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Histomorphological Descriptive Analysis Of Salivary Gland Neoplasms – A Retrospective StudyIn A South Indian Tertiary Care Hospital

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Abstract:
Objectives:*Tumors arising in salivary glands comprise about 4% of all malignant epithelial neoplasms encountered in head and neck. To evaluate the incidence and nature of salivary gland masses presenting to this Institute of Pathology, Madras Medical College, Chennai. To categorize the tumors presenting as per recent WHO classification, with routine Haematoxylin and Eosin staining.To compare and analyze our data with similar studies.*
Materials & Methods*: This study was undertaken to evaluate the incidence and nature of salivary gland masses presenting to this tertiary care hospital. This study was done retrospectively from January,2014 to March,2015 with available samples from the archives of the department.*
Results: *A total of 100 cases of salivary gland masses were studied and tumors were categorized. 75 cases were neoplastic and 25 were non neoplastic. The frequency of benign neoplasm were 66.67% and malignant tumors were 33.33%. The mean age of presentation of benign tumors were 39.28 years while for malignant tumors it was 50.88 years. The salivary gland tumors showed female preponderance with peak incidence of benign tumors in 4th decade and malignant tumors in 6thdecade. The most common benign tumor was Pleomorphic Adenoma and the most common malignant tumor was Mucoepidermoid Carcinoma. The commonest site of presentation of salivary gland tumors were parotid, while non neoplastic lesions were common in submandibular gland.*
Conclusion: *Though salivary gland tumors represent only a small fraction of all neoplasms, their morphologic diversity and varied histological subtypes frequently impose diagnostic problems.Analysis of various tumors of salivary gland was in accordance with other demographic studies done throughout the world.This study paves way for further analysis using Immunohistochemical profile and Cytogenetics for prognostic indications and treatment.*
Key words: *Histomorphology, Mucoepidermoid Carcinoma, Pleomorphic Adenoma, Salivary gland neoplasm.*

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I. Introduction

Tumors arising in salivary gland comprise only about 4% of all epithelial malignant neoplasms encountered in head and neck and are in the range of 2% to 6.5%.[1,2,3] The age adjusted incidence is 1.5 per 100,000 person-years. Malignancies of the salivary gland are uncommon, accounting for 0.3% of all malignancies and accounting for 3-6% of all head and neckmalignancies.[3]Varieties of neoplasms originate from the salivary gland. The histopathology of these neoplasms is most complex and diverse. About 80% of these tumors occur in the parotid, 15% in the submandibular gland and 5% in the sublingual and minor salivary glands. About 80% of parotid tumors, 50% of submandibular tumors and less than 40% of sublingual and minor salivary gland tumors are benign.[1,4] Their clinical importance is due to their confounding histological and behavioural diversity and their management challenges.[4,5]

Though neoplasms of salivary glands are comparatively uncommon, their multifaceted clinical features, varied morphological presentation and unpredictable prognosis evoke significant interest. Hereditary and environmental factors influence on the geographical distribution of neoplasms.[1,4] The first classification scheme of salivary gland tumors was proposed by Foote and Frazell, leading to most recent WHO classification published in 2005. Under this WHO classification, around 40 neoplasms are listed, many of which show significant variable histological features that posts a diagnostic challenge.

1.1.Materials And Methods: *This retrospective study included all salivary gland biopsy specimens submitted for histopathological examination to the Institute of Pathology, Madras Medical College from January,2014 to March,2015 with the available samples from the archives of department.*

1.2.Inclusion criteria*:All cases of Salivary gland tumors submitted for histopathology examination were included irrespective of age and sex of the patient.*

1.3.Exclusion criteria: *All cases with inadequate clinical details and inadequate samples were excluded from study. Total of 100 salivary gland specimens were analysed for this study.*

