

A clinicopathological study of salivary gland tumors

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Abstract

Background: To evaluate tumors involving major and minor salivary glands, histopathology is an essential diagnostic method and is the gold standard. This study was carried out to know the incidence of salivary gland tumors, their clinical presentation and diverse morphological patterns. **Materials and Methods:** A prospective cross-sectional descriptive study was carried out over a period of two years in the department of pathology, Yenepoya Medical College hospital, Mangalore. Data regarding patient demographics was also recorded. All the epithelial salivary gland tumors were classified according to WHO (2005) histological classification. **Results:** In the present study, a total of 65 cases of salivary gland tumours was found and an age range of 10-79 years was observed. The most common site affected was the parotid gland 47 (72.31%). Among the 48 (73.85%) benign tumors, pleomorphic adenoma 40 (61.54 %) was most common tumor and remaining 17 (26.15%) cases were malignant, of which mucoepidermoid carcinoma 8 (12.31%) was frequently observed. **Conclusion:** This study highlights the usefulness of histopathological study of salivary gland tumors with various morphological patterns of benign and malignant salivary gland tumors, which are of utmost value in planning the further management of the patient.

Key words: Histopathology, Neoplastic, Pleomorphic adenoma, Salivary gland

Introduction

Salivary gland tumors show diverse morphological patterns between various tumor types and on rare occasions with in the same tumor, thus causing interpretation challenges among the pathologists [1].

Studies from different countries have shown geographic variations in the relative incidence and clinicopathological discrepancies between benign and malignant salivary gland tumors [2]. The annual incidence worldwide ranges from 0.4 to 13.5 cases per 1,00,000 people. Majority of salivary gland tumors show a female preponderance [3].

Although the aetiology of salivary gland tumors is unknown, literature reports certain risk factors implicated in causation of these tumors. Among the viruses, Epstein-Barr virus, polyoma virus, cytomegalovirus, human immune deficiency virus and human papilloma virus types 16,18 are likely to cause salivary gland neoplasms.

Patients exposed to head and neck radiation for treatment showed increased incidence. Certain occupations such as asbestos mining, manufacturing of rubber products and plumbing (exposure to metals) and working in the automobile are other risk factors [4,5,6]. Clinically, salivary gland tumors present as a slow growing mass, however, rapid growth, pain, nerve involvement and fixation to skin or underlying muscles indicate malignancy [7].

Benign tumors commonly occur in the age group of 30-70 years whereas peak incidence of malignant tumors is in the 6th to 7th decades. Malignant tumors are more frequent in women than men [8]. Among the pediatric age group, 35% of salivary gland tumors are considered malignant [2].

Majority of Epithelial tumors are benign (75%) among which pleomorphic adenoma is the most common tumor and constitutes about 65% of all salivary gland neoplasms. Among the malignant neoplasms, mucoepidermoid carcinoma is the commonest. Of the major salivary glands, parotid gland is frequently involved [4,5].

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The distribution of salivary neoplasm's between sites has followed a rule of 100:10:10:1 ratio for parotid, submandibular, minor salivary glands and sublingual tumors, respectively [9].

Aims & Objectives

- To study the age, sex and site distribution of the salivary gland tumors regarding their origin from major and minor salivary glands.
- To study histomorphology of salivary gland lesions and to classify benign and malignant lesions according to World Health Organisation (WHO) 2005 Classification [3].

Material and Methods

Study design: A prospective cross-sectional descriptive study was carried out over a period of two years in the department of pathology, Yenepoya Medical College from patients admitted to Yenepoya Medical College, hospital Mangalore.

Sample size calculation

Formula for calculation of sample size [10]

$$\text{Estimate sensitivity: } n \geq \frac{Z_{1-\frac{\alpha}{2}}^2 \times p(1-p)}{d^2}$$

Alpha (α) -0.05

Estimated proportion (p) -0.83

Results

A total of 65 specimens of salivary gland tumors were received during the study period of which, 48 (73.84%) were benign tumors and 17 (26.15 %) were malignant tumors. The age incidence of salivary gland tumors in the present study ranged from 10 to 79 years and the male to female ratio of distribution of salivary gland tumors was 1:1.03 (Table 1). Male to female ratio in adenomas and carcinomas was 1:1.25 and 1:0.5 respectively.

