

# Spectrum of salivary gland diseases: A 24-year single-institution retrospective study

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## Abstract

**Introduction:** Salivary glands are exocrine glands and are classified as major and minor salivary glands. Salivary gland pathologies are classified as neoplastic and non-neoplastic. The neoplasms of salivary glands can be benign or malignant.

**Aim:** The aim of the study was to describe the frequency of various salivary gland diseases reported in our institution from 1997 to 2021.

**Methodology:** This was a 24-year retrospective study of salivary gland lesions processed and reported by the Department of Oral Pathology and Microbiology. Data regarding age, gender, site, and diagnosis were obtained and studied.

**Results:** Amongst the total 5928 biopsied cases reported, 6% were salivary gland pathologies. Two hundred sixty-six were non-neoplastic lesions and 81 were neoplastic. The most common non-neoplastic lesion was mucous extravasation cyst. The most common neoplastic lesion was pleomorphic adenoma.

Among the total number of mucous extravasation cyst reported, there was male predilection and the peak age of incidence was between 11 and 20 years. The most common site of occurrence was the lower lip.

There was a higher number of benign neoplasms than malignant. The most common benign salivary gland neoplasia was pleomorphic adenoma with male predilection. The peak age of occurrence was the third decade. Two cases of Warthin tumour and one case each of lipoma of the parotid gland and sialadenoma papilliferum were reported.

The most common malignant salivary gland neoplasia was mucoepidermoid carcinoma with female predilection. The peak age of occurrence was the fourth decade. The most commonly involved site was the minor salivary glands of the palate. Two cases each of polymorphous adenocarcinoma and carcinoma ex pleomorphic adenoma were reported. There was one case of acinic cell carcinoma and adenocarcinoma not otherwise specified (NOS) reported.

**Conclusion:** The frequency of occurrence of salivary gland lesions in the last 24 years of this institution is almost similar to that stated in other published studies.

**Keywords:** Adenocarcinoma, carcinoma ex pleomorphic adenoma, lipoma, mucocele, mucous extravasation cyst, pleomorphic adenoma, salivary gland neoplasm, salivary gland, sialadenoma papilliferum

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**Submitted:** 05-Sep-2022, **Revised:** 17-Oct-2022, **Accepted:** 16-Dec-2022, **Published:** 21-Mar-2023

### Access this article online

#### Quick Response Code:



#### Website:

www.jomfp.in

#### DOI:

10.4103/jomfp.jomfp\_371\_22

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**How to cite this article:** Sabarinath B, Murali P, Vijayashree RJ, Sivapathasundharam B, Kavitha B. Spectrum of salivary gland diseases: A 24-year single-institution retrospective study. *J Oral Maxillofac Pathol* 2023;27:238.

## INTRODUCTION

Salivary glands are exocrine glands. They are classified as major and minor salivary glands. The three pairs of major salivary glands are the parotid, submandibular, and sublingual salivary glands. They are present on the extra-oral location. Around 600 to 1000 minor salivary glands are present and are situated in the mucosa and submucosa of the oral cavity and the oropharynx.<sup>[1]</sup> The salivary glands synthesize and secrete saliva. Saliva helps in digestion, keeps the oral cavity wet and moist, possesses antimicrobial properties mediated by the action of lysozymes, immunoglobulins, lactoferrin, and also contains several signalling molecules.<sup>[2]</sup>

The clinical manifestations of salivary gland diseases are implicated to their morphological and functional impairments. However, the aetiopathogenesis can vary. Salivary gland pathologies are thus classified as neoplastic and non-neoplastic. The neoplasms of salivary glands can be benign or malignant. According to the 2017 World Health Organization (WHO) classification of salivary gland tumours, there are 33 different entities of salivary gland neoplasms.<sup>[3]</sup> Non-neoplastic lesions include inflammatory, autoimmune, infection, traumatic, obstructive, drug-induced and metabolic lesions.<sup>[1]</sup> Among the salivary gland neoplasms, about 80% are benign. Malignant salivary gland neoplasms form less than 8% of all head and neck malignancies.<sup>[3,4]</sup>

## AIM

The aim of the study was to describe the frequency of various salivary gland diseases reported in Meenakshi Ammal Dental College and Hospital, Chennai, India, from 1997 to 2021.

## OBJECTIVES

1. To describe the total number of salivary gland diseases reported during the study period.
2. To describe the incidence of neoplastic and non-neoplastic diseases reported during the study period.

