

Cytomorphological study of major salivary gland lesions with histopathological correlation

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Abstract

Background: Fine needle aspiration cytology (FNAC) is a very useful test for evaluating the salivary gland lesions. FNAC is useful to differentiate between benign and malignant and non-neoplastic lesions. A preoperative diagnosis will guide the surgeon to plan a surgery according to the nature of the tumor and proper management of the patient. FNAC is the most preferred method to biopsy because incisional biopsy is associated with the risk of contamination and infections.

Methods: A prospective observational study was done in the pathology department of a medical college after obtaining approval from the institutional ethical committee. FNAC from all patients with salivary gland lesions and surgically resected specimens sent for histopathology.

Results: A total of 173 cases were studied, of which 84 (48.55%) cases were reported as non-neoplastic lesions and 89 (51.44%) cases were reported as neoplastic lesions on FNAC. Among these, 71 (79.77%) cases were benign and 18 (20.22%) cases were malignant. Among non-neoplastic lesions, sialadenitis was the most common lesion. Pleomorphic adenoma and mucoepidermoid carcinoma were the most common benign and malignant lesions, respectively. Parotid gland was the most frequently involved gland. Histopathology correlation was seen in 66 cases that underwent surgery.

Conclusion: FNAC is a safe, reliable, and accurate method of diagnosis of salivary gland lesions. FNAC provides effective information about salivary gland lesions and prevents unnecessary surgery of non-neoplastic lesions, and it can establish the diagnosis of the major salivary gland neoplastic lesions and can be recommended as an adjunct to histopathology.

Keywords: Fine needle aspiration cytology; salivary gland neoplasm; pleomorphic adenoma.

Introduction:

A pre-operative diagnosis by this simple, rapid, and less complicated procedure will guide the surgeon to plan a surgery according to the nature of the tumor and about proper management of the patient^[1,2]. In the meta-analysis, it was found that neoplastic tumors have a sensitivity of 96% and a specificity of 98%, while benign and malignant tumors have 79% and 96%, respectively^[3,4]. The present study was undertaken to analyze the cytomorphology of major salivary gland lesions and to study the prevalence of non-neoplastic and neoplastic lesions along with the correlation of cytological and histopathological findings. In clinical practice, the prompt and accurate diagnosis of salivary gland lesions through FNAC, followed by histopathological confirmation, can significantly influence treatment decisions. Benign

lesions often require conservative management or simple excision, while malignant tumors may necessitate more aggressive surgical interventions, radiotherapy, or chemotherapy. Thus, accurate cytological diagnosis can lead to more personalized treatment plans, reducing unnecessary surgical interventions and improving patient outcomes. This study aims to evaluate the diagnostic accuracy and efficiency of FNAC.

Material and methods:

This is a prospective observational study that was performed in a single institute from May 2020 to June 2023 in the department of pathology. A total of 173 cases were studied. Prior informed consent was taken from all patients coming for FNAC of salivary gland lesions. All patients with salivary gland masses presented in the pathology OPD of our medical

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institute were included in the study. A detailed and relevant clinical history and local examination were performed on all the patients with salivary gland masses. After taking informed consent and clinical history from the patients, the swelling was palpated, fixed, and a fine needle aspiration of salivary gland lesions was performed under aseptic conditions with a 22-24 gauge needle with a 10 cc syringe. Aspiration material was taken from different sites of the salivary gland lesions. All alcohol-fixed wet smears are stained with hematoxylin-eosin (H&E) and papanicolaou stain, and all air-dried smears are stained with May-grunwald giemsa and Leishman stain. All included patients underwent histopathological examination of the specimens, which were fixed in 10% formalin and recorded. The gross measurements, size, encapsulation, cut surface, colour, consistency, contents, cystic spaces, hemorrhage, and necrotic areas were examined and then grossed, routinely processed, and cut. The slides were stained with hematoxylin and eosin stain. Smears were examined under light microscopy and diagnosed as per standards and classified with associated pathology if any were also recorded.

Results:

In our study, there were a total of 173 cases of major salivary gland lesions studied. The age of the patients ranged from 7 to 76 years, with a mean age of 39 years (Figure 1).

