

Histopathological analysis of salivary gland tumors at Pathology Department of King Edward Medical University Lahore

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ABSTRACT

Background: Salivary gland tumors are distributed in the head and neck area. The purpose of the study was to see the distribution of these tumors. The tumors were studied against the demographic variables like age and sex.

Patients and Methods: This was a descriptive cross-sectional study conducted at department of pathology of King Edward Medical University from 01 January 2010 to 31 December 2017. Three hundred and nineteen cases were included. Their diagnosis and demographic details like site, age and sex were recorded in a proforma. Statistical package for social sciences (SPSS) version 20 was used for descriptive analysis and the results were tabulated.

Results: Total 319 cases of salivary gland tumors (SGT) were enrolled in the study. Female to male ratio was 1.3:1. Minimum and maximum age of the patients were 5 and 80 years. Mean age was 37.45±15.7 years. Malignant tumors were seen in relatively older age group as compared to benign tumors. Majority cases were benign 214 (67.1%) while malignant cases were 105 (32.9%). The commonest benign tumor was pleomorphic adenoma 203 (63.6%) and the commonest malignant tumor was mucoepidermoid carcinoma (MEC) 43 (13.5%) followed by adenoid cystic carcinoma (AdCC) 42 (13.2%). Most of the tumours 146 (45.8%) were located in parotid area followed by submandibular gland 45 (13.8%) and hard palate area 37cases (11.6%). Overall, 194 (60.8%) cases were found in major salivary glands and 125 (39.2%) were distributed in minor salivary glands. Benign versus malignant tumors in major SG were 150 and 44 (3.4:1) as compared to 64 versus 61 (1.04:1) in minor salivary glands.

Conclusion: Pleomorphic adenoma was the commonest benign salivary gland tumor whereas mucoepidermoid carcinoma remained the commonest malignant tumor followed by adenoid cystic carcinoma. Parotid and minor salivary glands were predominant locations for benign and malignant tumors respectively.

Keywords:

Salivary gland tumors; pleomorphic adenoma; adenoid cystic carcinoma; mucoepidermoid carcinoma; minor salivary glands.

INTRODUCTION

Salivary glands (SG) constitute important organs in the faciomaxillary area. They are divided into major and minor salivary glands. Major salivary glands are parotid, submandibular and sublingual while minor are randomly distributed in the oral cavity. Sialadenitis and salivary gland tumors (SGT) are commonly encountered pathologies of these glands. SGTs

comprise about 3-10% tumors of head and neck area. Both benign and malignant SGT carry significant morbidity and mortality. These tumors have variable distribution among different types of salivary tissues. Majority of benign tumors are seen in major salivary glands as compared to malignant tumors which are mainly confined to minor salivary glands. So, the likelihood of malignancy is inversely proportional to the size of salivary glands.¹⁻³ The commonest benign tumor is pleomorphic adenoma which is mainly seen in parotid area, but fair numbers of this tumor are also noticed at other sites. Other tumors which are mentioned in the

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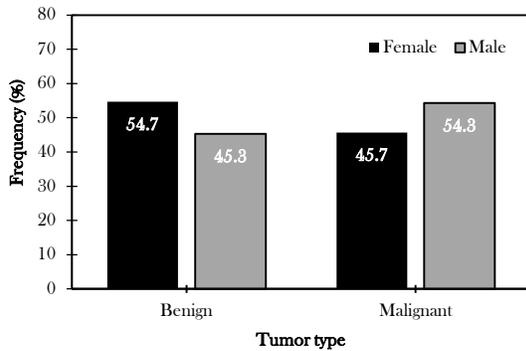