II. Observation and Results

Among the salivary gland lesions, non neoplastic lesions accounted for 25 cases (25%) and neoplastic 75 cases (75%). Out of the 75 neoplasms 50 were benign and 25 were malignant as represented in (TABLE-1).**2.1.BenignTumors**:

Among the 75 neoplastic cases, 50 cases were benign and 25 cases were malignant. Benign tumors accounted for 66.67% of all neoplasms of salivary gland. Benign tumors were more common in females with peak incidence in 31-40years age group. 50% of the tumors were reported in the age group of 31-50 years. (TABLE-2). The benign tumors include Pleomorphic adenoma (84%), Myoepithelioma (10%), Warthin tumor (2%), Basal cell adenoma (2%), and Ancient schwannoma (2%) (TABLE-3)

Pleomorphic adenoma, the commonest benign tumor in our study was seen predominantly in parotid gland with female preponderance (67%). The peak incidence was in 31-40 years age group.The variants reported in Pleomorphic adenoma were myoepithelial predominant Pleomorphic adenoma in 9 cases(21%) which were common in females and epithelial predominant (cellular Pleomorphic adenoma) reported in 1 case(2%).

Myoepithelioma was the second common benign tumor in our study. It was also predominantly seen in parotid gland and among females with peak incidence occurring in 51-60 year age groups.One case each of Warthin tumor in 66 year old male patient, Basal cell adenoma in 65 year female and Ancient schwannoma in 40 year female were reported in parotid gland.

2.2.MalignantTumors:.

Malignant tumors accounted for 25% of the total lesions and 33.33% of all salivary gland tumors. They were more common among females with peak incidence in 51-60 year age group(TABLE-4).The percentage of occurrence in malignant tumors alone includes Adenocarcinoma at 8%, Mucoepidermoid carcinoma (MEC) at 36%, Acinic cell carcinoma (ACC) at 8%, Salivary duct carcinoma (SDC) at 8%, Carcinoma ex pleomorphic adenoma (CA ex PA) at 8%, Epi-Myo Ca(12%), Adenoid cystic carcinoma (ADCC) at 4%, Polymorphous low grade adenocarcinoma (PLGA) at 4%,Squamous cell carcinoma (SCC) at 8%, Malignant Oncocytoma(4%) (TABLE-5,6)The commonest salivary gland involved was parotid followed by submandibular gland. The Mucoepidermoid carcinoma was the commonest malignant tumor followed by Epithelial myoepithelial carcinoma. Mucoepidermoid carcinoma was seen exclusively in parotid gland and frequently in male population with peak incidence at 61-70 year age group. The cases were distributed from 2^{nd} to 7^{th} decade.Low grade MEC occurred in 6 cases and intermediate grade in 3 cases.

Low Grade - MEC	Intermediate Grade - MEC	HighGrade - MEC
6	3	0
66%	34%	0

Grading of MEC in received cases.

Epithelial myoepithelial carcinoma was the second commonest malignant tumor accounting for 12% of malignant tumors and 4% of salivary gland tumor and 3% of salivary gland lesion. It occurred predominantly in parotid gland. Two cases of Acinic cell carcinoma was reported in parotid gland with equal sex prevalence. Two cases of Carcinoma ex pleomorphic adenoma were reported in parotid gland and occurred exclusively in males.Among the two reported cases of Squamous cell carcinoma one was Well differentiatedSquamous cell carcinoma in a 60 year female and the other was poorly differentiated in a 30 year female.One each of Adenoid cystic carcinoma in submandibular gland in a 33year female, one case of PLGA in minor gland of 42year female, one case of Monomorphic adenocarcinoma and another case of Adenocarcinoma- NOS were reported in 50year female in parotid gland. One case in the seventh decade was reported as Malignant oncocytoma of submandibular gland.