History of tobacco chewing (30.36%), alcohol consumption (29.23%) and smoking (23.07%) was noted. The most common presenting complaint was a localised swelling. Only a small percentage (18.46%) of patients also presented with pain along with swelling.

The parotid gland 47 (72.31%) was the commonest site for various tumors, notable exception being adenoid cystic carcinoma, adenocarcinoma NOS, clear cell carcinoma NOS, which showed predilection for the minor salivary glands 15 (23.08%). Two cases (4.62%) involved the submandibular gland. However, no case was seen in the sublingual gland. Histology of Pleomorphic adenoma revealed classical histological features. Five cases showed squamous metaplasia of the ducts with epithelial pearl formation (figure 1) and one case showed adenoid cystic – like areas.

Seven cases of Warthin's tumor accounted for 10.77% of total, occurring in an age range of 50 and 59 years, frequent in males. In the present study, one case of oncocytoma was found in a 40 year female patient involving the parotid gland and showed typical histological features.

The commonest malignant tumor of parotid (23.52%) and submandibular gland (5.88%) was mucoepidermoid carcinoma, whereas of the minor salivary gland (23.52%) was adenoid cystic carcinoma.

Estimation error (d) -0.1

Minimum total sample size needed: 55

Inclusion Criteria: Epithelial tumors involving major and minor salivary glands.

Exclusion Criteria: Inflammatory, non-neoplastic and non-epithelial tumors of salivary gland were excluded.

Sample collection and sampling methods: Salivary gland specimens received in 10% formalin in the department of pathology were processed and paraffin blocks were made.

Hematoxylin and eosin (H & E) stained sections were studied under microscope and in selected cases special stains like Periodic acid Schiff (PAS), Alcian Blue, Toluidine blue were done.

The tumors were classified, employing the World Health Organization (WHO) 2005 histological classification of tumors of the salivary glands.

Clinical information regarding age, sex, presenting symptoms, past history was recorded. The study was commenced after obtaining approval from the institutional ethics committee.

Statistical analysis: Data was analysed in the form of tables, proportions and graphs

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Table-1: Number, percentage and Sex distribution of salivary gland tumors

S No.	Tumors	No.	%	Male	Female	Total
1	Benign Tumors					
	Pleomorphic adenoma	40	61.54	15	25	40
	Warthin's tumor	7	10.77	6	1	7
	Oncocytoma	1	1.54	0	1	1
	Total	48	73.85	21	27	48
2	Malignant Tumors					
	Acinic cell carcinoma	1	1.54	0	1	1
	Mucoepidermoid carcinoma	8	12.31	6	2	8
	Adenoid cystic carcinoma	4	6.15	3	1	4
	Clear cell carcinoma,NOS	1	1.54	1	0	1
	Salivary duct carcinoma	1	1.54	0	1	1
	Adenocarcinoma,NOS	1	1.54	1	0	1
	Squamous cell carcinoma arising in Warthin's tumor	1	1.54	1	0	1
	Total	17	26.15	12	5	17
Grand Total	65	100	32	33	65	

Table 2 displays various morphological types of benign tumors. Pleomorphic adenoma 40(83.33%) was the commonest histologic type followed by warthin's tumor 7(14.58%).

Table 3 shows the distribution of malignant salivary gland tumors. The predominant histologic type was mucoepidermoid carcinoma 8(47.06%).