## METHODOLOGY

This was a 24-year retrospective study of salivary gland lesions reported by the Department of Oral Pathology and Microbiology, Meenakshi Ammal Dental College and Hospital, Chennai, India. Those lesions that did not require biopsy were not included in this study. All the specimens were processed for routine haematoxylin and eosin (H&E)

staining. Special stains were used wherever required. Data regarding age, gender, site, and diagnosis were obtained from the department archives.

## RESULTS

The total number of biopsied cases reported in the Department of Oral Pathology and Microbiology from 1997 to 2021 was 5928. Amongst this, a total of 347 cases (6%) were salivary gland pathologies that necessitated biopsy. A wide spectrum of salivary gland diseases were reported [Table 1], of which 266 were non-neoplastic lesions and 81 were neoplastic. The most common non-neoplastic lesion was mucous extravasation cyst ( $n = 232$ ). The most common neoplastic lesion was pleomorphic adenoma ( $n = 44$ ).

Among the total number of mucous extravasation cysts reported, 140 were from male and 92 were from female patients. The peak age of incidence of mucocele was between 11 and 20 years ( $n = 80$ ), followed by 21 and 30 years ( $n = 74$ ). Very few were reported from adult patients above 60 years of age ( $n = 4$ ) [Table 2]. The most common site of occurrence of mucocele was the lower lip ( $n = 174$ ), followed by floor of the mouth ( $n = 20$ ) [Table 3].

**Table 1: Number of each salivary gland pathology diagnosed**

Diagnosis	Frequency
Mucous extravasation cyst	232
Mucous retention cyst	7
Pleomorphic adenoma	44
Mucoepidermoid carcinoma	16
Chronic sialadenitis	13
Adenoid cystic carcinoma	11
Sialolithiasis	5
Sjogren's syndrome	4
Necrotizing sialometaplasia	3
Polymorphous adenocarcinoma	2
Carcinoma ex pleomorphic adenoma	2
Warthin tumour	2
Lipoma of parotid gland	1
Adenocarcinoma	1
Acinic cell carcinoma	1
Hyperplasia of minor salivary glands	1
Hyperplasia of submandibular salivary gland	1
Sialadenoma papilliferum	1

**Table 2: Age of occurrence of mucous extravasation cyst**

Age (years)	Mucous extravasation cyst
0-10	31
11-20	80
21-30	74
31-40	33
41-50	8
51-60	3
61-70	2
71-80	1
Total	232

Among the neoplastic lesions, there were more benign neoplasms ( $n = 48$ ) than malignant ( $n = 33$ ).

The most common benign salivary gland neoplasia was pleomorphic adenoma ( $n = 44$ ). Twenty-nine cases were from male and 15 from female patients. The peak age of occurrence was the third decade with 15 cases reported. The most common gland involved was the parotid gland with 30 cases reported. The second most common was the minor salivary glands of the palate with 14 cases. Two cases of Warthin tumour and one case each of lipoma of parotid gland and sialadenoma papilliferum were reported.

The most common malignant salivary gland neoplasia was mucoepidermoid carcinoma ( $n = 16$ ). Women were most commonly involved ( $n = 10$ ). The peak age of occurrence was the fourth decade ( $n = 9$ ) [Table 4]. The most commonly involved site was the minor salivary glands of the palate ( $n = 12$ ) [Chart 1].

The second most common malignant salivary gland neoplasm was adenoid cystic carcinoma ( $n = 11$ ). Two cases each of polymorphous adenocarcinoma and carcinoma ex pleomorphic adenoma were reported. There was one case of acinic cell carcinoma and adenocarcinoma not otherwise specified (NOS) reported.

**DISCUSSION**

The salivary gland diseases are not very common and many salivary gland neoplasms are relatively difficult to diagnose due to their morphological and histopathological

appearances. Most of the salivary gland neoplasms present as painless growing mass.<sup>[5]</sup> Salivary gland diseases can be broadly classified as neoplastic and non-neoplastic. Very few studies on the incidence of salivary gland pathology have been published. Usually, non-neoplastic lesions of the salivary glands are more, compared to the neoplasms. Therefore, the study aimed to describe the frequency of the various salivary gland pathologies reported to our institution in the 24-year period.

The total percentage of salivary gland diseases reported were only 6% of all the biopsied cases reported, similar to the study done by Colonia-García *et al.*<sup>[6]</sup> (7.4%). Valuable comparisons with other studies could not be made as they do not mention the percentage of salivary gland diseases reported.