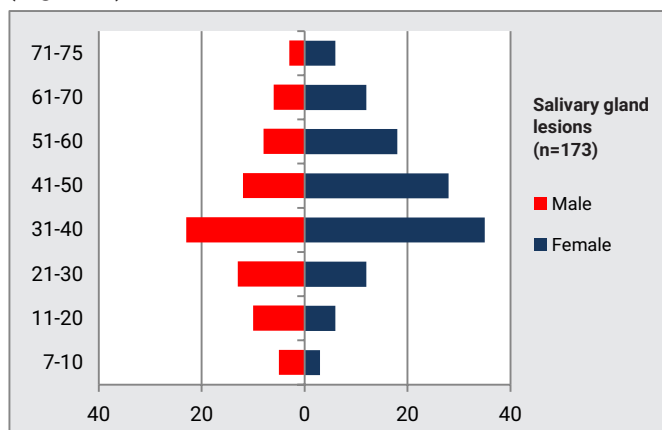


Figure 1. Age distribution of salivary gland lesions.

60 (34.6%) patients were male and 113 (65.3%) were females, with a male-to-female ratio of 1:1.8 (Figure 2).

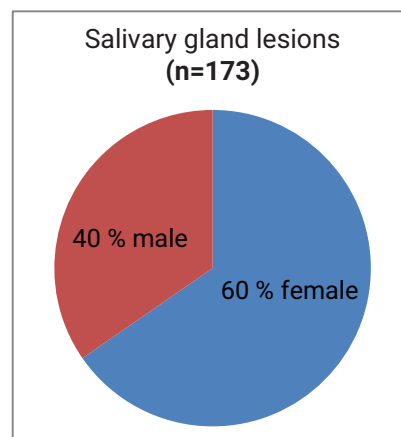


Figure 2. Gender distribution of salivary gland lesions.

Out of 173 cases, 83 (47.97%) cases were diagnosed as non-neoplastic lesions, and 90 (52.0%) cases were diagnosed as neoplastic lesions on fine needle aspiration cytology (Figure 3).

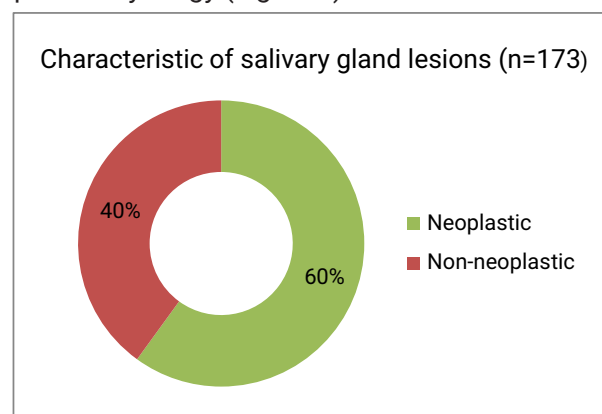


Figure 3. Categorization of neoplastic and non-neoplastic salivary gland lesions.

Out of 90 neoplastic cases, 71 cases were diagnosed as benign neoplastic lesions, and 19 cases were diagnosed as malignant neoplastic lesions on a cytological basis (Figure 4).

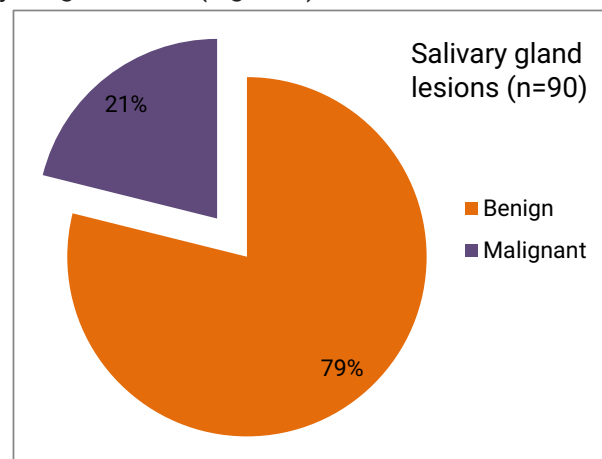
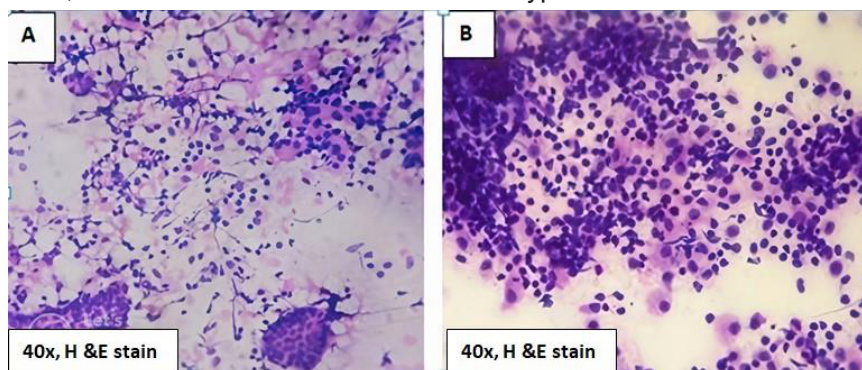


