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Review Article

Salivary Gland Tumors in Nigerian Patients – a 10 year review

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Keywords

- Salivary gland
- Tumors
- Survival
- Pattern

Abstract

Objective: This study was carried out to examine the pattern and treatment outcomes of salivary gland tumors in Nigerian patients attending Radiotherapy clinic at the University College Hospital, Ibadan.

Methodology: Retrospective review of clinical records of patients with salivary gland tumors seen in the Department of Radiotherapy UCH Ibadan, from 2001-2010 was done. Information collected included bio data, tumor site histology, degree of differentiation, and survival among others.

Results: 108 cases of histologically diagnosed salivary gland tumors were recorded in the department in a 10 year period. The commonest recorded presenting complaint was facial swelling seen in all the 108 patients. Mucoepidermoid was the most common histological type in 40 (37.0%) of the cases. Social habits such as tobacco smoking and alcohol consumption did not have any strong association with development of these tumors. The stage at presentation, histology and grading were found to be of prognostic significance.

Conclusion: This study shows that salivary gland tumors are not common in our environment; almost 50% of the patients presenting with locally advanced, fungating disease, usually inoperable and treatment intent is more of palliation. A high index of suspicion by the primary physician is required to improve early detection and treatment. There is a need for establishment of multidisciplinary tumor board for ease of referral and management of these patients for better control.

INTRODUCTION

Salivary glands are anatomical and functional adnexae of the oral cavity that seldom give rise to tumuors. These tumuors are rare and constitute between 8-10.5% of all head and neck cancers in Western studies [1,2], and 2.8% to 10% of all head and neck cancers in African studies [3]. The incidence of salivary gland tumours in Nigeria is 2.8% [4]. It accounts for about 2% of all cancers [5].

Though rare,salivary gland tumours constitute one of the most varied pathology in human body,similar to those of breast and thyroid gland cancers. They present a large varieties of histopathological types of benign and malignant tumours whose aetiological factors are unknown or poorly understood. According to the World Health Organization (WHO) [6], epidemiological studies have shown many cancers including salivary gland to be avoidable in that 80-90% of human cancers are attributed to environmental and lifestyle factors such as tobacco, alcohol and dietary habits.

Evidence suggest a variation in the age, sex and site of distribution of salivary gland tumours between western and african populace. The most recent data suggest an increase in the annual presentation of salivary gland tumours in University College Hospital compared with previous studies [7]. Although researchers have learned much from the study of these diverse tumours over the years, diagnosis and treatment remain very complex and challenging [7]. Salivary gland tumours are classified as major and minor salivary gland types. The major salivary gland tumours arise from the parotid,submandibular and sublingual glands. The parotid is by far the commonest site accounting for 80%. 70% of salivary gland tumours originates in the parotid gland, 8% in the submandibular while 22% in the minor salivary gland. Although 75% of parotid gland tumours are benign, slightly more than 50% tumours of the submandibular and 60-80% of minor salivary gland tumours are said to be malignant.The proportion of malignant tumours increases from parotid 25% to submandibular gland 43% and minor salivary gland 65% [8,9].

There is little or no documented literature on salivary gland tumours in Nigeria. This study was conducted to examine salivary tumors in our practice.

MATERIALS AND METHODS

A retrospective review was conducted, using clinic records of all histologically confirmed patients with salivary gland tumours, between January 2001 and December 2010. These were regular attendees of the Radiotherapy clinic, University College Hospital, Ibadan, Nigeria. Patients' referral was from all over Nigeria to the Radiotherapy Department for treatment. A checklist was used to retrieve information on demographic data, presenting complaints, site of tumor, histological type,pattern of presentation,different doses of external Radiotherapy and other adjuvant treatment recieved were documented.Treatment outcomes were correlated with different stage, histology,and grade of the disease. Early stage were stages 1 and 2 while late stage were stages 3 and 4 diseases. Well diffentiated means low grade tumors, moderately differentiated means internediate grade, while poorly and undifferentiated mean high grade tumors.