Table-2: Distribution of benign tumors in salivary glands

Benign Tumors	No. of Cases	Parotid	Parotid Percentage	Sub-mandibular	Sub-mandibular Percentage	Minor	Minor Percentage
Pleomorphic adenoma	40	33	68.75	2	4.16	5	10.41
Warthin's tumor	7	7	14.58	0	0.00	0	0.00
Oncocytoma	1	1	2.08	0	0.00	0	0.00
Total	48	41	85.41	2	4.16	5	10.41

Table-3: Distribution of malignant tumors in salivary glands

Malignant Tumors	No. of Cases	Parotid	Parotid Percentage	Sub-mandibular	Sub-mandibular Percentage	Minor	Minor Percentage
Acinic cell carcinoma	1	1	5.88	0	0.00	0	0.00
Mucoepidermoid carcinoma	8	4	23.52	1	5.88	3	17.64
Adenoid cystic carcinoma	4	0	0.00	0	0.00	4	23.52
Clear cell carcinoma,NOS	1	0	0.00	0	0.00	1	5.88
Salivary duct carcinoma	1	1	5.88	0	0.00	0	0.00
Adenocarcinoma, NOS	1	0	0.00	0	0.00	1	5.88
Squamous cell carcinoma arising in Warthin's tumor	1	0	0.00	0	0.00	0	0.00

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Total	17	6	35.29	1	5.88	9	52.94
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Eight cases of mucoepidermoid carcinoma accounted for 12.31% of total, occurring in an age range of 50-59 years with a male predominance. Parotid gland was the commonest site followed by minor salivary glands and showed typical histological features (figure 1). There was a higher incidence of low grade tumors and only one tumor with intermediate grade showed lymph node metastasis. Four cases of adenoid cystic carcinoma accounted 6.15% of total, with an age range of 50-59 years and involving mainly males and minor salivary glands. Microscopically, cribriform arrangement was the predominant pattern observed and two cases showed perineural invasion and one case showed muscle invasion.

One case of Acinic cell carcinoma was observed in a 45 year female affecting the parotid gland with characteristic morphological features. One case of clear cell carcinoma, NOS was observed in a 52 year male, involving the minor salivary gland with lymph node metastasis and one case of salivary duct carcinoma was seen in a 60 year male affecting the parotid gland.

A 58 year male, presented with morphological features of adenocarcinoma, NOS involving the minor salivary gland. A rare case of squamous cell carcinoma arising in Warthin tumor was seen in a 65 year male, involving the parotid gland. Microscopically, the tumor showed two components, the first component showed cystic spaces and papillae lined by double layered cuboidal to columnar epithelium with benign cytological features. The second component showed nests and sheets of pleomorphic cells with moderate amount of eosinophilic cytoplasm and centrally placed pleomorphic nuclei (figure 2).

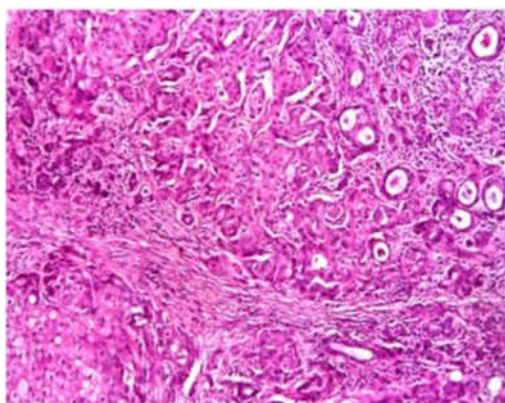


Fig.-1: Photomicrograph reveals predominately solid epidermoid areas and focal cystic areas in a case of mucoepidermoid carcinoma (H & E stain, 100 X)

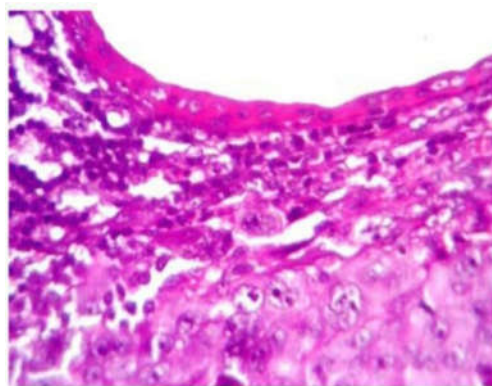


Fig.-2: Photomicrograph reveals Squamous cell carcinoma arising in Warthin tumor showing tumor cells infiltrating the stroma (H & E stain, 100 X)

Discussion

The mean incidence of salivary gland tumors per year at our hospital was 33 cases which is similar to the study by Vuhahula EAM [9] however, lower incidence of these tumors was reported in the literature [1,3]. Ahmed et al, Tilakaratne WM et al and Subhashraj K et al [8,11,12] series showed a higher incidence.