The present study showed predominance of non-neoplastic lesions, as reported in the literature. Since the institute is not a referral/primary cancer centre, the neoplastic lesions are not reported in increased numbers.

The majority of the cases were mucous extravasation cysts, among all salivary gland pathologies, including neoplastic and non-neoplastic. Mucocele is the pooling of mucous within the connective tissue [Figure 1]. Based on the etiopathogenesis and histopathology, it may be either mucous retention cyst or extravasation cyst. In mucous extravasation cyst, the cavity is not lined by epithelium, whereas the mucous retention cyst is a true cyst lined by epithelium.<sup>[1]</sup> Since the trauma to the minor salivary glands due to various reasons, such as sharp teeth and lip biting, are very common, increased number of mucous extravasation cysts are reported.<sup>[7]</sup>

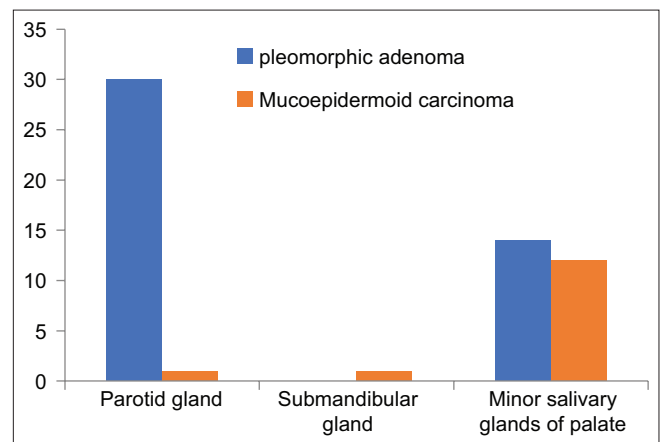
The present study showed slight male predominance, with peak age of occurrence in the second decade and followed

**Table 3: Site of occurrence of mucous extravasation cyst**

Site	Frequency (n)	Percentage
Lower lip	174	75
Floor of the mouth	20	8.6
Buccal mucosa	14	6
Upper lip	11	4.7
Tongue	9	3.9
Palate	3	1
Submandibular gland	1	0.4
Total	232	

**Table 4: Age of occurrence of pleomorphic adenoma and mucoepidermoid carcinoma**

Age	Pleomorphic adenoma	Mucoepidermoid carcinoma
0-10	0	0
11-20	4	0
21-30	15	4
31-40	4	9
41-50	14	1
51-60	5	0
61-70	2	1
71-80	0	1
Total	44	16



**Chart 1: Site of occurrence of pleomorphic adenoma and mucoepidermoid carcinoma**

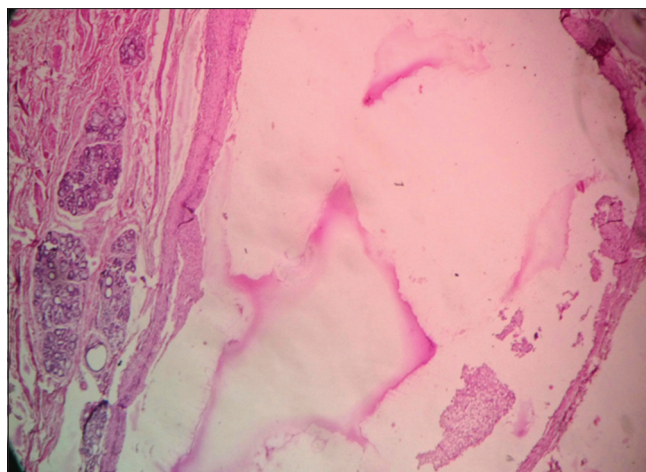
by the third decade for mucous extravasation cyst. Also, there was a predilection for the lower lip. These findings are consistent with many other published studies.<sup>[6-12]</sup>

The psychological stress that a person has during their adolescence, along with dental mal-alignment can be the aetiology for habitual lip biting, resulting in increased incidence of mucoceles in the second decade.<sup>[7]</sup> Various other reasons like sharp tooth, lip piercing, and ill-fitting prosthesis may result in trauma, which in turn increases the incidence of mucoceles in the lower lip.<sup>[7,13]</sup>