Data analysis was done using SPSS version 16.0. Categorical variables were presented as frequencies and percentages, continuous variables as means ± SD. Chi-square analysis was done to determine associations between categorical variables while t-test was used to compare two variables. Level of significance was set at $p<0.05$

TREATMENT

All the patients received one form of surgery ranging from biopsy to curative.

All patients received external beam radiotherapy using megavoltage machine (Co^{60} equipment – average photon-beam energy of 1.25Mev). Average radical radiation dose received by 80 patients was 55Gy ± 6.15 Gy (Dose range of 45- 64 Gy in 4 to 6 weeks); average palliative radiotherapy dose was 25Gy ± 10.2Gy in 28 patients. Patients that received adjuvant chemotherapy were those with malignant disease and some of the Pleomorphic adenoma that had features suggestive of malignant transformation (Infiltration of adjacent stucture). The chemotherapy combination was either vincristine, Bleomycin, Methotrezate (VBM) or Methotrezate, vincristine, Adriamycin and cyclophosphamide (MVAC).

SURVIVAL

Patients were seen six weeks post radiation therapy as first follow-up visit then every three months or earlier as patient's condition dictated for the first one year and six monthly thereafter. Full patient examination with complete blood count and other appropriate investigations were performed at follow-up visits to monitor progression free survival with intention to treat. Patient's survival was measured from the date of diagnosis of disease to the date of death or last follows up. For this study, complete treatment response was defined as disappearance of all clinical evidence of active tumor for a minimum of 4 weeks, partial response was 50% or greater disease in the sum of products of perpendicular diameter of all measured lesions. Stable disease is tumor growth or progression not quantifying for partial remission or progression and no worsening of symptoms. Progressive disease is unequivocal increase of at least 50% in the size of any measureable lesion or appearance of new lesion.

Approval for the study was obtained from the Joint Ethical Review Committee of the University of Ibadan/University College Hospital (UCH), Ibadan.

RESULTS

A total of 108 cases of salivary gland tumors were seen in the study period. There were 63 (58.3%) males and 45 (41.7%) females and mean ages were 47.9±3.1 and 46.5±3.7 respectively (Table 1). Majority of the patients 61 (56.5%) were within the middle age group (Figure 1). Sixty-eight (62.7%) were married while 19 (17.6%) of the patients had no formal education. Their social habits showed that, 10(9.3%) of these patients consumed alcohol, 3(2.8%) indulged in both tobacco and alcohol. 1(0.9%) indulged in tobacco and alcohol as well as other substances such as snuff.

Facial swelling 108(100%) was the commoness mode of presentation followed by pain 56(51.9%) (Figure 2). Mucoepidermoid carcinoma had the highest frequency 40 (37.0%) followed by Adenoid cystic 28 (25.9%), Adenocarcinoma 11 (10.2%) and Pleomorphic Adenoma 17 (15.7%) of which 4(23.5%) patient were carcinoma ex pleomorphic adenoma. Others such as warthins tumour, oncocytoma and acnic cell made up to 10 (9.3%) (Figure 3). Sixty-six (61.1%) patients had their tumour located on the right side of the face, 37 (34.3%) on the left and 5 (4.6%) were bilateral.

The parotid gland has the highest anatomical site of affectation with 83(76.8%) and the mucoepidermoid carcinoma 37(92.5%) having the highest histological occurrence (Table 2).

The grade of the histology had a significant association with the treatment outcome. Table 3 shows that well differentiated tumors' had a better outcome after treatment with 60.5% complete response while the undifferentiated had 31.5% of progressive disease indicating that treatment outcome was

Table 1: Demography of patients with salivary gland tumors (N=108).