Figure 1. Gender distribution of benign and malignant tumors

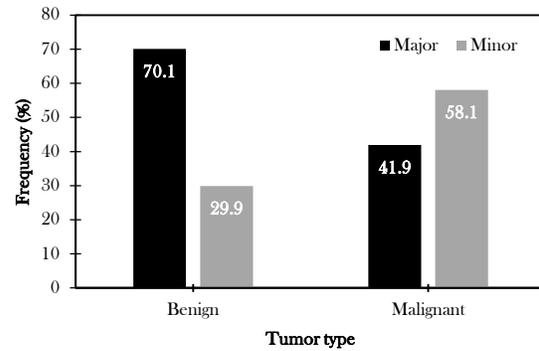


Figure 2. Distribution of tumors in major and minor salivary glands

literature are Warthin tumor and oncocytoma etc.^{4,5} Malignant tumors are classified into mucoepidermoid carcinoma (MEC), adenoid cystic carcinoma (Ad.CC), adenocarcinoma (NOS), malignant mixed tumor, acinic cell carcinoma (ACC) etc. Out of these MEC is the commonest malignant tumor followed by Ad.CC and majority of these are seen in minor salivary glands.^{6,7}

PATIENTS AND METHODS

This was a descriptive cross-sectional study. The study was conducted at pathology department of King Edward Medical University Lahore with collaboration of four surgical and faciomaxillary units of Mayo Hospital Lahore from January 2010 till December 2017. The results and demographic details were retrieved using computer software and clinical records.

Hematoxylin and eosin (H&E) stained slides were retrieved from the records and reviewed again. Diagnosis and demographic details like age, sex and site were entered on the proforma. Cases like sialadenitis and mucocele were excluded from the study.

Statistical package for social sciences (SPSS) version 20 was used for analysis. Frequency, percentages and ratios were calculated. Results obtained were compared with data in local and international publications.

RESULTS

A total of 319 cases were studied, out of which 214 (67.1%) were benign and 105 (32.9%) malignant. Mean age was 37.45±15.7 years (range, 5 to 80 years). There was slight female dominance with female to male ratio of 1.3:1. Gender-wise distribution of benign and malignant tumors is depicted in Figure 1.

In females, 106 (64.2%) cases were seen in major and 59 (35.8%) cases in minor SGs while in males this was 88 (57.1%) and 66 (42.9%) respectively. Over all 194 (60.8%) and 125 (29.2%) cases were seen in major and

minor salivary glands respectively (Figure 2). In major and minor salivary glands, 150 (70.1%) and 64 (29.9%) cases were benign while in case of malignancy these were 44 (41.9%) and 61 (48.1%) respectively. A total of 77.3% cases of benign nature were seen in major salivary glands while only 22.7% cases were malignant. In minor salivary tissues, 51.2% benign cases were noticed as compared to 48.8% of malignant diagnosis. Distribution of benign and malignant tumour in females were 117 (70.9%) and 48 (29.1%) whereas this distribution was 97(63%) and 57(37%) in males respectively.

Pleomorphic adenoma (PA) was the commonest benign tumor with a total of 203 (63.6%) cases, while MEC was the commonest malignant tumor comprising 43 cases (13.5%) followed by Ad.CC, 42 cases (13.2%). Six cases of polymorphous low-grade adenocarcinoma (PLGA), seven of Warthin tumor, four of malignant mixed tumor, three of salivary duct carcinoma, three of ACC and two cases of adenocarcinoma (NOS) were also noticed. Only a single case each from myoepithelioma, myoepithelial carcinoma, carcinosarcoma, basal cell adenoma, oncocytoma and lipoma was appreciated (Table 1). Majority of the tumors 146 (45.8%) were located in parotid gland with benign and malignant distribution as 117 (80.1%) and 29 (19.9%) respectively. This was followed by submandibular area with 45 cases (14%); 34 (75.6%) benign and 11 (24.4%) being malignant. Females to male ratio was double in favor of females in submandibular glands. Cases in hard palate were 37(11.6%); out of which 23 (62.2%) cases were benign with female predominance against malignant diagnosis 14 (37.8%). Cheek (7.8%), orbit (6.0%), lip (2.8%), soft palate (3.8%), maxillary sinus (2.8%) and sublingual gland (1.3%) were other notable locations. Cheek, orbit, sublingual, maxillary sinus, nostril and tongue area carried predominance of malignant cases