Among the 65 cases of salivary gland tumors, 48 (73.85%) were benign and 17 (26.15%) were malignant which was similar to other studies [1,4,14,17] except in observations made by Nagarkar et al and Tilakaratne WM et al [2,11] wherein malignant tumors were predominant.

The mean age observed was 40 years with an age range of 10 to 79 years. Benign tumors were common in age group of 40 to 49 years and the peak age incidence for malignant tumors was 50 to 59 years; which is in

accordance with the observation by Chatterjee et al [1] wherein benign tumors occurred at a lower age group as compared to malignant tumors. A slight female preponderance (33 cases among 65) with a sex ratio of 1:1.03 was noted. Our findings were similar to the previous studies [15].

A female predominance was observed among benign tumors supporting the findings of previous studies [9,15]. However; other authors [16,17] have observed a male predominance. A male predominance was seen in

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malignant tumors of salivary glands in our study which was similar to the previous studies [8,11,12].

Parotid gland 47 (72.31%) was the commonest site involved followed by minor salivary glands 15 (23.08%) and 3 (4.62%) submandibular gland. Thus, minor salivary gland was more likely to be involved than the submandibular gland in our study as well as in previous studies [1,12,13]. However, in other series [14,15] the sequence of involvement of the tumors was parotid gland followed by submandibular gland and minor salivary glands. Palate was the commonest site involved, among the minor salivary glands, which is similar to the study reported in literature [4].

Pleomorphic adenoma was the most common tumor accounting for 40 (83.33%) of benign tumors and 61.54% of all tumors. This is similar to the results of other studies [5,12,13,18]. The peak age incidence of pleomorphic adenoma was 40-49 years with a female preponderance. These findings are similar to De Oliveria FP et al [19].

Pleomorphic adenoma commonly involved the Parotid gland 33 (82.05%) and is agreeable with other studies [12,13,19]. However, Vuhahula E A M series [9] showed submandibular gland as the most common site. No case was recorded in the sublingual gland. Five cases showed squamous metaplasia of the ducts with epithelial pearl formation and in one case, adenoid cystic-like areas was seen. Similar observations have been recorded by Ellis et al [6].

Three cases showed fatty change and one case was of a recurrent pleomorphic adenoma. Calcification and ossification were not observed in the present study. Chondromyxoid areas showed strong metachromatic reaction with toluidine blue and stained strongly with alcian blue.

Warthin's tumor constituted 7 (10.77%) of all salivary gland tumors and 14.58% of benign tumors. Thus, in our study, warthin's tumor showed an higher incidence as compared to the other series [8,9,12,13].

Peak age distribution was between 50 and 59 years which correlates with other studies [14] where as Ito et al [13] showed an higher age incidence. A male predominance in all studies is similar to the present study, probably related to the environmental factor. Parotid gland was the only gland involved which was similar with the results obtained by other studies [12,17]. No case was seen in minor salivary gland.

One case of oncocytoma was recorded, accounting for 1.53% of all salivary gland tumors. In other studies, Tilakaratne WM et al, Subhashraj K et al, Ito et al [11,12,13] studies found oncocytoma accounting for less than 1% of all salivary gland tumors. However in Vuhahula E A.M [9] series, it accounted for 2.6%. Parotid gland was the commonest site involved which was similar to that observed by Vuhahula E A.M [9] and Subhashraj K et al [13]. The present study showed an higher incidence of mucoepidermoid tumors which was similar to the findings of Ito et al [13]. Other studies [1,9,12,19] showed a lower incidence as compared to the present study. The peak incidence was 50-59 years which was similar to study of De Oliveria FP et al [19].