Figure 4. Distribution of benign and malignant salivary gland lesions.

Non- neoplastic lesions

In non-neoplastic lesions, sialadenitis was the most common type of lesion.



(Figure 5-A) - Chronic sialadenitis

(Figure 5-B) - Lymphoepithelial cyst

Table 1. Site distribution of salivary gland lesions.

Type of Salivary Gland Lesion	Parotid	Submandibular	Submental	Total Number of Cases
Non neoplastic cysts	08	4	0	12
Sialadenosis	14	4	0	18
Sialadenitis	24	14	2	40
Lymphoepithelial cyst	06	3	4	13
Pleomorphic adenoma	40	12	4	56
Warthin's tumor	06	03	0	09
Schwannoma	01	0	0	01
Oncocytoma	04	01	0	05
Mucoepidermoid carcinoma	04	01	0	05
Adenoid cystic carcinoma	02	0	0	02
Carcinoma ex pleomorphic adenoma	02	0	0	02
Low grade salivary gland carcinoma	03	01	0	04
Acinic cell carcinoma	02	01	0	03
Metastasis/ primary malignant tumor	02	01	0	03
Total	118	45	10	173

In our study, we observed that the parotid gland was the most frequently involved salivary gland in 118 (67.6%) cases, and the second most commonly involved was the submandibular gland, seen in 45 (26.5%) cases, followed by the submental gland, seen in 10 (5.7%) cases (Table 1).

Table 2. Cytological diagnosis of non-neoplastic salivary gland lesions

Cytological diagnosis	Frequency	percentage
Sialadenosis	18	21.68%
Sialadenitis	40	48.19%
Lymphoepithelial cysts	13	15.66%
Non neoplastic cysts	12	14.45%
Total	83	100%

In non-neoplastic lesions, sialadenitis was the most common type of lesion. Among these acute sialadenitis was 18 (21.68%) cases, and chronic sialadenitis was 22 (26.50%) cases. Sialadenosis had 18 (21.68%)

cases. Lymphoepithelial cyst in 13 (15.66%) cases and non-neoplastic cysts in 12 (14.5%) cases (Table 2).

Neoplastic lesions

Out of 90 cases of neoplastic lesions, 71 (78.88%) cases were reported as benign, and 19 (21.11%) cases were reported as malignant on the basis of fine needle aspiration cytology. Among benign neoplastic lesions, pleomorphic adenoma was the most common lesion.

Table 3. Cytological diagnosis of benign neoplastic lesions

Cytological diagnosis	Frequency	Percentage
Pleomorphic adenoma	56	78.87%
Warthin's tumor	9	12.67%
Oncocytoma	5	7.04%
Schwannoma	1	1.40%
Total	71	100%

Out of 71 cases of benign neoplastic lesions, 56 (78.87%) cases were reported as pleomorphic adenoma on a cytological basis, of which parotid gland 40 cases (56.3%) were most frequently involved, followed by submandibular 12 (16.9%) cases and submental 4 cases (5.6%) glands. Among benign neoplastic lesions, warthin's tumor was reported in 9 (12.67%) cases, oncocytoma in 5 (7.04%) cases, and schwannoma in 1 (1.40%) cases (Table 3).

Malignant neoplasms

A total of 19 cases was reported as malignant neoplasms, in which mucoepidermoid carcinoma was the most common lesion and the second most common lesion was low-grade carcinoma of the salivary gland, of which parotid is exclusively involved.

Table 4. Cytological diagnosis of malignant salivary gland lesions.

