



## HISTO-MORPHOLOGICAL SPECTRUM OF SALIVARY GLAND LESIONS

<b>Dr. Suwarna Patil</b>	Associate Professor, Department of Pathology, GMC, Akola, Maharashtra, India.
<b>Dr. Manjiri Khade</b>	Assistant Professor, Department of Pathology, GMC, Akola, Maharashtra, India.
<b>Dr. Shweta Dhage</b>	Assistant Professor, Department of Pathology, GMC, Akola, Maharashtra, India.
<b>Dr. Swarada Kangate*</b>	Assistant Professor, Department of Pathology, GMC, Akola, Maharashtra, India. *Corresponding Author
<b>Dr. Pradip Umap</b>	Professor and Head, Department of Pathology, GMC, Akola, Maharashtra, India.
<b>Dr. Shahnawaz Khan</b>	Junior Resident, Department of Pathology, GMC, Akola, Maharashtra, India.
<b>Dr. Deji Talekar</b>	Junior Resident, Department of Pathology, GMC, Akola, Maharashtra, India.

**ABSTRACT**

**Introduction:** Salivary gland neoplasms consist of a group of heterogeneous lesions with complex clinicopathological characteristics and distinct biological behaviors, accounting for less than 1% of all tumors and 3-5.5% of all head and neck tumors. Pleomorphic adenoma is the most common tumor, accounting 70% of benign tumors. Muco-epidermoid carcinoma is the most common malignant tumor which involves mostly the parotid gland. In the present study, the wide histopathological spectrum of salivary gland neoplasms in patients presenting to a tertiary care center, were studied. **Materials and Methods:** The present study was a retrospective cross-sectional study, carried out at Tertiary Care Teaching Hospital, in Department of Pathology, over a period of five years from July 2015 to June 2020 and a total of 134 cases were studied. **Results:** Out of 134 cases, 87 were males (64.9%) and 47 were females (35.1%). Male to female ratio was 1.8:1. Most common age group was 41-50 years (32%). Most common site of involvement was parotid gland (62%), followed by minor salivary glands (17%). Benign neoplasms were 72% and malignant were 28%. Most common benign tumor was found Pleomorphic Adenoma (43%), followed by Warthin's tumor (20%). In malignant tumors, muco-epidermoid carcinoma was most common (10.4%), followed by carcinoma ex-pleomorphic adenoma (3.7%). **Conclusion:** Proper diagnosis needs consideration of histological findings to differentiate between benign and malignant neoplasms. Hence, Histopathology remains the Gold standard procedure.

**KEYWORDS :** Salivary gland, Histopathology, Pleomorphic Adenoma, Muco-epidermoid carcinoma

**INTRODUCTION:**

Salivary gland neoplasms consist of a group of heterogeneous lesions with complex clinicopathological characteristics and distinct biological behaviors,<sup>1</sup> accounting for less than 1% of all tumors and 3-5.5% of all head and neck tumors. The worldwide annual incidence of salivary gland tumors ranges from 0.4 to 13.5 cases per 1 lakh. There is a wide variety of benign and malignant salivary gland tumors.<sup>2</sup> These tumors commonly pose problems in diagnosis due to rarity, broad morphologic spectrum (resulting from multiple tumor cell differentiation<sup>3</sup>) and morphologic overlap among the different tumor types. They exhibit differences in biological behavior and also in prognosis. Parotid gland accounts for nearly 80% of the salivary gland tumors followed by the submandibular gland (approximately 10-15%). 80-85% of the tumors are benign in nature. Pleomorphic adenoma is the most common tumor, accounting 70% of benign tumors. Salivary gland tumors are commonly seen in 6th and 7th decades of life. Incidence of benign salivary gland tumors are more in females whereas malignant tumors are more in males. Muco-epidermoid carcinoma is the most common malignant tumor which involves mostly the parotid gland followed by the minor and submandibular gland. Adenoid cystic carcinoma is a highly malignant neoplasm which is more commonly seen in the minor salivary glands.<sup>2</sup>

Acinic cell carcinoma is rare (1-3%) of all salivary gland tumor with male predominance and a peak incidence in the third decade of life. Although FNAC is a valuable diagnostic tool for pre-operative evaluation, Histopathology still remains the gold standard.<sup>2</sup>

In the present study, the wide histopathological spectrum of salivary gland neoplasms in patients presenting at a Tertiary Care Center, were studied.

