, gingivobuccal complex, tongue, and parotid, palate, submandibular and sublingual regions, including scalp skin among others.[11,13,21] The tumors that presented in this study affected both the hard and soft tissues due to the contiguous spread of the lesions which is attributable to late presentation by the patients.

The tumors that were identified in this study and their clinical features have been reported earlier by other researchers.[2,4,6,13-15] Each patient presented with an average of 10 clinical symptoms and signs which suggests that the lesions were in the late stages of their clinical progression and course. Evidence suggests that surgical resection is technically not possible in locally advanced oral cavity malignancy as the oral cavity is anatomically close to the infra-temporal fossa and masticator space, and also the possibility of metastasis.[30] These patients that present early (Stage I: $T_1N_0M_0$ and Stage II: $T_2N_0M_0$) whose tumors are often localized to the organ of origin are usually treated by surgery, radical radiotherapy with or without chemotherapy with an estimated 5-year survival of 40–60%.[2,4,5] Stages III ($T_3N_0M_0$, or T_1, T_2 or $T_3N_1M_0$) and IV (any T_4 lesion, any N_2 or N_3 lesion, or any M_1 lesion), the tumors spread beyond the organ of origin have worse prognosis with survival rate of 41% and 15%, respectively, over a period of 3 years for patients treated with radiotherapy and chemotherapy.[4,8,9,15] Factors that may influence the use of nonsurgical treatment include unresectability of the

lesion, tumor volume, distant metastases, comorbidity, age, patient's preference, functional imaging parameters, and response on induction chemotherapy among other variables.[1,16,17,21,31] The mortality resulting from orofacial malignancy is strongly related to the stage of diagnosis, as detection of early stage lesions is associated with significantly improved survival with lower morbidity while it is the reverse for late stage lesions.[4,16,17] The patients in this study that needed radiotherapy treatment were referred to other centers for treatment because of unavailability of this service at the study center.

Locally advanced orofacial malignancies are of clinical significance because of their site of occurrence, spread to contiguous structures, high morbidity and mortality rates coupled with late presentation for clinical evaluation and treatment due to ignorance, traditional belief in alternative therapy, and low socioeconomic status of most patients.[3-6] In the present study, tumors presented with facial disfigurement and functional impairment, and due to their clinical stage spread to contiguous and distant sites, presenting management challenges. This study has determined the prevalence of these tumors in this community, in addition to their clinicodemographic characteristics and histopathological pattern which will enhance the recognition of the significance of universal coverage and equity in health services by the agencies concerned in this environment irrespective of the socioeconomic status of the patients.

It is possible that not all the patients afflicted with orofacial malignancy and Stage IV locally advanced inoperable lesions in our community presented for clinical evaluation and treatment during the study period. This would have negatively affected the prevalence rate obtained in this study. This limitation is supported by an earlier study carried out in the same environment.[32]

Conclusion

The synopsis of these lesions includes a prevalence of 11.2%, and shows that all has undergone metastasis. Salivary gland malignancies were the most common with maxilla as the commonest site. In addition, majority of the patients were in the lower socioeconomic class and each presented with an average of 10 symptoms and signs because of late presentation. Consequently, the recognition of the significance of universal coverage and equity in health services by government and non-governmental agencies will ensure universal coverage for all patients which will directly benefit these patients irrespective of their socioeconomic status and minimize late presentation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Acknowledgements

The authors are grateful to the staff of the Oral and Maxillofacial Surgery Department of this institution who were of immense assistance during the management of the patients and data collection, particularly the dental surgeons, nurses, information technology and health record staff, dental surgery assistants, and dental therapists.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Wadhwan V, Chaudhary MS, Gawande M. Fibrosarcoma of the oral cavity. Indian J Dent Res 2010;21:295-8.
2. Kumar S, Heller RF, Pandey U, Tewari V, Bala N, Oanh KT. Delay in presentation of oral cancer: A multifactor analytical study. Natl Med J India 2001;14:13-7.
3. Banon JN, Saad MN. Operative Plastic and Reconstructive Surgery. 1st ed. Edinburgh, London Melbourne and New York: Churchill Living Stone; 1980.
4. Jaafari-Ashkavandi Z, Mohammad-Javad A. A clinic-pathologic study of 142 orofacial tumors in children and adolescents in Southern Iran. Iran J Pediatr 2011;21:367-72.
5. Clegg LX, Reichman ME, Miller BA, Hankey BF, Singh GK, Lin YD, *et al*. Impact of socioeconomic status on cancer incidence and stage at diagnosis: Selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study. Cancer Causes Control 2009;20:417-35.
6. Ibikunle AA, Taiwo AO, Braimah RO. Oral and maxillofacial malignancies: An analysis of 77 cases at an academic medical hospital. J Orofac Sci 2016;8:80-5.
7. Vishak S, Ranqarajan B, Kekatpure VD. Neoadjuvant chemotherapy in oral cancers: Selecting the right patients. Indian J Med Paediatr Oncol 2015;36:148-53.
8. Seoane-Romero JM, Vázquez-Mahía I, Seoane J, Varela-Centelles P, Tomás I, López-Cedrún JL. Factors related to late stage diagnosis of oral squamous cell carcinoma. Med Oral Patol Oral Cir Bucal 2012;17:e35-40.
9. Gorsky M, Dayan D. Referral delay in diagnosis of oro/oropharyngeal cancer in Israel. Eur J Cancer B Oral Oncol 1995;31:166-8.
10. Kalburge JV, Sahuji SK, Kalburge V, Kini Y. Osteosarcoma of mandible. J Clin Diagn Res 2012;6:1597-9.
11. Patil VM, Noronha V, Joshi A, Banavali SD, Muddu V, Prabhash K. Preoperative chemotherapy and metronomic scheduling of chemotherapy in locally advanced oral cancers. Oncology 2016;91(Suppl 1):35-40.
12. Lakshmaiah KC, Suresh TM, Babu KG, Sirsath NT, Dasappa L, Abraham LJ. Locally advanced oral cavity squamous cell