III. Discussion

This study analysed the histomorphological pattern of salivary gland tumors presented to this tertiary care hospital. The lesions were classified into non neoplastic and neoplastic and neoplastic were further classified into benign and malignant and co-relation done with the demographic data.Incidence of salivary gland tumors were 0.5% to 2% of all neoplasms and salivary gland tumors were 0.95%[6]. In our study the benign tumors accounted for 66.67% of total salivary gland neoplasms and malignant tumors accounted for 33.33%. The various studies conducted showed an incidence of benign tumors to be from 60% to as high as 86%. The malignant tumors showed an incidence as low as 14% to 40%. So our study correlates with most of the studies done across continents and more so with other Asian and Indian studies. In our study most cases were presenting in 31-40years age group. Most of the benign cases presented in 31-40year age group with a mean age incidence of 39.28 years. Malignant cases had a peak incidence in 51-60year age group with mean age incidence of 50.88 years. Our analysis showed that benign tumor incidence is in 3rd-4th decade and it co-relates with above data.In our study of 100 cases, females account for 60 and males 40 in the ratio of 1:1.5(male to female). In exclusively tumors, the sex incidence were female 47 cases and male 28 cases in the ratio of M:F [1:1.67]

3.1Benign Neoplasm- Analysis:

Pleomorphic adenoma accounted for 42 cases(42%). Of the salivary gland tumors, Pleomorphic adenoma accounted for 56% and in benign tumors, Pleomorphic adenoma accounted for 84%. The average age in our study was 37.6 years. Pleomorphic adenoma was the commonest benign tumor with female preponderance.[1,7,8,9], Our study has 66.66% female prevalence similar to other studies.Also pleomorphic adenoma was commonest[4] with female preponderance with mean age of 37.6 years and most common location being parotid as with above literature. Also 33 out of 42 cases occurred under age of 50years. This co-relates with most of studies stated above. Our prevalence was from 13years to as high as 70 years.[10]Out of 42 cases reported, epithelial and mesenchymal elements intermingled with myxoid and chondroid elements.[FIG-1,2] Two cases showed squamoid metaplasia[12,13,14] constituting about 4.8%. Nine cases were classified as myoepithelial predominant and 1 case as epithelial predominant Pleomorphic adenoma.[11]

Second most common tumor was Myoepithelioma in our study. Five cases were received accounting for 66.6% of salivary gland neoplasms and 10% of benign tumors. The peak incidence was in the 5th decade with female preponderance. In our study, ocurrence in female was 60%. Three cases occurred in parotid and 2 cases in submandibular gland.[15] Two cases of spindle cell variant and 1 case of spindle cell, hyalinising variant were reported. It is composed of solid to trabecular pattern [FIG-3] with polygonal cells, plasmacytoid hyaline cells exhibiting myoepithelial differentiation with hyalinised stroma. One case of hyalinising variant with clear cells and abundant hyalinised stroma were seen.

Warthin tumor accounts for 1 case of all salivary gland tumors accounting for 2% of benign tumors. It occurred in parotid gland in a 66 years male patient.[16] Our case was characterized by cyst with papillary projections lined by columnar oncocytic luminal cells with a layer of basal cells demarcated from underlying lymphoid stroma.[11,12]One case of Basal cell adenoma was reported in a 65year female accounting for 1.33% of all salivary gland tumor and 2% of benign lesions of salivary gland[17]occurring in parotid predominantly and in elderly woman.[11] One case of Ancient schwannoma was reported in 40years/female in parotid gland, constituting 2% of benign tumors of salivary gland.[18,19]