**MATERIALS AND METHODS:**

The present study was a retrospective cross-sectional study, carried out at Tertiary Care Teaching Hospital, in Department of Pathology, over a period of five years from July 2015 to June 2020. Among 12,750 histopathological specimens received, total 134 cases were found to be of salivary gland neoplasm. All salivary gland neoplasm specimens

along with their operative findings were received from Department of Surgery and Otorhinolaryngology. Clinical history with age, presenting signs & symptoms, radiological findings were studied. Gross examination of 10% formalin fixed specimen was done and sections were taken from the surgical margins, base and representative area, along with normal looking area. Further histopathological processing of sections was done and slides stained with Haematoxylin and Eosin (H&E) were studied. Where ever indicated, special stains like Periodic Acid Schiff (PAS) and Mucicarmine were studied.

All the tumors were classified as per the WHO-2018 classification.

**INCLUSION CRITERIA:**

All epithelial origin, major and minor salivary gland tumors

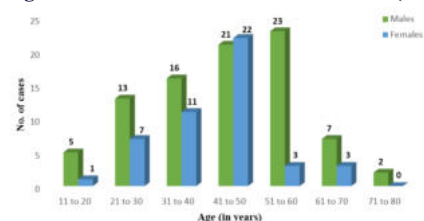
**EXCLUSION CRITERIA:**

1. All inflammatory and cystic lesions of salivary glands. 2. All mesenchymal origin salivary gland tumors. 3. Metastasis in salivary glands.

**RESULTS:**

In the present study, during the study period, total 12,750 histopathological specimens were received, out of which 134 cases (1.1%) were found to be of salivary gland neoplasm.

**Figure 1: Age-wise and Sex-wise distribution of cases (n=134)**



As shown in fig 1, out of 134 cases, total 87 were males (64.9%) and 47 were females (35.1%), with the male to female ratio of 1.8:1. Most

common age group was 41-50 years (43 cases – 32%) and minimum cases were seen in the age group of 71-80 years (two cases – 1.5%). Youngest patient was Carcinoma ex-pleomorphic adenoma.

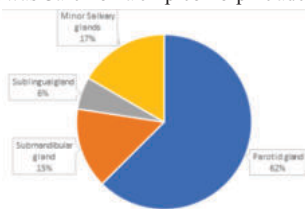


Figure 2: Site-wise distribution of cases (n=134)

Fig 2 shows that most common site of involvement in the present study was parotid gland (62%), followed by minor salivary glands (17%) and submandibular gland (15%). While least commonly sublingual glands were involved (6%).

Table 1: Distribution of cases according to the diagnosis (n=134)

Diagnosis		No. of cases	Percentage (%)
Benign (96 cases – 72%)	Pleomorphic adenoma	57	43
	Warthin's tumor	26	20
	Oncocytoma/ Oxyphil adenoma	04	03
	Basal cell adenoma	04	03
	Schwannoma	03	2.2
	Neurofibroma	02	1.5
	Malignant (38 cases – 28%)	Muco-epidermoid carcinoma	14
Carcinoma ex-pleomorphic adenoma	05	3.7	
Adenoid cystic carcinoma	04	03	
Salivary duct carcinoma	04	03	
Acinic cell carcinoma	03	2.2	
Polymorphous low-grade adenocarcinoma	03	2.2	
Epithelial-myoepithelial carcinoma	02	1.5	
Lymphoma	02	1.5	
Squamous cell carcinoma	01	0.7	
<b>Total</b>		<b>134</b>	<b>100</b>

Out of 134 cases, benign neoplasms were found in 96 cases (72%) and malignancy was found to be in 38 cases (28%). (Table 1)

Most common benign tumor was found to be Pleomorphic Adenoma in 57 cases (43%), followed by Warthin's tumor in 26 cases (20%). Pleomorphic Adenoma was most commonly found in parotid gland (30%), followed by submandibular gland and sublingual gland (1.5% each) and least commonly in minor salivary gland (10.4%). Four cases (03% each) were found to be of Oncocytoma and Basal Cell Adenoma. Three cases of Schwannoma were also included in the present study (2.2%). Least common benign tumor was found to be Neurofibroma in two cases (1.5%). (Fig 3)