Age	***Mean age (years)***	***Range***
Male	47±3.1	12-72 years
Female	46.5±3.7	22-80 years
Sex	***Frequency***	***Percentage***
Male	63	58.3
Female	45	41.7
Marital Status		
Single	24	22.2
Married	68	62.7
Widow/widower	13	12.0
Separated	3	2.8
Level of Education		
Primary	21	19.4
Secondary	36	33.4
Tertiary	32	29.6
None	19	17.6

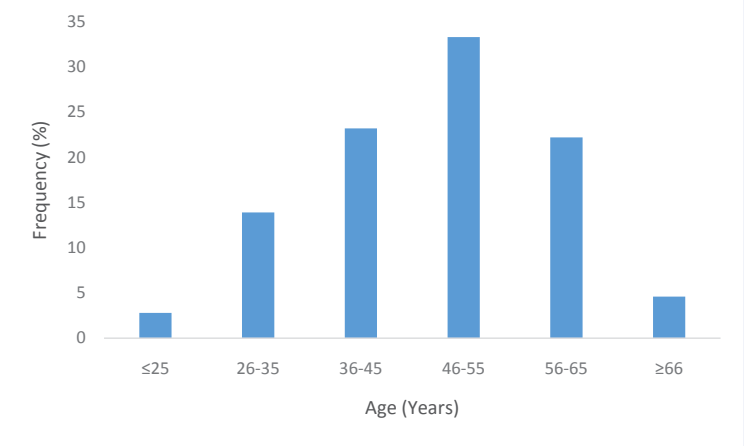

Figure 1 Age distribution of patient with salivary gland tumors.

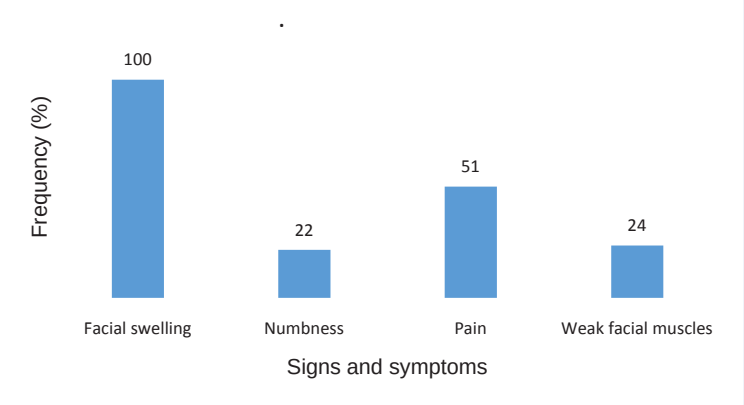

Figure 2 Clinical presentation of salivary gland tumors.

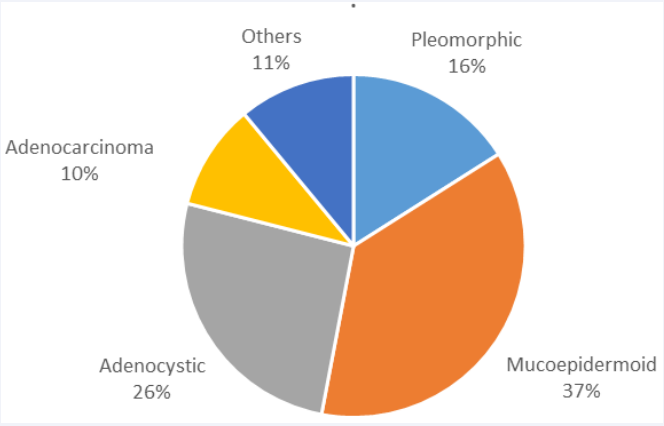

Figure 3 Frequencies of histological types of salivary gland tumors.

dependent on degree of differentiation (X^2 6=24.25. p=0.0005)

Histological classification had significant association with the treatment outcome (X^2 8=40.01 p=0.0001).

Mucoepidermoid carcinoma 18/43(41.9%) had highest frequency for complete response compared with the Adenoid cystic carcinoma 22/46(47.8%) with higher progressive disease (Table 4).