3.2 Malignant Neoplasm- Analysis:

Malignant neoplasms account for 33.33% of all salivary gland neoplasms. In our study mucoepidermoid carcinoma was most common malignant tumor accounting for 36% of neoplastic tumors and 12% of salivary gland tumors. All cases occurred in parotid gland.Mucoepidermoid carcinoma[FIG-4] had a slight male preponderance, 55.5% occurring in males with a peak incidence in 61-70 years and in females in the 31-40 years age group,[20,21] and showed equal sex distribution in separate studies. Our study showed prevalence in 19-70 years age group and an incidence of 12% for MEC in all salivary gland tumors. Various studies showed an incidence varying from 7.2% to 13.9%. Adenoid cystic carcinoma occurred in a 33year female with perineuralinfiltration,[FIG-5] with tumor invasion into the underlying muscle and capsular invasion is also noted.In our study carcinoma ex pleomorphic adenoma[FIG-6] accounted for 2(8%) cases of malignant tumors and 2.6% of salivary gland tumors with the median age being 55years.[22,23] with male predominance. [24,25]. Both cases occurred in the parotid gland[16] Malignant oncocytoma, in a 73year female was reported in submandibular gland[FIG-8].[11]

Epithelial myoepithelial carcinoma[FIG-10] was reported in 3cases of our study which comprises 12% of malignant tumors and 4% of overall salivary gland tumors. [15] All the cases occurred in major salivary glands especially in parotid with male preponderance and median age being 58.3years[27,28] Polymorphous low grade

adenocarcinoma **[**PLGA**](**1%) presented in our study which occurred in the minor gland in a 42year female[FIG-7].[29]. Adenocarcinoma- NOS: Two cases were reported in female patients in our study which occurred in the parotid glands accounting for 2.66% of salivary gland tumors.Salivary duct carcinoma [FIG-9] accounted for 2.66% of salivary gland tumors. [30,20]. Of the 2 cases reported, 1 case showed nodal metastasis.

1V. FIGURES AND TABLES

Pathology	No of cases	%
Non neoplastic	25	25%
Neoplastic 1. Benign 2. Malignant	75 50 25	75% 50% 25%

Table-1, Incidence of salivary gland tumors

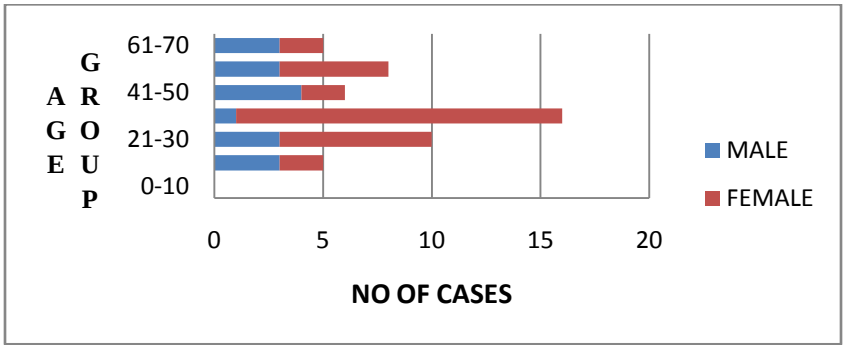

Table-2, Age & sex incidence of benign tumors.

HPE Diagnosis	No: Of Cases	% Of All SGT	% Of All Benign SGT	Male	Female
1.Pleomorphic adenoma	42	56	84	14	28
2.Myoepithelioma	5	6.66	10	2	3
3.Warthin tumor	1	1.33	2	1	-
4.Basal cell adenoma	1	1.33	2	-	1
5.Ancient schwannoma	1	1.33	2	-	1
TOTAL	50			17	33

SGT- Salivary gland tumor

Table-3, Distribution and sex incidence of various benign tumorsin salivary gland