In malignant tumors, Muco-epidermoid Carcinoma was most common (10.4%), followed by Carcinoma ex-pleomorphic adenoma (3.7%) and Adenoid Cystic Carcinoma and Salivary Duct Carcinoma (03% each). Muco-epidermoid carcinoma was most commonly found in submandibular gland (6.7%) followed by parotid (3%) and minor salivary gland (0.7%). Adenoid Cystic Carcinoma was most commonly found in the minor salivary glands. Acinic Cell Carcinoma and Polymorphous low-grade adenocarcinoma (PLGA) were found in three cases each (2.2% each). While two cases each were found to be of Epithelial-Myoepithelial Carcinoma and Lymphoma. One case of 70-years male with squamous cell carcinoma was also found. (Fig 4)

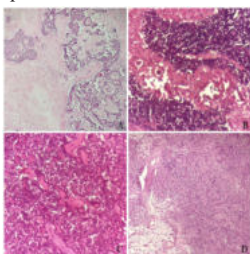


Figure 3: Microphotographs of Benign Salivary Gland Tumors

Figure A – Pleomorphic Adenoma (H&E, 400x)  
 Figure B – Warthin's tumor (H&E, 400x)  
 Figure C – Basal Cell Adenoma (H&E, 400x)  
 Figure D – Schwannoma (H&E, 400x)

Figure 4: Microphotographs of Malignant Salivary Gland Tumors

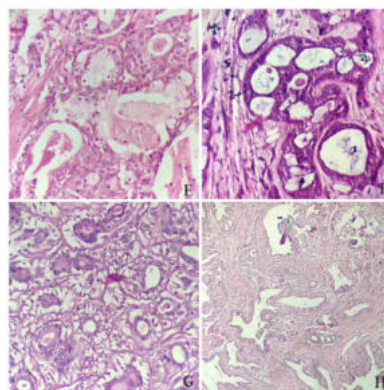


Figure E – Muco-epidermoid carcinoma (H&E, 400x)  
 Figure F – Adenoid cystic carcinoma (H&E, 400x)  
 Figure G – Epithelial-myoepithelial carcinoma (H&E, 400x)  
 Figure H – Salivary duct carcinoma (H&E, 400x)

**DISCUSSION:**

In the present study, out of total 12,750 histopathological specimens, 134 cases (1.1%) were found to be of salivary gland neoplasm, while it is found to be 2% in the Western World. A very little information is available on the tumors of head and neck over the last two-three decades.<sup>3</sup>

Present study included maximum male patients (64.9%) and female patients were 35.1%, similar to the study done by Otoh EC<sup>4</sup>. While Dr. Aneesha Asok Kumar<sup>2</sup>, de Oliveira FA<sup>1</sup>, Bobati SS<sup>5</sup>, Dandapat MC<sup>6</sup> and Rewusuwan S<sup>7</sup> reported female preponderance in their studies.

Most common age group, in the preset study, was found to be 41-50 years (32%) and minimum cases were seen in the age group of 71-80 years (1.5%). While benign tumors were most commonly seen in the age group of 41 to 50 years and malignant tumors were seen most commonly in the advanced age group of 51 to 60 years. These findings were comparable to the studies in the literature.<sup>1,2,5</sup>

Parotid gland (62%) was the commonest tumor site in the present study. This was again similar to the findings of studies available in the literature.<sup>1,2,5,7,8</sup> Minor salivary glands (17%) was the second common site, followed by submandibular gland (15%) as the third one.

Benign tumors (72%) were more common in the present study, as compared to the malignant one (28%). Similar results were observed in the studies done by Dr. Aneesha Asok Kumar<sup>2</sup>, de Oliveira FA<sup>1</sup>, Bobati SS<sup>5</sup>, Nepal A<sup>9</sup>, Naeem Sultan Ali<sup>10</sup>, Moghadam Sa<sup>11</sup>.