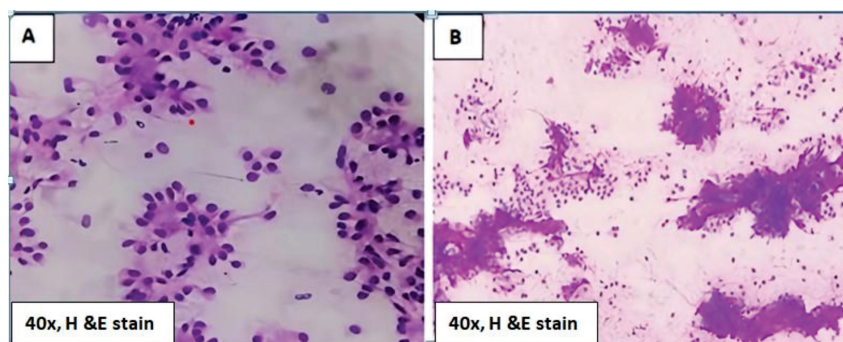
Cytological diagnosis	Frequency	Percentage
Mucoepidermoid carcinoma	5	26.31%
Acinic cell carcinoma	3	15.78%
Adenoid cystic carcinoma	2	10.52%
Carcinoma ex pleomorphic adenoma	2	10.52%
Low grade salivary gland tumor	4	21.05%
Metastatic malignancy	3	15.78%
Total	19	100%

Mucoepidermoid carcinoma was reported in 5 (26.3%) cases, of which parotid gland involvement was most commonly present in 4 (80%) cases. Low-grade carcinoma of the salivary gland was reported in 4 (21.05%) cases, of which parotid gland 3 (75%) cases were most frequently involved. Acinic cell carcinoma and metastasis/primary malignant tumors were reported in 3 (15.7%) cases each, of which 2 (66.6%) cases each in parotid and 1 (33.3%) case each in the submandibular gland. Adenoid cystic carcinoma and carcinoma ex pleomorphic adenoma were 2 (10.5%) cases each (Table 4).

Discussion:

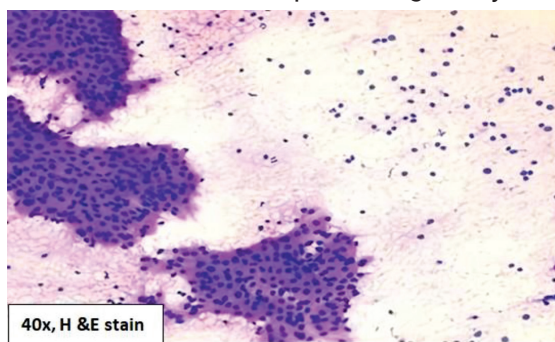
The FNAC procedure is found to be a simple, rapid, and cost-effective diagnostic tool for assessing various salivary gland lesions^[5]. Salivary gland tumors exhibit a diverse group of benign and malignant tumors, which showed a multifaceted clinical scenario and different morphological architectures with unpredictable prognostic status^[6]. Salivary gland swellings, mostly parotid and submandibular gland, are readily visible and create havoc among patients. Because of the easy accessibility of the lesion and superficial location of these lesions, FNAC diagnostic tools provide a