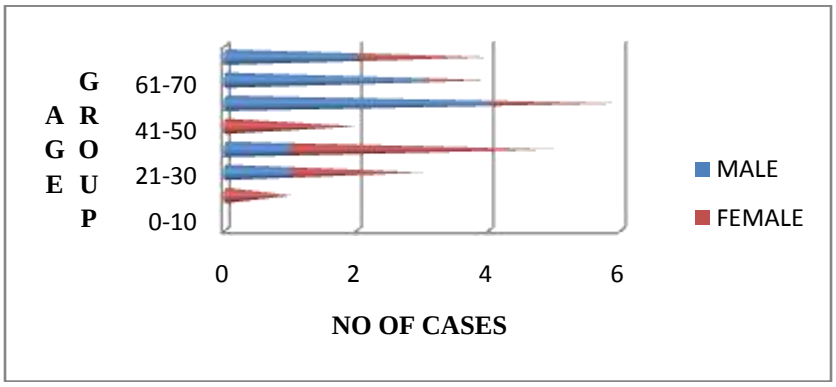

TABLE-4, Frequency of age and sex distribution in malignant neoplasms

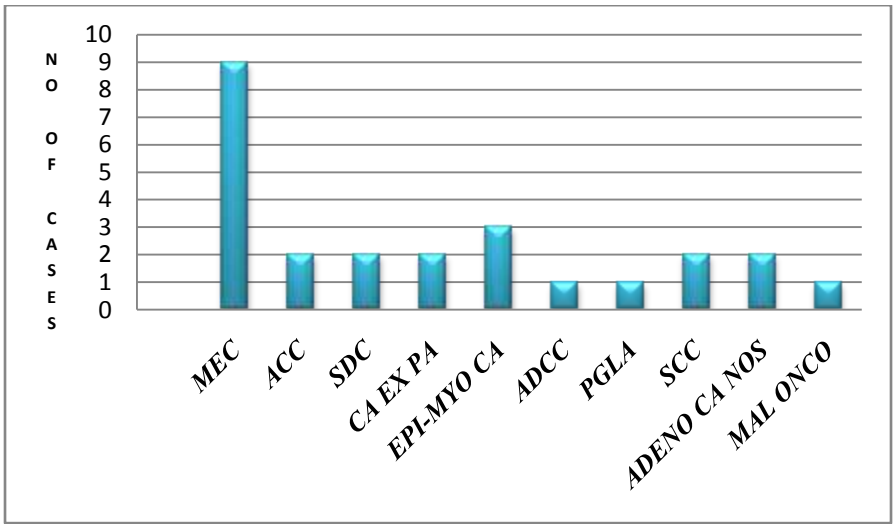

Table-5,Frequency of distribution of various malignant tumors

S.No	Hpe Diagnosis	No Of Cases- %	Male	Female	Gland
1.	Adenocarcinoma - NOS	2(2.66%)	-	2	Parotid
2.	Mucoepidermoid Ca	9(12%)	5	4	Parotid
3.	Acinic Cell Ca[ACC]	2(2.66)	1	1	Parotid
4.	Salivary Duct Ca[SDC]	2(2.66)	1	1	1Parotid+1S/M
5.	Carcinoma Ex PA	2(2.66)	2	0	Parotid
6.	Epi Myo Ca	3(4%)	2	1	2Parotid+1S/M
7.	Adenoid cystic Ca[ADCC]	1(1.33%)	0	1	S/M
8.	PLGA	1(1.33%)	0	1	Minor
9.	Squamous Cell Ca[SCC]	2(2.66%)	0	2	1Parotid+1S/M
10.	Malignant Oncocytoma	1(1.33%)	0	1	S/M
	TOTAL	25	11	14	

Table-6, Distribution of malignant tumors in salivary gland with sex incidence

FIG-1**,** Cellular pleomorphic adenoma showing encapsulated, solitary mass with solid grey white areas and areas of degeneration.