Pleomorphic Adenoma was the most common benign tumor in parotid gland, predominant in females and consisted of 43% of all tumors. All epidemiological studies on the salivary gland tumors have shown a pronounced predominance of 42%–80% Pleomorphic Adenoma.<sup>3,12,13</sup> Histopathological feature shows both epithelial and mesenchymal differentiation. Epithelial component includes the well-formed ductal structures formed of inner epithelial and outer myoepithelial cells with associated features of spindle, squamous, basaloid, cuboidal, oncocytoid, mucous, sebaceous, round, plasmacytoid, polygonal or clear cells. Cytologic features of epithelial cells were bland, and the mesenchymal component consisted myxoid, hyaline, cartilaginous or osseous differentiation. Variants include cellular with predominant epithelial element and myxoid type having myxochondromatous mesenchymal elements. Thickness of fibrous capsule varied, often absent in predominantly myxoid tumors. Special stains and immunohistochemistry (IHC) are noncontributory.<sup>5</sup> Similar predominance of Pleomorphic Adenoma was seen in the series reported by Dr. Aneesha Asok Kumar<sup>2</sup>, de Oliveira FA<sup>1</sup>, Bobati SS<sup>5</sup>, Shrestha S<sup>14</sup>, Naeem Sultan Ali<sup>10</sup>, Bashir S<sup>8</sup>.

Second most common benign tumor was Warthin's tumor, which was comparable to study done by Dr. Aneesha Asok Kumar<sup>2</sup>, Shrestha S<sup>14</sup>,

Naeem Sultan Ali<sup>10</sup>, Bashir S<sup>8</sup> and Bobati SS<sup>5</sup>. Smoking habits are the main etiological factor for Warthin's tumor mainly affecting the elderly patients and rarely occurs in <30 years of age, with a peak incidence in the sixth decade of life. The differences in results could be affected by racial, behavioral, geographical and unknown environmental factors. Microscopically, epithelial tall columnar with basaloid oncocytic cells lining cysts form prominent papillae, the cystic spaces are filled with lymphoid stroma and few show lymphoid follicles. Other techniques for diagnosis are noncontributory.<sup>5</sup>

Mucoepidermoid carcinoma was reported to be the most common malignant salivary gland tumor (10.4%). It was most commonly found in submandibular gland (6.7%) followed by parotid (3%) and Minor salivary gland (0.7%). Dr. Aneesha Asok Kumar<sup>2</sup>, Richardson et al<sup>15</sup> and Ali et al<sup>10</sup> also observed mucoepidermoid carcinoma to be the most common salivary gland tumor in their studies. Mucoepidermoid carcinoma on microscopy is composed of varying proportions of mucous, epidermoid and intermediate-type cells with cystic or papillary mucin-filled cystic lumens, often have pools of extravasated mucin in surrounding tissue which are strongly positive for mucicarmine stain. These carcinomas may also have clear cells with clear cytoplasm mainly glycogen and less mucin. This carcinoma is reported on a grading system of low (Grade I - Predominant cystic), intermediate (Grade II - Cystic and cellular) and high (Grade III - Predominant solid pattern).<sup>5</sup>

Carcinoma ex-pleomorphic adenoma was second most common malignant tumor (3.7%), which was followed by Adenoid Cystic Carcinoma and Salivary Duct Carcinoma (0.3% each). Adenoid Cystic Carcinoma was the second most common tumor in the study done by Dr. Aneesha Asok Kumar<sup>2</sup>, and was present in minor salivary glands, which was similar to the observations done in the present study and also that by Bhavani et al<sup>16</sup> and Rewusuwan et al<sup>7</sup>.

Oncocytoma and Basal cell adenoma each were noted in 3% of cases. While rare cases like, Schwannoma and Neurofibroma were also noted (2.2% and 1.5% each). In the present study, we also found Acinic cell carcinoma and PLGA in 2.2% cases each. While Epithelial-myoepithelial carcinoma and Lymphoma were also seen in 1.5% cases each. One rare case of Squamous Cell Carcinoma was also found. These reported cases have no or negligible impact on the presented data, as no consistent data were found in the literatures.

#### CONCLUSION:

Our study revealed that benign tumors are more common than malignant tumors in salivary gland. Pleomorphic adenoma is the most common benign tumor and mucoepidermoid carcinoma is the common malignant tumor in this study. Most common age group for salivary gland tumor is between 40-60 years. Among the tumors, female preponderance is seen in all except Warthin tumor. Parotid gland is the commonest site for various tumors, notable exception being adenoid cystic carcinoma, which showed predilection for the minor salivary glands. Salivary gland neoplasms show overlapping features. Proper diagnosis needs consideration of histological findings to differentiate between benign and malignant neoplasms. Hence, Histopathology remains the Gold standard procedure.

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