Table 1. Tumor diagnosis with frequency and percentages

| Diagnosis | Frequency (%) |
|----------------------|---------------|
| Benign Tumors | |
| Pleomorphic adenoma | 203 (63.6) |
| Warthin tumor | 7 (2.2) |

| | |
|-------------------------|---------|
| Basal cell adenoma | 1 (0.3) |
| Oncocytoma | 1 (0.3) |
| Lipoma | 1 (0.3) |
| Myoepithelioma | 1 (0.3) |
| Malignant Tumors | |

| | |
|--|-----------|
| Mucoepidermoid carcinoma | 43 (13.5) |
| Adenoid cystic carcinoma | 42 (13.2) |
| Polymorphous low- grade adenocarcinoma | 6 (1.9) |
| Malignant mixed tumor | 4 (1.3) |
| Acinic cell carcinoma | 3 (0.9) |
| Salivary duct carcinoma | 3 (0.9) |
| Adenocarcinoma (NOS) | 2 (0.6) |
| Myoepithelial carcinoma | 1 (0.3) |
| Carcinosarcoma | 1 (0.3) |

with 60.0%, 63.2%, 100%, 100%, 100%, 100% respectively. Lip tumors were 100% benign. Male dominance of tumors was seen in orbit (57.9%), nostril (100%), lip area (66.7%), soft palate (83.3%), cheek (56%) and tongue (100%). Tumors in parapharyngeal area and sublingual gland carried female predominance (100%) (Table 2).

In parotid gland, out of 146, 74% tumors were PA followed by MEC (11.0%), Warthin tumor (4.1%), malignant mixed tumor (2.7%), salivary duct carcinoma (2.1%) and ACC (1.4%). Forty-five cases were seen in submandibular gland and PA remained the predominant tumor (73.3%), followed by MEC (15.6%) and Ad.CC (6.7%). Hard palate carried situation with PA (59.5%), MEC (13.5%), Ad.CC (16.2%) and PLGA (5.4%). All the tumors in lip were PA. Significant number of tumors were diagnosed as Ad.CC in cheek (36%), orbit (52.9%), maxillary sinus (88.9%) and nostril (100%). All the tumors in sublingual and tongue area were MEC and PLGA respectively. Orbit has also significant 36.8% cases of PA.

Nine out of twelve cases from soft palate tumors were PA along with three cases of Ad. CC (Table 3).

DISCUSSION

Salivary gland tumors are well known for their diverse morphological patterns and constitute an important part of faciomaxillary and oral tumors.⁷⁻⁹ This study is a detailed analysis of SGTs located in major and minor salivary glands. Total 319 cases were analyzed including 214 (67.1%) benign and 105 (32.9%) malignant tumors. Females slightly dominate in the study with 1.30:1, which is significantly different from the studies by Zaman and colleagues and Etit and coauthors with almost equal gender distribution.^{2,10} However, male dominance has been reported by other authors.^{1,11,12} This may be due to geographic differences and sample size. We noticed slight increase in number of benign cases as compared to malignancy with similar study Qureshi and coauthors at the same institution which included 62.5% benign cases and 37.6% malignant cases.¹³ Another local study showed overall 58.2% benign cases.² Similar results were seen by Etit and group in Turkey with benign 62.1% and malignant 37.8%.¹⁰ Whereas a study from Iran reported in favor of benign 67.8% verses malignant 32.2%.¹¹ Conflicting results were obtained by authors from America and China who described benign diagnosis with 84.3%, 77.1% and only 15.7%, 22.9% malignancies respectively.^{5,14} Another important deviation was reported by Lawal and coauthors from Nigeria with malignant 53.5% and 46.5% benign diagnosis.¹⁵