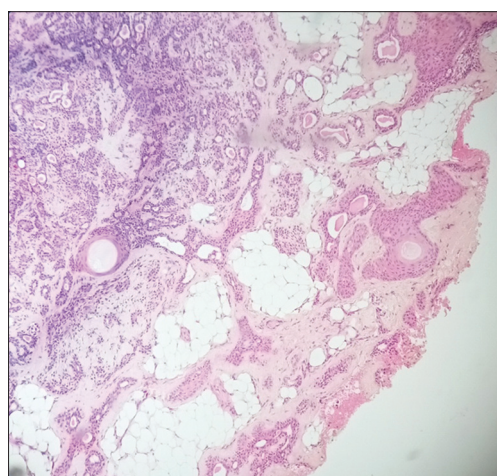
Regarding the neoplastic lesions of the salivary glands, the present study showed predominance for benign neoplasms. Pleomorphic adenoma was the most common neoplastic lesion in the present study. The reason for pleomorphic adenoma being the most common benign salivary gland neoplasia is elusive. The neoplasm showed an increased male predilection, with increased age of occurrence in the third and fifth decades and the parotid gland being the most common site involved. These findings are consistent with many other studies published across the world.<sup>[14,15]</sup>

Pleomorphic adenoma is the most common salivary gland neoplasia of both the major and the minor salivary glands. The tumour is composed of epithelial cells (luminal) and myoepithelial cells (abluminal) in varying proportions within the connective tissue stroma [Figure 2]. Though the tumour is called a mixed tumour, owing to the assumption that it is derived from more than one germ layer, immunohistochemical studies have shown it to be a pure epithelial tumour. In spite of the tumour being called pleomorphic, there is actually no true pleomorphism of the tumour cells. Pleomorphic adenoma has an increased rate of recurrence. Inadequate excision, tumour spillage, pseudopodia, and satellite nodules are some of the reasons for their increased recurrence rate.<sup>[1]</sup>

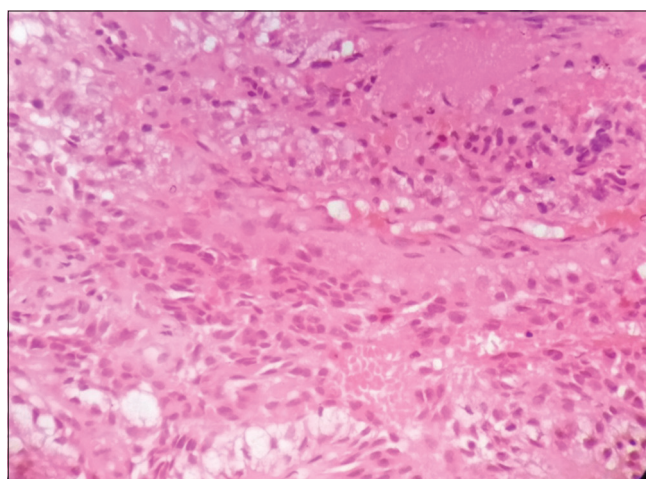
In the present study, the most common malignant neoplasia was mucoepidermoid carcinoma [Figure 3], followed by adenoid cystic carcinoma [Figure 4]. Mucoepidermoid carcinoma showed female predilection with increased occurrence in the palatal minor salivary glands. These findings are similar to numerous published studies.<sup>[14-18]</sup> Mucoepidermoid carcinoma is the most common malignant salivary gland neoplasm in most published studies. It can be histopathologically graded as high, low, or intermediate based on certain histological features such as neural invasion, lymphovascular invasion, bone invasion, mitosis, and intracystic component.<sup>[5]</sup> Usually, tumours arising from the smaller salivary gland are more likely to be malignant;



**Figure 1:** Mucous retention cyst (10x magnification)

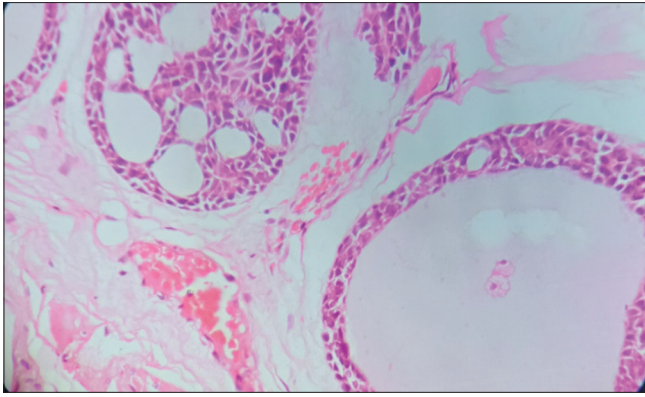


**Figure 2:** Pleomorphic adenoma (10x magnification) showing the presence of epithelial in acinar and tubular pattern in myxoid stroma. Also, note the presence of adipose tissue



**Figure 3:** Mucoepidermoid carcinoma (40 x magnification) showing the presence of mucous and epidermoid cells

for example, almost 90% of sublingual salivary gland neoplasms are malignant.<sup>[5]</sup>



**Figure 4:** Adenoid cystic carcinoma (10× magnification). Tumour cells arranged in Swiss cheese pattern

However, some studies differ from the present study in certain features. The probable reason could be the variation in the geographical distribution, race, and ethnicity between the lesions.