convenient way to obtain a tissue-based diagnosis and therefore become a diagnostic test of choice^[7]. Although FNAC is a minimally invasive technique that provides an important role in the diagnosis and management of patients with salivary gland lesions^[8]. Preoperative cytological diagnosis and categorization of benign and malignant lesions will guide the surgeons to select an appropriate surgical procedure^[9]. In the present study, a total of 173 cases underwent FNAC procedures for various salivary gland lesions. The lesions were categorized as neoplastic and non-neoplastic based on the cytological diagnosis. The cytological diagnosis was correlated with the histopathological diagnosis, which was available in 40 (23.1%) of cases. In the present study, the age range was from 8 to 70 years, with a mean age of 39 years. A slight female preponderance was observed in our study with a male: female ratio of 1:1.8, which was similar to the few other studies^[10-12]. A male predominance was seen in malignant tumors of the salivary gland in our study, which supports the findings of previous studies done by Dharwadkar et al and Rameeza et al. Parotid gland was the most commonly involved site, followed by submandibular gland and submental gland in our study as well as in previous studies done by Todase v et al^[13], Sengupta et al^[14], Verma et al^[15], and Theresa et al^[16]. There was a slightly higher incidence of non-neoplastic lesions in the parotid gland than neoplastic lesions. Out of 173 cases, 83 (47.9%) cases were diagnosed as non-neoplastic lesions, and 90 (52.0%) cases were diagnosed as neoplastic lesions on fine needle aspiration cytology. The cytological diagnosis revealed a slightly higher incidence of neoplastic lesions, 90 cases (52%), compared to non-neoplastic lesions, 83 cases (47.9%), these findings were similar to the studies done by Theresa et al and Gore et al^[17]. Das et al^[18] a slightly higher incidence of non-neoplastic lesions compared to neoplastic lesions. Among non-neoplastic lesions, inflammatory lesions were predominant. Among them, chronic sialadenitis was the most common entity; these findings support the findings of previous studies. In the present study, neoplastic lesions were reported in 90 (52.0%) cases; among them, 71 (78.8%) cases were benign neoplastic lesions, and 19 (21.1%) cases were malignant neoplastic lesions. Among benign neoplasms, pleomorphic adenoma was the most frequently involved lesion in our study, with a higher incidence of occurrence in the parotid gland; similar findings were quoted in the other studies^[19-21]. The cytological diagnosis that supports the features of pleomorphic adenoma was ductal epithelial cells in varying proportions, metachromatic chondromyxoid stroma, myoepithelial cells, and extracellular matrix^[22].

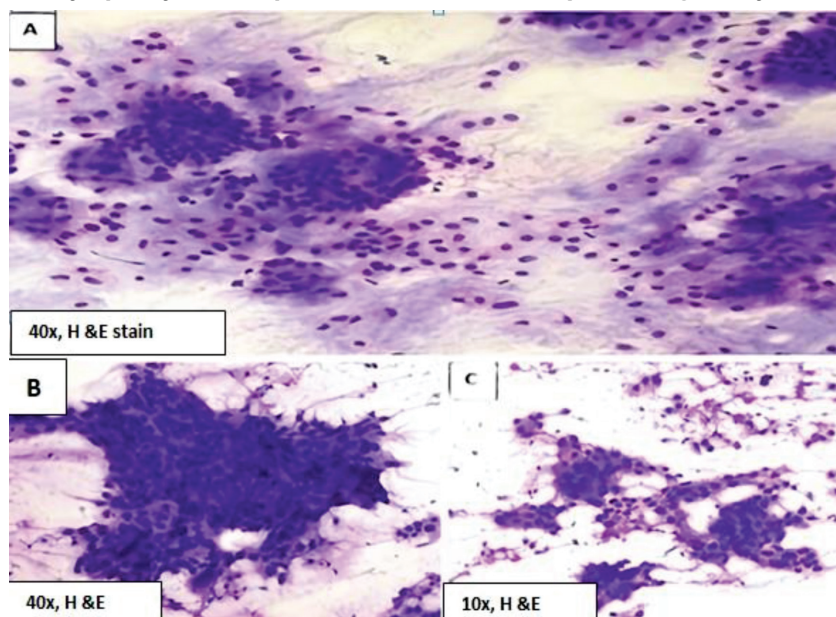


(Figure 6 –A, B)- Pleomorphic adenoma: ductal epithelial cells in varying proportions, metachromatic chondromyxoid stroma, myoepithelial cells, and extracellular matrix.

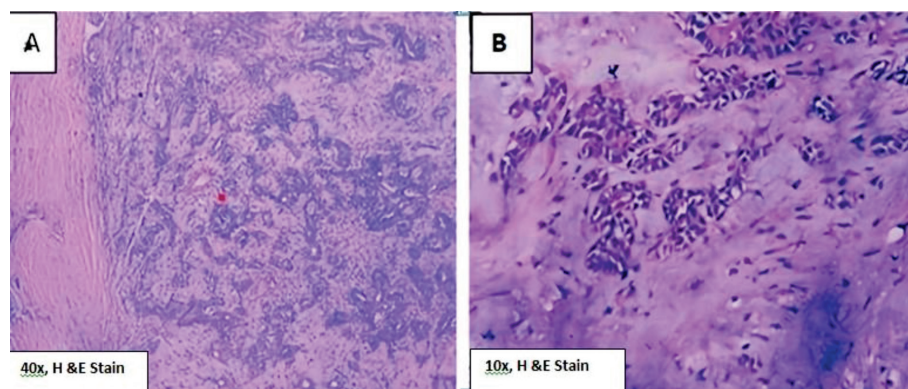
The diagnostic difficulty we will face when there are secondary changes like fibrosis, cystic degeneration, and hyalinization may lead to sampling error. In our study, 4 cases of pleomorphic adenoma showed cystic changes cytologically. A study done by Aruna S et al also quoted cystic change in pleomorphic adenoma. A similar study done by Saldanha et al^[23], quoted adenoid cystic-like areas in the pleomorphic adenoma. After pleomorphic adenoma, the second most common lesion was warthin's tumor among benign neoplastic lesions, with a higher incidence of occurrence in parotid gland. These findings support the findings of other studies. In our study, we observed the diagnostic triad of cohesive, monolayered sheets of uniform oncocytic epithelial cells with small bland nuclei, lymphocytes, and proteinaceous material representing the cystic fluid.