Table 2. Site distribution of salivary gland tumors with frequency and percentage against benign/malignant types and gender

| Tumor Site | Benign | Malignant | Male | Female | N (%) |
|----------------|--------|-----------|------|--------|------------|
| Parotid | 117 | 29 | 74 | 72 | 146 (45.8) |
| Submandibular | 34 | 11 | 15 | 30 | 45 (13.8) |
| Hard palate | 23 | 14 | 10 | 27 | 37 (11.6) |
| Cheek | 10 | 15 | 14 | 11 | 25 (7.8) |
| Orbit | 7 | 12 | 11 | 8 | 19 (6.0) |
| Soft palate | 9 | 3 | 10 | 2 | 12 (3.8) |
| Lip | 9 | 0 | 6 | 3 | 9 (2.8) |
| Max.sinus | 0 | 9 | 6 | 3 | 9 (2.8) |
| Sublingual | 0 | 4 | 0 | 4 | 4 (1.3) |
| Nostril | 0 | 2 | 2 | 0 | 2 (0.6) |
| Parapharyngeal | 2 | 0 | 0 | 2 | 2 (0.6) |
| Post auricular | 0 | 2 | 1 | 1 | 2 (0.6) |
| Tongue | 0 | 2 | 2 | 0 | 2 (0.6) |
| Tonsil | 1 | 0 | 0 | 1 | 1 (0.3) |
| Alveolus | 1 | 0 | 1 | 0 | 1 (0.3) |
| Supraglottic | 0 | 1 | 1 | 0 | 1 (0.3) |

Table 4. Comparison of studies of various countries

| Author with country and Year of Study | Total No. of tumors | Major vs. Minor SGT | Benign vs. Malignant Major SGT | Benign vs. Malignant Minor SGT | PA vs. Warthin tumor | MEC | Ad.CC |
|---------------------------------------|---------------------|---------------------|--------------------------------|--------------------------------|----------------------|-----|-------|
| Bradeley and McGurk (2012). UK | 1065 | 967 vs. 98 | N =967 859 vs. 108 | N = 98 59 vs. 39 | 651 vs. 203 | 38 | 32 |
| Luksic et al (2012). Croatia | 779 | 567 vs. 212 | N = 567 413 vs. 154 | N = 212 87 vs. 125 | 348 vs. 87 | 67 | 94 |
| Kizil et al (2013). Turkey | 510 | 413 vs. 97 | N =413 316 vs. 97 | N = 97 42 vs. 55 | 231 vs. 91 | 29 | 39 |
| Torabinia et al (2014). Iran | 229 | 134 vs. 95 | N = 134 87 vs. 47 | N = 95 40 vs. 55 | 111 vs. 4 | 54 | 24 |
| Qureshi et al (2014). Pakistan | 117 | 94 vs. 23 | N =94 | N = 23 | 60 vs. 5 | 30 | 9 |

| | | | | | | | |
|--------------------------------|-----|-------------|-----------------------|----------------------|-----------|----|----|
| | | | 66 vs. 28 | 7 vs. 16 | | | |
| Zaman et al (2014). Pakistan | 91 | 66 vs. 25 | N = 66 40 vs. 26 | N = 26 13 vs. 12 | 43 vs. 2 | 15 | 16 |
| Current study (2018). Pakistan | 319 | 194 vs. 125 | N = 194 150 vs. 44 | N = 125 64 vs. 61 | 203 vs. 7 | 43 | 42 |

SGT= Salivary gland tumor, PA= Pleomorphic adenoma, MEC=Mucoepidermoid carcinoma, Ad.CC=Adenoid cystic carcinoma

Regarding location of SGT present study is dominated by the tumors in major salivary glands with bulk of the tumors being benign whereas malignancy was more common in minor salivary glands. This is in accordance with the study by Kizil and others from Turkey, who noticed benign and malignant tumors in parotid, submandibular, sublingual and minor salivary glands as 78.5%, 60%, 0%, 43.3% and 21.5%, 40%, 100%, 56.7% respectively.¹ Yet another analysis by Jaafari and colleagues reported 57.5%, 13.1%, 28.5% cases in parotid, submandibular and minor salivary glands, which is also supporting this study.¹¹ Further supporting evidence was from Laishram and associates in India who pointed out parotid being the commonest site with 56.6% of the tumors.¹⁶ In one large series from Croatia, parotid still dominated by 65.3% tumors verses 27.2% in minor salivary glands which further strengthens results of this study.⁶ Niazi and coauthors relatively supported the findings of this study with large sample size as 77.2% and 2.8% cases in major and minor salivary glands with dominance of benign diagnosis (67%) in the former and 52.5% of malignancy in minor salivary glands.⁷