Our study showed male predominance as compared to study done by De Oliveria FP et al [19] which showed a female predominance. Parotid gland was frequently involved which correlates with other studies [2,12] Adenoid cystic carcinoma constituted 4 (6.15 %) of all tumors of salivary glands and 23.53% of malignant tumors. Our study showed a male predominance whereas the other studies [19] showed a female predominance. Minor salivary glands was commonly involved which was similar to other studies [12,19].

One case of clear cell carcinoma, NOS was observed in a 52 year male, accounting for 1.54% of all salivary gland tumors which was located in the minor salivary gland which correlates with the study by Yang S et al [20].

One case of salivary duct carcinoma was seen in a 60 year male, comprising 1.54% of all tumours involving the parotid gland, which correlates with the study of Gonzalez-Alva P et al [21].

One case of adenocarcinoma, NOS was seen in a 58-year male, accounting for 1.54% of all tumors located in minor salivary gland which was similar to the study observed by Ashkavandi ZJ [22].

A single case of acinic cell carcinoma was seen in 45 year female, accounting for 1.54% of all tumor slocated in parotid gland which was similar to the findings reported in literature [1,12].

The present study revealed a peculiar case of squamous cell carcinoma arising in warthin's tumor in a 65-year old male, involving the parotid gland which accounted for 1.54% of all salivary gland tumors and 5.88% of malignant tumors. Until now only 32 cases are reported in the literature [23].

Conclusion

It is evident from the present study that the histopathological examination of salivary gland lesions is the most important method to differentiate between benign as well as malignant tumors and also in predicting the incidence. It is also useful in typing, staging and grading of malignant lesions.

What is new in this study?

Our distribution of histomorphological spectrum of epithelial tumors salivary gland is similar to most of the other studies worldwide as stated in discussion. However, in our study, minor salivary glands (23.08%) was more likely to be involved as compared to the submandibular glands (4.62%).

A rare case of squamous cell carcinoma arising in Warthin's tumor was seen in a 65 year old male patient, located in parotid gland was noted in our study.

Contribution by different authors

- Dr. Cryslesaldanha contributed to literature review, data acquisition and analysis, statistical analysis, manuscript preparation and editing.
- Dr. Parasappa Yaranal contributed to study designing, manuscript preparation and editing.
- Dr. Krishnaraj Upadhyaya contributed to study designing, data analysis.

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References

1. Chatterjee T, Panda PK. A pathological study of benign and malignant tumours of salivary glands. *Med J Armed Forces India*. 2000 Oct; 56 (4): 282-286. doi: 10.1016/S0377-1237(17)30208-3. Epub 2017 Jun 12.
2. Nagarkar NM, Bansal S, Dass A, et al. Salivary gland tumors - our experience. *Indian J Otolaryngol Head Neck Surg*. 2004 Jan; 56 (1):31-4. doi: 10.1007/BF02968769.
3. Barnes LB, Eveson JW, Reichart P, Sidransky D. editors. *Pathology and Genetics of Head and Neck Tumors*. Lyon: IARC Press; 2005.
4. Hashemi P, Zarei MR, Chamani G, Rad M. Malignant salivary gland tumors in Kerman province: a retrospective study. *Dent Res J* 2007; 4: 4-10.