(Figure-7): Warthin's tumor- cohesive, monolayered sheets of uniform oncocytic epithelial cells with small bland nuclei, lymphocytes, and proteinaceous material representing the cystic fluid.



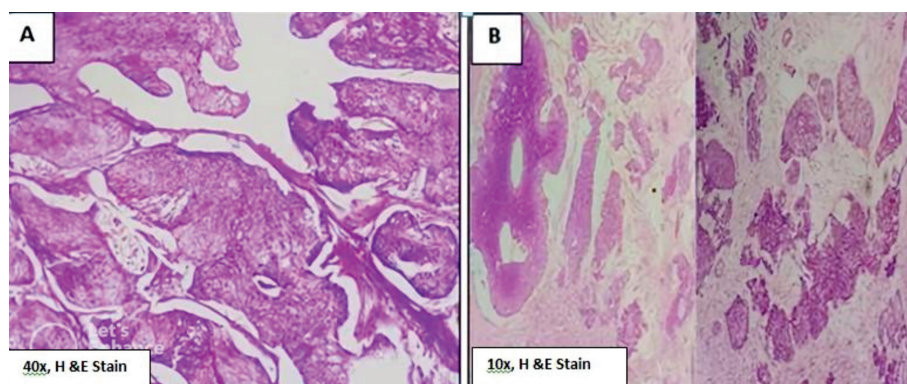
(Figure -8 A, B, and C): Carcinoma ex pleomorphic adenoma- Pleomorphic, hyperchromatic cells, clumped chromatin, high N:C ratio, dense fibrillary metachromatic background.



(Figure 9-A, B): Histopathology of pleomorphic adenoma- Mixture of ductal and myoepithelial cells and extracellular fibrillary matrix.

These findings were in concordance with the previous studies^[24,25]. After Warthin's tumor, the most common lesion among benign neoplasms was oncocytoma. Cytological features that support the oncocytoma were cohesive, multi-layered aggregates of oncocytic cells with small regular nuclei, abundant eosinophilic cytoplasm. These findings are also reported by other studies done by Dey P, Griffith CC et al^[25,26]. Cells with abundant cytoplasm from non-oncocytic tumors can resemble oncocytes in MGG-stained preparations. Cells from acinic cell carcinoma, mucoepidermoid tumors, and adenocarcinoma sometimes also have this appearance. Oncocytomas may be cystic, and their relationship to Warthin's tumors is then uncertain. In general, cyst fluid with debris, oncocytes, and lymphoid cells indicates a Warthin's tumor, especially if the oncocytes lie in flat sheets. Multifocal oncocytic hyperplasia of the salivary gland may suggest oncocytoma in FNAC smears^[27,28]. In our study, one rare case of benign mesenchymal tumor (schwannoma) was reported cytologically in a parotid gland, which was confirmed through histopathology.