Pleomorphic adenoma is the commonest benign tumor in present study constituting 203 cases (63.6%). It is followed by Warthin tumor with 7 cases (2.2%). Tumors in parotid gland are dominated by 74% by PA and also in submandibular gland with 73.3%. In lip all the cases were PA whereas hard and soft palate carried 59.5% and 75% respectively of this tumor. Present study is well supported by studies from United Kingdom, America, China and Pakistan wherein PA has been reported as 71%, 65.6%, 69% and 56.4% respectively.^{4,5,7,17} Similar results have been reported by other local and international authors.^{14,18,19} However other authors have come up with 47.2% , 54.3% which could be due to different population and small sample size.^{2,11,12} Warthin tumor ranked second in present study with 2.1% of the total benign and malignant cases. It was documented as 4.3% and 3% in two previous studies from same institute.^{7,13} Difference exists between present study and a study from America who referred to it with 29.2% of overall tumors.⁵ Yet another study quoted Warthin tumor as 22% of benign tumors.⁴ Studies from Croatia and Turkey also mentioned high percentages of Warthin tumor.^{1,6} This may be due to environmental and genetic reasons (Table 4).

Present study evaluated 105 (32.9%) cases of malignancies which were dominated by MEC and Ad.CC with 13.5% and 13.2% respectively of total SGTs. PLGA also contributed 6 cases (1.9%) and malignant mixed

tumor with 4 cases (1.3%). Other malignant cases comprised of minor fraction. Major fraction of these (58.1%) were present in minor salivary glands with predominance in cheek, hard palate, sublingual gland, maxillary sinus and orbit. Significant numbers i.e., 29 were also seen in parotid area. These frequencies are relatively low in comparison to the study by Zaman and group where Ad.CC and MEC constituted 17.5% and 16.4% of the total SGTs and 62.5% were located in minor salivary tissues.² Results from United Kingdom were different with only 14% malignant cases with predominance of MEC (26%) followed by Ad. CC with 40% of total malignant cases located in minor salivary glands which is different from this study.⁴ Qureshi and coauthors described only 25.6% cases of MEC followed by Ad.CC at 7.7%.¹³ This variation may be due to relatively small sample size of that study. Out of the 37.4% malignant cases Niazi and associates mentioned MEC being the commonest malignancy (44.3%) with Ad.CC (30.9%) at the second place. Frequency of Ad. CC was low in their study, probably because the present also included cases of Ad.CC from orbit. However, figures similar to present study have been reported in the study by Andreoli and colleagues.²⁰ who did epidemiological study about lacrimal gland in which they discussed 702 cases of malignant lacrimal gland tumors and Ad.CC constituted 13.4% of cases. Just like our study palate was the commonest site of minor salivary gland tumors in their analysis. They also discussed rare SGTs which is quite in accordance with this study.

CONCLUSION

From this study it is clear that SGTs are mainly distributed in major salivary glands with malignant cases mainly confined to minor salivary glands. Tumors are more common in females. Pleomorphic adenoma is the commonest benign tumor followed by Warthin tumor. Among the malignancies, adenoid cystic and mucoepidermoid carcinoma exist in almost same percentages which is different from most of other studies. Further studies to look into the genetic and environmental etiological factors to search the difference of frequencies of malignancies and Warthin tumor in this area are suggested.