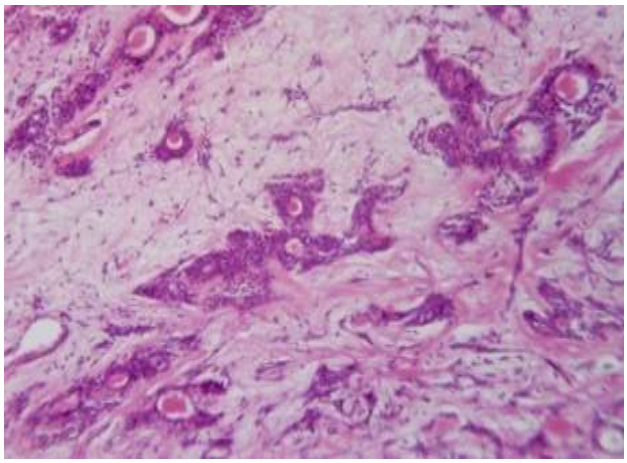

FIG-2,Pleomorphic adenoma showing tubules lined by inner layer of ductal cells and outer layer of myoepithelial cells in a chondromyxoid stroma.

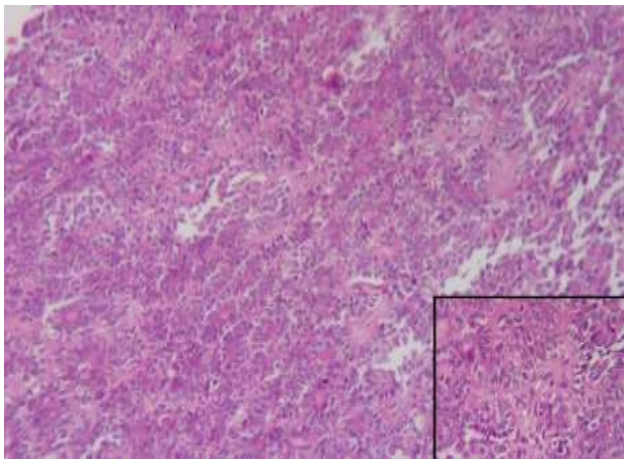

FIG-3,Myoepithelioma showing solid to trabecular growth pattern of myoepithelial cells.

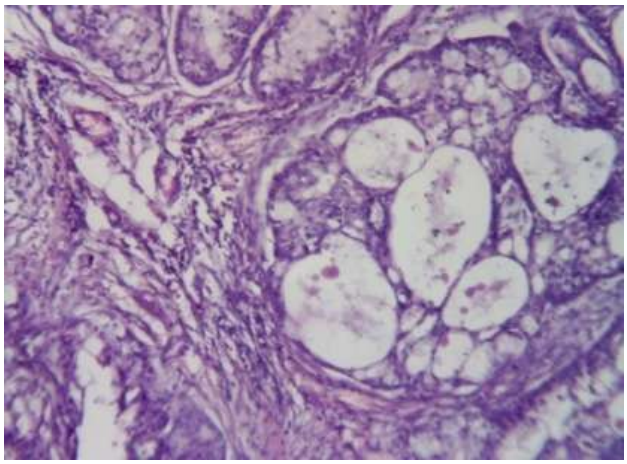

FIG-4, Mucoepidermoid carcinoma showing multiple mucin filled cystic structures lined by mucouscells.

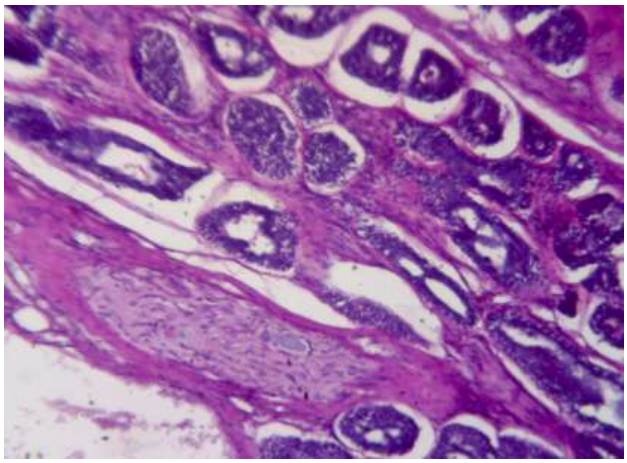

FIG-5, Adenoid cystic carcinoma showing perineural invasion.