Only one case each of the rare benign mesenchymal salivary gland neoplasia, lipoma of the parotid gland, and sialadenoma papilliferum was reported in the 24 years. Mesenchymal neoplasms of salivary gland origin account for only 1.9% to 5% of the major salivary gland neoplasms. These include haemangioma, lipoma, neurogenic origin, solitary fibrous tumour, liposarcoma, leiomyosarcoma, and synovial sarcoma.<sup>[19]</sup> Lipoma is a common benign soft tissue tumour; however, it is a very rare entity of the parotid gland. Histologically, the tumour consists of well encapsulated mass of mature adipocytes with no cellular atypia. There are two variants of parotid lipoma: periparotid and intraparotid.<sup>[1]</sup>

Sialadenoma papilliferum is a very rare benign salivary gland neoplasm that is presented most commonly on the hard palate. Histopathologically, the neoplasm shows the presence of epithelial component with papillary growth and an adjacent contiguous salivary gland ductal proliferation that is unencapsulated.<sup>[20,21]</sup>

Two rare types of salivary gland malignancies—clear cell adenocarcinoma and adenocarcinoma NOS—were also reported with one case each. Clear cell adenocarcinoma most commonly occurs in minor salivary glands. Histologically, the disease contains sheets, islands, or cords of monomorphic clear cells with eccentrically placed nuclei and small nucleoli, and separated by fibrous septa of varying thickness. The cells exhibit nuclear pleomorphism and rarely mitotic figures. The neoplasia has a tendency to invade adjacent tissues.<sup>[22]</sup>

Adenocarcinoma NOS is defined as a salivary gland malignancy with glandular or ductal differentiation that

does not show the histopathological features characteristic of other malignant epithelial salivary gland neoplasms.<sup>[23]</sup> Based on the degree of differentiation, they are graded as low grade, moderate grade, and high grade.<sup>[23]</sup>

The molecular aspects of salivary gland neoplasms are now widely studied. Various genomic alterations such as gene mutations and fusions are identified. Overexpression of various oncogenes, such as increased levels of human epidermal growth factor (HER2), c-KIT tyrosine kinase receptor, and epidermal growth factor receptor (EGFR). More than 50% of mucoepidermoid carcinomas show mastermind-like transcriptional coactivator-2 (*MAML2*) gene fusions (mostly through a recurrent t (11; 19) (q21; p13) translocation resulting in (CREB Regulated Transcription coactivator-1) *CRTC1-MAML2* fusion; less commonly through t (11; 15) (q21; q26) resulting in *CRTC3-MAML2* fusion). Few cases also show EWS RNA binding protein 1–POU domain, class 5 transcription factor 1 (*EWSR1-POU5F1*) gene fusions. Similarly, 60% of adenoid cystic carcinomas show t (6; 9) (q22-23; p23-24) translocation resulting in myeloblastostosis gene–neurofibromatosis 1 gene (*MYB-NF1B*) gene fusion. Genetic abnormalities involving pleomorphic adenoma gene 1 (*PLAG1*) and high mobility group AT-Hook 2 (*HMG2*) are seen in both pleomorphic adenoma and carcinoma ex pleomorphic adenoma cases.<sup>[24]</sup>

The derived results were consistent with other single-institution studies. Retrospective analysis of salivary gland pathologies at the global level is needed for studying these lesions in a larger scale.

## CONCLUSION

Salivary gland pathologies form less than 7% of all biopsied cases. As per this study, the non-neoplastic lesions, particularly the mucous extravasation cyst, are the most common salivary gland pathology, which is followed by the benign neoplasm pleomorphic adenoma. Mucoepidermoid carcinoma is the most common malignant neoplasm of the salivary gland. It is also the third most common salivary gland lesion reported. The frequency of occurrence of the salivary gland lesions in the last 24 years of this institution is almost similar to the other published studies.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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