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REFERENCES

1. Kızıl Y, Aydil U, Ekinci Ö, Dilci A, Köybaşıoğlu A, Düzlü M, et al. Salivary gland tumors in Turkey: demographic features and histopathological distribution of 510 patients. *Indian J Otolaryngol Head Neck Surg* 2013; 65(1):112-20.
2. Zaman S, Majid S, Chughtai O, Hussain M, Nasir M. Salivary gland tumours: a review of 91 cases. *J Ayub Med Coll Abbottabad* 2014;26(3):361-3.
3. Fonseca FP, Carvalho Mde V, de Almeida OP, Rangel AL, Takizawa MC, Bueno AG, et al. Clinicopathologic analysis of 493 cases of salivary gland tumors in a Southern Brazilian population. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2012; 114(2): 230-9.
4. Bradley PJ, McGurk M. Incidence of salivary gland neoplasms in a defined UK population. *Br J Oral Maxillofac Surg* 2013; 51(5): 399-403.
5. Pinkston JA, Cole P. Incidence rates of salivary gland tumors: results from a population-based study. *Otolaryngol Head Neck Surg* 1999;120(6): 834-40.
6. Lukšić I, Virag M, Manojlović S, Macan D. Salivary gland tumours: 25 years of experience from a single institution in Croatia. *J Craniomaxillofac Surg* 2012;40(3): e75-81.
7. Niazi S, Arshad M, Iqbal A, Jaffery A, Bokhari MH. The morphological spectrum of salivary gland tumours at K and Mayo hospital, Lahore. *Biomedica* 2013; 29: 1-11.
8. Torabinia N, Khalesi S. Clinicopathological study of 229 cases of salivary gland tumors in Isfahan population. *Dent Res J (Isfahan)* 2014; 11(5): 559-63.
9. Araya J, Martinez R, Niklander S, Marshall M, Esguep A. Incidence and prevalence of salivary gland tumours in Valparaiso, Chile. *Med Oral Patol Oral Cir Bucal* 2015; 20(5): e532-9.
10. Etit D, Ekinci N, Tan A, Altinel D, Dag F. An analysis of salivary gland neoplasms: a 12-year, single-institution experience in Turkey. *Ear Nose Throat J* 2012; 91(3):125-9.
11. Jaafari-Ashkavandi Z, Ashraf MJ, Moshaverinia M. Salivary gland tumors: a clinicopathologic study of 366 cases in southern Iran. *Asian Pac J Cancer Prev* 2013;14(1): 27-30.
12. Jude UO, Olu-Eddo AN. Salivary gland tumors, a twenty-year retrospective study. *African J Med and Health Sciences* 2014;13(1): 24-9.
13. Qureshi A, Rehman K, Husain S, Khawaja NH, Qureshi GR, Naveed I. Salivary gland tumours-a three years experience at King Edward Medical College, Lahore. *AKEMU* 2004;10(2): 200-2.
14. Wang XD, Meng LJ, Hou TT, Huang SH. Tumours of the salivary glands in northeastern China: a retrospective study of 2508 patients. *Br J Oral Maxillofac Surg* 2015; 53(2):132-7.
15. Lawal AO, Adisa AO, Kolude B, Adeyemi BF, Olajide MA. A review of 413 salivary gland tumours in the head and neck region. *J Clin Exp Dent* 2013; 5(5): e218-22.
16. Laishram RS, Kumar KA, Pukhrabam GD, Laishram S, Debnath K. Pattern of salivary gland tumors in Manipur, India: A 10 year study. *South Asian J Cancer* 2013; 2(4):250-3.
17. Tian Z, Li L, Wang L, Hu Y, Li J. Salivary gland neoplasms in oral and maxillofacial regions: a 23-year retrospective study of 6982 cases in an eastern Chinese population. *Int J Oral Maxillofac Surg* 2010; 39(3): 235-42.
18. Shishegar M, Ashraf MJ, Azarpira N, Khademi B, Hashemi B, Ashrafi A. Salivary gland tumors in maxillofacial region: a retrospective study of 130 cases in a southern Iranian population. *Patholog Res Int* 2011; 2011: 934350.
19. Memon JM, Sheikh B, Baloch I. Histopathological audit of salivary gland neoplasms. *AKEMU* 2014; 20(1): 81-4.
20. Andreoli MT, Aakalu V, Setabutr P. Epidemiological trends in malignant lacrimal gland tumors. *Otolaryngol Head Neck Surg* 2015;152(2): 279-83.