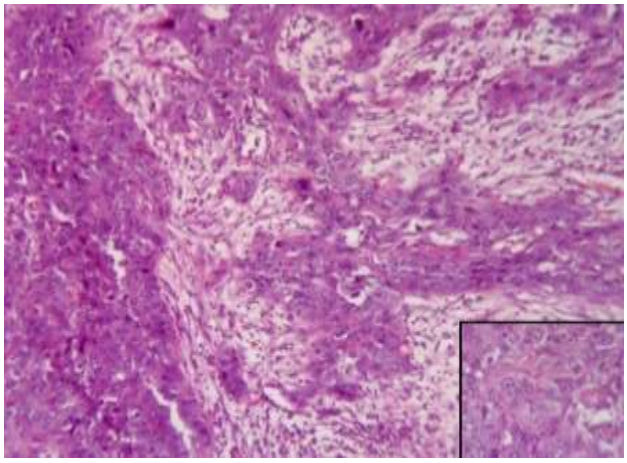

FIG-6, Carcinoma ex pleomorphic adenoma showing infiltration of wide spread pleomorphic tumor cells.

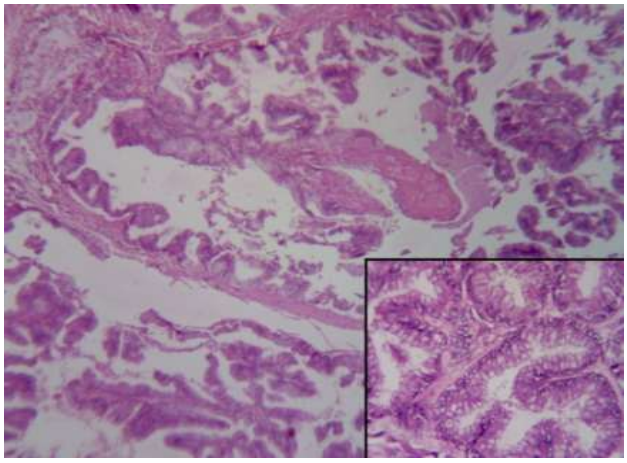

FIG-7, PLGA showing tumor cells arranged in papillary cystic pattern with dilated cysts showing intraluminal projections.

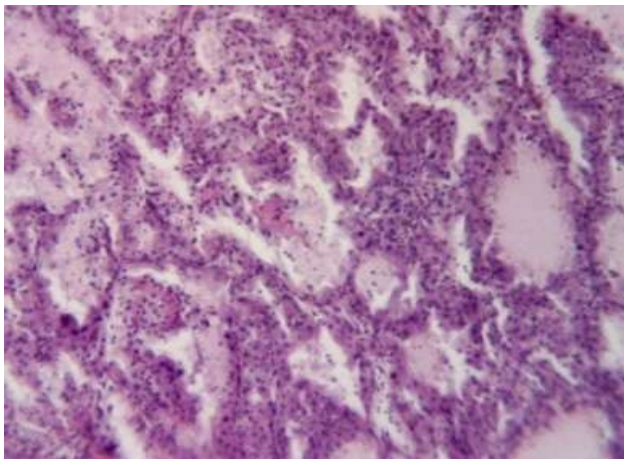

FIG-8, Malignant oncocytoma showing malignant oncocytic cells in nests.

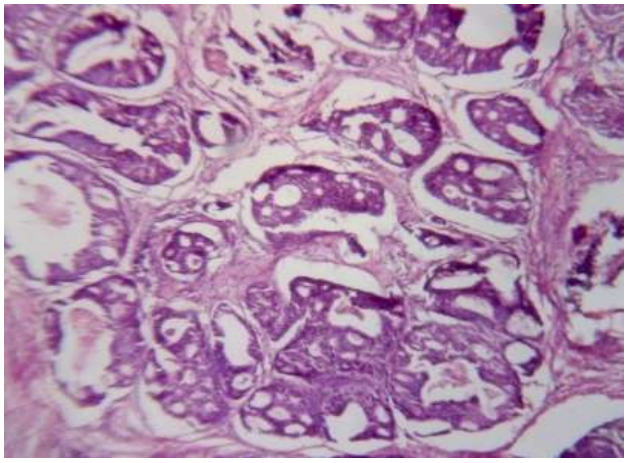

FIG-9, Salivary duct carcinoma showing cribriform, papillary cystic with comedo necrosis.