carcinoma: Barriers related to effective treatment. South Asian J Cancer 2015;4:61-4.
13. Braimah RO, Soyele OO, Aregbesola SB, Rasheed MA. Pattern of histologically diagnosed orofacial tumour and disparity in number managed in a Nigerian teaching hospital: A 5 year review. J Dent Allied Sci 2017;6:60-4.
14. Parkins GE, Armah GA, Tettey Y. Orofacial tumours and tumour-like lesions in Ghana: A 6-year prospective study. Br J Oral Maxillofac Surg 2009;47:550-4.
15. Ketabchi A, Kalavrezos N, Newman L. Sarcomas of the head and neck: A 10-year retrospective study of 25 patients to evaluate treatment modalities, function and survival. Br J Oral Maxillofac Surg 2011;49:116-20.
16. González-González R, Bologna-Molina R, Molina-Frechero N, Domínguez-Malagon HR. Prognostic factors and treatment strategies for adult head and neck soft tissue sarcoma. Int J Oral Maxillofac Surg 2012;41:569-75.
17. Patil VM, Noronha V, Joshi A, Muddu VK, Gullia S, Bhosale B, *et al*. Induction chemotherapy in technically unresectable locally advanced oral cavity cancers: Does it make a difference? Indian J Cancer 2013;50:1-8.
18. Lydiatt WM, Patel SG, O'Sullivan B, Brandwein MS, Ridge JA, Migliacci JC, *et al*. Head and Neck cancers-major changes in the American Joint Committee on cancer eight edition cancer staging manual. CA Cancer J Clin 2017;67:122-37.
19. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, *et al*. The eight edition AJCC cancer staging manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin 2017;67:93-9.
20. Adedeji GA. Socio-economic and cultural background of hospitalized children in Ilesha, Nigeria. Niger J Paediatr 1985;12:111-7.
21. Rudresha AH, Chaudhuri T, Lakshmaiah KC, Babu KG, Dasappa L, Jacob LA, *et al*. Induction chemotherapy in technically unresectable locally advanced T4a oral cavity squamous cell cancers: Experience from a regional cancer center of South India. Indian J Med Paediatr Oncol 2017;38:490-4.
22. Fomete B, Ogbeifun JO. Soft tissue sarcoma of the orofacial region: Our experience with 64 cases. Niger J Surg Res 2015;16:3-10.
23. Conway DI, Petticrew M, Marlborough H, Berthiller J, Hashibe M, Macpherson LM. Socioeconomic inequalities and oral cancer risk: A systematic review and meta-analysis of case-control studies. Int J Cancer 2008;122:2811-9.
24. Zygogianni AG, Kyrgias G, Karakitsos P, Psyrri A, Kouvaris J, Kelekis N, *et al*. Oral squamous cell cancer: Early detection and the role of alcohol and smoking. Head Neck Oncol 2011;3:2-5.
25. Znaor A, Brennan P, Gajalakshmi V, Mathew A, Shanta V, Varghese C, *et al*. Independent and combined effects of tobacco smoking, chewing and alcohol drinking on the risk of oral, pharyngeal and esophageal cancers in Indian men. Int J Cancer 2003;105:681-6.
26. Amanda P, Caitlin M, Jeff H. Low Socioeconomic Status and Cancer Prevention in the American Cancer Society Great West Division. 1st ed. Atlanta, Georgia: Center for Disease Control (CDC); 2013.
27. Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and neck cancer. New Engl J Med 1993;328:184-94.
28. Enwonwu CO, Meeks VI. Bio-nutrition and oral cancer in humans. Crit Rev Oral Biol Med 1995;6:5-17.
29. Lawal AO, Kolude B, Adeyemi BF. Oral cancer: The Nigerian experience. Int J Med Med Sci 2013;5:178-83.
30. Wei Y, Xiao J, Zou L. Masticator space: CT and MRI of secondary tumor spread. AJR Am J Roentgenol 2007;189:488-97.
31. Tovey P, Broom A, Chatwin J, Hafeez M, Ahmad S. Patient assessment of effectiveness and satisfaction with traditional medicine, globalized complementary and alternative medicines, and allopathic medicines for cancer in Pakistan. Integr Cancer Ther 2005;4:242-8.
32. Anyanechi CE, Saheeb BD. Reasons underlying failure to seek early dental treatment among patients presenting in a Nigeria Tertiary Hospital. J Med Biomed Res 2013;12:37-45.