Similar to our study, many authors also reported schwannoma in parotid gland cytology and confirmed by histopathology^[29,30]. Spindle cell variants of myoepithelioma can mimic schwannoma. Nuclei of schwannoma are elongated with wavy pointed ends rather than round ends in cells of myoepithelioma. Rows of palisaded nuclei in hypocellular fibrillar stroma (Verocay bodies) may also be seen. In case of difficulty, a panel of immunocytochemistry, particularly myoepithelial markers, may be helpful. A total of 19 cases of malignant tumors are reported cytologically, and 14 (73.68%) cases were confirmed by histopathological examination. In the present study, mucoepidermoid carcinoma was the most frequently involved malignant tumor, similar results are obtained by the studies done by Omhare et al, Rajdeo et al, Desai et al^[31], Mukundapai et al^[32], Devi et al^[33]. Various studies reported the characteristic cytological features of mucoepidermoid carcinoma, mainly having three types of cells: (1) squamoid cells, (2) intermediate cells, and (3) mucus secreting cells



(Figure 10-A): Histopathology of mucoepidermoid carcinoma, mainly having three types of cells: (1) squamoid cells, (2) intermediate cells, and (3) mucus secreting cells. (Figure 10-B) : Histopathology of basaloid cells with hyperchromatic nuclei and coarse chromatin adhering to large hyaline stromal globules.

The background of the tumor is dirty with mucus and debris. The squamoid or epidermoid cells are polygonal with orangeophilic cytoplasm in papanicolaou stain. The intermediate cells are smaller, columnar to polygonal,

and have enlarged hyperchromatic nuclei with a high N:C ratio. The mucus-secreting cells are round with abundant vacuolated cytoplasm. The nuclei are eccentrically placed and indented and often give a signet ring-like appearance. The nuclei of mucus secreting cells show a low N: C ratio and almost no nuclear enlargement. These cells can easily be mistaken for histiocytes. However, the histiocytes exhibit multiple vacuoles, phagocytosed material, and often centrally placed nuclei. In our study, the second most common tumor after mucoepidermoid carcinoma was low grade carcinoma of the salivary gland, which was similar to the studies done by Aruna et al, but few authors reported adenoid cystic carcinoma more frequently involved than mucoepidermoid carcinoma among malignant neoplastic lesions. Acinic cell carcinoma was reported in 3 (15.7%) cases, of which 2 (66.6%) cases in parotid and 1 (33.3%) case in submandibular gland. The features supporting the acinic cell carcinoma were epithelial cell fragments composed of cells with abundant vacuolated cytoplasm and relatively bland nuclei, resembling normal acinar cells, many naked nuclei, scanty, thin fibrovascular stroma and absence of well-formed acinar epithelial structures. These similar findings were also quoted in the studies done by Desai et al and Aruna et al. Adenoid cystic carcinoma and carcinoma ex pleomorphic adenoma were 2 (10.5%) cases each, of which parotid is exclusively involved. Darwadkar et al and Theresa et al also quoted that adenoid cystic carcinoma is exclusively involved in parotid gland. In contrast to this, Aruna et al and Saldanha et al were observed in submandibular and minor salivary glands, respectively. Aruna et al were quoted in her study that adenoid cystic carcinoma was the most frequently involved malignant salivary gland tumor. The cytological features supporting adenoid cystic carcinoma are basaloid cells with hyperchromatic nuclei and coarse chromatin adhering to large hyaline stromal globules. Tumor cells are attached to hyaline globules. The similar cytological features for adenoid cystic carcinoma were also reported by other studies. 2 cases of carcinoma ex pleomorphic adenoma were diagnosed on cytology, which was confirmed by histopathological examination. A male predominance was seen in malignant tumors of the salivary gland in our study, which supports the findings of previous studies done by Rameeza et al^[34]. Cytological diagnosis of metastasis/primary malignant tumor was reported in 3 cases, in which one case was reported as secondary metastatic deposits from squamous cell carcinoma, which was further confirmed by immunohistochemistry. Histopathological correlation is available for 43 cases,

of which 2 cases were diagnosed as lymphoepithelial cysts, 19 cases were diagnosed as pleomorphic adenoma. 2 cases were oncocyoma, 2 cases were warthin's tumor, 4 cases were chronic sialadenitis, and 5 cases were mucoepidermoid carcinoma. Carcinoma ex pleomorphic adenoma and low grade salivary gland carcinoma are 3 cases each. Acinic cell carcinoma and adenoid cystic carcinoma, metastatic carcinoma, and 1 case each.

Conclusion:

FNAC is a safe, reliable, and accurate method of diagnosis of salivary gland lesions. FNAC provides effective information about salivary gland lesions and prevents unnecessary surgery of non-neoplastic lesions, and it can establish the diagnosis of the major salivary gland neoplastic lesions and can be recommended as an adjunct to histopathology.

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