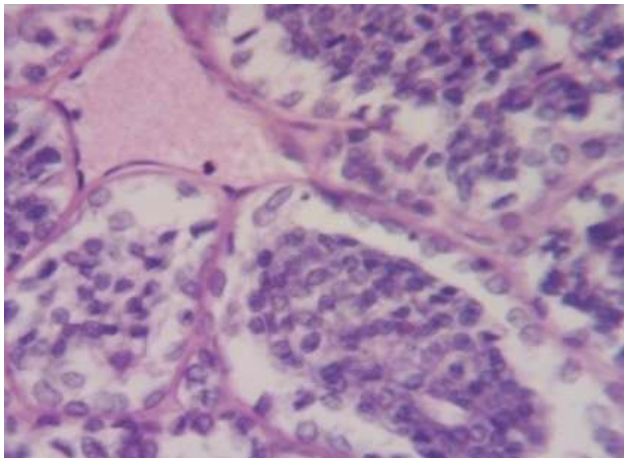

FIG-10, Showing tubules lined by inner epithelial and outer clear myoepithelial cells separated by sclerotic stroma.

V. Conclusion

1. Total number of 100 salivary gland lesions were studied retrospectively to evaluate the incidence and nature of salivary gland tumors presenting. The different types of salivary gland lesions both non neoplastic and neoplastic occurring in the region of this tertiary care hospital in Southern India and found to be correlated with other studies conducted in western and asian populations. The tumors were categorized as per recent WHO classification under conventional processing and H&E stain study.
2. The peak incidence of the lesions of salivary gland were in 30-40 year group with benign tumors showing peak incidence in 3rd – 4th decade and in malignant tumors the peak incidence was in 5th – 6th decade followed by non neoplastic lesions in 3rd and 4th decade.
3. In our study of 100 cases, incidence of salivary gland lesions in females were higher occurring in 60% of cases and the female: male ratio was 1.5:1. In exclusively salivary gland tumors, the incidence was 47 females out of 75 cases and the female: male ratio was 1.67:1.
4. The mean age for benign tumor was 39.28 years while for malignant tumors it was 50.88 years. Among 100 cases majority of lesions were in parotid gland the incidence being 76.2%, in submandibular 19% and minor glands accounting for 4.8%.
5. Of the 50 cases of benign tumors 38 cases occurred in parotid gland and out of 25 malignant cases, nineteen cases were present in parotid. Benign tumors were common in minor salivary glands. Non neoplastic inflammatory lesions were more common in submandibular glands.
6. The frequency of benign neoplasms was 66.67% and malignant tumors were 33.33%.
7. The most common benign salivary gland neoplasm was Pleomorphic adenoma with an incidence of 56% of total salivary gland neoplasm and accounted for 84% of total benign tumors. The second most common wasMyoepithelioma accounting for 6.66% of total salivary gland neoplasms.
8. The most common malignant neoplasm in our study was Mucoepidermoid carcinoma accounting for 12% of overall salivary gland tumors and 36% of malignant salivary gland neoplasms. The second most common malignant tumor was Epithelial myoepithelial carcinoma accounting for 4% of all salivary gland neoplasms.
9. Thus we conclude that, though salivary gland tumors represent only a small fraction of all neoplasms, their morphologic diversity and varied histological subtypes frequently impose diagnostic problems. This study paves way for further analysis using Immunohistochemical profile and cytogenetics for prognostic indications and treatment.

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