5. Jude U O, Olu-Eddo A N. Salivary gland tumors, a twenty-year retrospective study. *Afr J Med Health Sci* 2014; 13(1):24-9.
6. Dardick I. Histogenesis and Morphogenesis of salivary gland neoplasms. In : Ellis GL, Auclair PL, Gnepp RD, eds. *Surgical pathology of the salivary glands*, Vol 25. Philadelphia : WB Saunders Co. 1991 : 108-28.
7. Shafkat Ahrnad, Mohainmad Lateef, Rouf Ahmad. Clinicopathological study of primary salivary gland tumors in Kashmir. *JK-Practitioner* 2002; 9(4): 231- 33.
8. Ahmed S, Lateef M, Ahmad R. Clinicopathological study of Primary Salivary-gland tumors in Kashmir. *JK Pract* 2002; 9 (4): 231-3.
9. Vuhahula E A.M. Salivary Gland tumors in Uganda: Clinical Pathological study. *African Health Sciences* 2004; 4 (1): 15-23.
10. Shetty Archana, V Geethamani. Spectrum of Major Salivary Gland Tumours: Clinicopathologic Study. *Sch. J. App. Med. Sci.* 2014; 2(3):1088-90.
11. Tilakaratne WM, Jayasooriya PR, Tennakoon TM, et al. Epithelial salivary tumors in Sri Lanka: a retrospective study of 713 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009 Jul; 108 (1): 90-8. doi: 10.1016/j.tripleo.2009.01.026. Epub 2009 Apr 29.
12. Subhashraj K. Salivary gland tumors: a single institution experience in India. *Br J Oral Maxillofac Surg*. 2008 Dec; 46 (8):635-8. doi: 10.1016/j.bjoms.2008.03.020. Epub 2008 Jul 11.
13. Ito FA, Ito K, Vargas PA, et al. Salivary gland tumors in a Brazilian population: a retrospective study of 496 cases. *Int J Oral Maxillofac Surg*. 2005 Jul; 34 (5): 533-6.
14. Nepal A, Chettri ST, Joshi RR, et al. Primary salivary gland tumors in eastern Nepal tertiary care hospital. *J Nepal Health Res Counc*. 2010 Apr; 8 (1): 31-4.
15. Kalburge JV, Kalburge V, Latti B, Kini Y. Salivary Gland Tumors: Clinicopathologic analysis of 73 cases. *J Cranio Max Dis* 2014; 3(2):111-5.

Original Research Article

16. Shrestha S, Pandey G, Pun C.B, Bhatta R, Shahi R. Histopathological Pattern of Salivary Gland Tumors. *Journal of Pathology of Nepal* 2014; 4(7): 520 –24.

17. Laishram RS, Kumar KA, Pukhrabam GD, et al. Pattern of salivary gland tumors in Manipur, India: A 10 year study. *South Asian J Cancer*. 2013 Oct;2(4): 250-3. doi: 10.4103/2278-330X.119886.

18. C. M. Dharaiya, M. B Patel. Comparative study of Cytodiagnosis of salivary gland neoplasm with Histopathology. *Trop J Path Micro* 2018;4(1):88-92.

19. de Oliveira FA, Duarte EC, Taveira CT, et al. Salivary gland tumor: a review of 599 cases in a Brazilian population. *Head Neck Pathol*. 2009 Dec;3(4):271-5. doi: 10.1007/s12105-009-0139-9. Epub 2009 Sep 16.

20. Yang S, Zhang J, Chen X, et al. Clear cell carcinoma, not otherwise specified, of salivary glands: a

clinicopathologic study of 4 cases and review of the literature. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod*. 2008 Nov;106 (5):712-20. doi: 10.1016/j.tripleo.2008.04.016. Epub 2008 Jul 7.

21. Gonzalez-Alva P, Tanaka A, Ohba K, Yoshizawa D, Ito S, Kusama K. Clinicopathological Study of Epithelial Salivary Gland Neoplasms : Retrospective Review of 156 Cases. *J. Meikai Dent Med* 2007; 36 (2): 135-43.

22. Jaafari-Ashkavandi Z, Ashraf MJ, Moshaverinia M. et al. Salivary gland tumors: a clinicopathologic study of 366 cases in southern Iran. *Asian Pac J Cancer Prev*. 2013;14(1):27-30.

23. Sharma M, Chintamani, Saxena S, Agrawal U. Squamous cell carcinoma arising in unilateral Warthin's tumor of parotid gland Case Report. *Journal of Oral and Maxillo Facial Pathology* 2008;12 (2): 82-4.

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