All 108 patients were grouped as those with early disease 57 (52.8%) and late disease were 51(47.2%) (Locoregionally advanced 41(80%) and those with metastatic disease were 10 (20%).

Table 2: Histology and anatomical site affected by salivary gland tumors.

Anatomical sites affected					
Histology	**Total**	**Parotid**	**Submandibular**	**Intraoral**	**Sublingual**
Pleomorphic adenoma	17	13(76.5%)	4(23.5%)	0(0.0%)	0(0.0%)
Mucoepidemoid	40	37(92.5%)	2(5.0%)	0(0.0%)	1(2.5%)
Adenoid cystic	28	18(64.3%)	7(25.0%)	1(3.6%)	2(7.1%)
Adenocarcinoma	11	7(63.6%)	4(25.0%)	0(0.0%)	0(0.0%)
Others	12	8(80.0%)	4(20.0%)	0(0.0%)	0(0.0%)
Total	108	83(76.8%)	21(19.4%)	1(0.9%)	3(2.8%)

Table 3: Treatment outcome and grade showing that grade is a determinant of outcome (p <0.0005).

Treatment response		**Grade of differentiation N (%)**			
	Total	**Well**	**Moderate**	**Poor**	**Undifferentiated**
Complete	43 (39.8%)	26(60.5%)	8 (7.4%)	6 (5.6%)	3 (2.8%)
Partial	46 (42.6%)	22(47.8%)	4 (8.7%)	12(26.1%)	8 (17.4%)
Progressive disease	19 (17.6%)	0 (.0%)	4(21.1%)	9 (47.3%)	6 (31.5%)
Total	108(100.0%)	48(44.4%)	16 (14.8%)	27(25.0%)	17 (15.7.0%)

Table 4: Treatment outcome according to histological type (P < 0.0001).

Histology	**Treatment response**			
	Complete Response	**Partial Response**	**No Response**	**Total**
Pleomorphic adenoma	14(32.6%)	3 (6.5%)	0 (0.0%)	17
Mucoepidemoid carcinoma	18 (41.9%)	22 (47.8%)	0 (0.0%)	40
Adenoid cystic c	6 (14.0%)	13 (28.3%)	9 (47.4%)	28
Adenocarcinoma	2 (4.7%)	5 (10.9%)	4 (20.1%)	11
Others	3 (7.0%)	3 (6.5%)	6 (31.6%)	12
Total	43 (39.8%)	46 (42.6%)	19 (17.6%)	108(100.0%)

The disease stage at presentation was significantly associated with treatment outcome. Table 5 showed 2 years post treatment disease free survival (DFS) 31/43 (72.1%) of patients with early disease while 39/51(76.5%) with late stage disease are living with the disease after 2 years of follow up clinic. Out of 10 patients with metastatic disease, 3 (30%) responded initially to treatment though they relapsed within two years of treatment and were alive with disease at two years. At two years overall follow-up of 108 patients, 43 (40%) were alive without disease while 4 (4%) were confirmed dead (Table 6).

ADVERSE EFFECT

Adverse effects were documented but not graded. These ranged from erthema 23(21%) patients, mucositis 36(33%) patients to late side effects of trismus 4 (4%) patients and hearing impairment in 1(1%) patient.

Table 5: Treatment outcome of salivary gland tumors at 2 years (by stage of disease).

Stage		**DFS**	**P value**	**Local Relapse**	**Persistent Disease**
	Early	31	<0.002	17	9
	Late	12		32	7
Total		43		49	16

DFS-Disease Free Survival

Table 6: Two years survival table of patients with salivary gland tumors.

Survival	**N (%)**
Disease free survival (DFS)	43(40%)
Alive with disease	32(30%)
Lost to follow up	29(27%)
Dead	4(4%)
Total	108(100%)

DISCUSSION

The study aimed at describing the pattern of presentations and treatment outcomes in patients with saliavary gland tumours. The study observed the disease was more common in males and amongst the middle aged. This disagrees with the previous report by Adeyemi et-al [10] which stated that there is no gender predilection and a study from Uganda that reported female to be affected more than males [11]. The finding of less than 25 percent of the study population being involved in cancer risk social habits is similar to previous study by Lawoyin et al. [11]. This emphasises the need to investigate other possible risk factors such as low fruits and vegatable intake in our environment, which has been implicated in gastrointestinal cancers.

However, the rare warthins tumor (papillary cystadenoma lymphomatosun) [12] strongly associated with tobacco smoking

was not recored in this study population.

A large number of patients in the study presented with loco-regionally advanced disease. The stage of presentation, histologic type and grading were found to be of prognostic importance in this study. The misconception by some maxillofacial and ear nose and throat surgeons that Radiotherapy has little or no role in the management of benign pleomorphic adenoma, may account for the low incidence seen in this study. The study observed that 14 (82.4%) of the seventeen patients with pleomorphic adenoma had complete response to radiotherapy treatment, supporting the fundamental role of radiotherapy in the management of both benign and malignant salivary gland tumors [13]. Over fifty per cent (55.6%) of patients presented after 1year of initial symptoms. This may be attributable to initial misdiagnosis and treatment for infection, which is often the practice in some resource poor, developing countries, mostly by non specialist private medical practitioners. Absence of pain at the early stage of the disease, delay in surgery and prompt histological diagnosis may contribute also to late presentation in our patient population. In this study, 56 (51.9%) patients had pain at presentation, due mainly to locally advanced stage [8] with associated fungating tumor and sepsis in some cases. Though up to one third of parotid cancer patients are said to have facial nerve involvement, only 10-20% of patients complain of pain [14,8]. Pain is also associated with involvement of deeper structures such as the masseter temporalis and pterigoid muscles.

Tumors of the mucoepidermoid origin 40 (38.9%) was the commonest in this study, similar to a study by Spiro et al. which stated that mucoepidermoid as the most common malignant tumor appearing in parotid gland [8]. Another study stated that muco-epidermoid accounted for 41% of all salivary gland tumors. A large proportion of salivary gland tumors from this study originated from the parotid 83(76.8%), this is similar to other studies which stated that 70% of salivary gland tumors originate from the parotid [7].The most common presentation was facial swelling, some patients however, presented with more than one symptom.

Adenocarcinoma and adenoid cystic showed worst treatment outcome. The high incidence of poor response of adenoid cystic carcinoma is due to the fact that adenoid cystic carcinoma is associated with high rate of pulmonary metastasis which is a significantly poor prognostic factor. Reported incidence of distant metastasis in patients with adenoid cystic carcinoma at 10yrs of follow up is around 40% [15,8]. Thus poorly differentiated adenoid cystic carcinoma had the highest rate of pulmonary metastases and mortality.

There was a significant association between the grade and outcome. Poorly differentiated tumors had poorer outcome compared with well differentiated histology.

There was also a significant association between stage of presentation and treatment outcome.

Post operative radiotherapy has been shown to improve loco regional control in patients with advanced salivary gland cancer, [16,17,18] and frequency of recurrence shown to be high in patients who had surgery without adjuvant radiotherapy. Post operative radiotherapy is recommended in bulky tumors, high grade histology irrespective of surgical margins [19,20,21]. Post treatment, about forty percent were symptom and disease free at study end point of two years, four cases were confirmed dead and 29 lost to follow up.

CONCLUSION

The burden of managing salivary gland tumors is enormous in our environment despite advances in diagnosis and treatment.

Major prognostic factors seen in this study were stage of presentation, histologic type and tumor grade. Adjuvant radiotherapy proved to be of value in the management of salivary gland tumors in spite of late presentation which remains a major challenge in our environment in the area of cancer management.

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