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Original Research Paper

Cytopathological spectrum of salivary gland lesions and classification according to the MILAN System

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ABSTRACT:

Background: Fine needle aspiration cytology (FNAC) is a minimally invasive useful procedure for evaluating lesions of salivary glands all over the world. Diverse morphological patterns in salivary gland lesions make diagnosis challenging at times hence Milan system of reporting was introduced to overcome this difficulty. **Method:** This is a two year retrospective and one year prospective study from January 2021 to January 2024 conducted on 73 cases of salivary gland lesions. Smears were stained with May-Grünwald Giemsa stain, Haematoxylin & Eosin and Papanicolaou stains. Smears of old cases were retrieved from records and were classified according to Milan system of reporting salivary gland cytology. Histopathological comparison was done wherever possible and sensitivity, specificity, positive predictive value, negative predictive value , diagnostic accuracy of FNAC for diagnosing benign and malignant lesions and risk of malignancy for each category was calculated. **Result:** 73 salivary gland lesions were included in the study with most common age group being 31-40 years (23.28%) and male to female ratio of 1.8:1. Acute sialadenitis (13.7%) was the most common non-neoplastic lesion and Pleomorphic adenoma (34.24%) was the most common benign lesion. The commonest malignancy was mucoepidermoid carcinoma (4.11%). Histopathology was received for 19 cases. Statistical analysis revealed the Sensitivity, Specificity, Positive predictive value, Negative predictive value and Diagnostic accuracy as 75% ,100%, 100%, 93.75% and 94.73% respectively. **Conclusion:** FNAC is a simple and cost-effective procedure with high sensitivity ,specificity and accuracy which makes it a reliable diagnostic tool for rapid and early diagnosis of salivary gland lesions.

Keywords : Salivary gland lesions, Pleomorphic adenoma, Mucoepidermoid carcinoma, Milan system .

INTRODUCTION:

Salivary glands are the organs which produce and secrete saliva. These include 3 major (parotid, submandibular, sublingual) and numerous minor glands present throughout mouth and oropharynx.[1] Fine needle aspiration cytology (FNAC) is a minimally invasive useful procedure for evaluating lesions of salivary glands all over the world. It has advantage over incisional biopsy and frozen section due to its low cost, minimum morbidity, rapid turn-around time, high accuracy in diagnosing various non neoplastic and neoplastic lesions and differentiating benign from malignant.[2][3][4] Thus, it helps in eliminating unnecessary surgeries for non-neoplastic lesions and planning further treatment strategy in neoplastic cases.[3] [5] Various studies show the high sensitivity (62 to 97%), specificity (80 to 100%), and accuracy (86 to 98%) of FNAC in salivary gland neoplasms. [6-10] Despite this, diverse morphological patterns and overlapping features of various salivary gland lesions make accurate diagnosis challenging at times hence making the management difficult. To overcome this, American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC) in 2015 proposed a six tiered international classification system called Milan system for reporting of salivary gland cytopathology (MSRSGC). It is a standard and uniform reporting system which provides the diagnostic criteria, risk stratification and plan of management of various categories. This study was conducted to observe the cytomorphological spectrum of various salivary gland lesions in our region and reclassify them according to Milan system.

MATERIAL AND METHODS:

This is a two year retrospective and one year prospective study from January 2021 to January 2024 conducted on all cases of salivary gland lesions coming for Fine needle aspiration to department of pathology, VCSGGIMS &R ,Srinagar, Uttarakhand and included a total of 73 cases. Patients of all ages and gender were included in the study and clinically evaluated by detailed history and examination.

Aspirations were performed from different sites of the salivary gland swelling by the standard procedure using a 23-gauge needle and 10-ml syringe. Air-dried smears were stained with May-Grünwald Giemsa (MGG) stain and alcohol fixed smears were stained with Haematoxylin and Eosin (H&E) and Papanicolaou(Pap) stains. Smears of old cases were retrieved from the records and were again classified according to Milan system of reporting salivary gland cytology into six categories including nondiagnostic, non-neoplastic, atypia of undetermined significance, neoplasm (benign or salivary gland neoplasm of uncertain malignant potential), suspicious for malignancy, and malignant.

We compared the histopathological findings with the FNAC diagnosis wherever possible and calculated sensitivity, specificity, positive predictive value, negative predictive value , diagnostic accuracy of FNAC for diagnosing benign and malignant lesions and risk of malignancy for each category.

OBSERVATION AND RESULTS:

Cytology of total of 73 salivary gland lesions were examined during the study period out of which 64.38% were males, and 35.62% females with a male to female ratio of 1.8:1. Most patients were in their 4thdecade with mean age of 43.15 years **[Table1].** The most frequent site of involvement was the parotid gland (59%) **[Table 2].**

The distribution of the cases as per the MSRSGC category was done. The majority of cases belonged to category II (non-neoplastic-42.46%), followed by category IV a (benign-39.72%) of MILAN. Acute sialadenitis (13.7%) was the most common non-neoplastic lesion and Pleomorphic adenoma (34.24%) was the most common benign lesion. The commonest malignancy was mucoepidermoid carcinoma (4.11%) **[Table2].**

Out of 73 cases, histopathology was received for 19 cases. Among these, 12 cases had the similar diagnosis as in cytology **[Table 3]**. The risk of malignancy for each category was calculated **[Table 3].**

Statistical analysis revealed the Sensitivity, Specificity, Positive predictive value, Negative predictive value and Diagnostic accuracy as 75% ,100%, 100%, 93.75% and 94.73% respectively.

Table 1. Age and gender distribution of the salivary gland lesions

Age group	Number of cases (%)	Male (%)	Female (%)
<10	2 (2.75%)	1 (1.37%)	1 (1.37%)
11-20	8(10.95%)	6 (8.22%)	2(2.75%)
21-30	6 (8.22%)	5 (6.84%)	1(1.37%)
31-40	17 (23.28%)	7 (9.60%)	10(13.69%)
41-50	12 (16.44%)	6 (8.22%)	6(8.22%)
51-60	14 (19.17%)	11(15.07%)	3 (4.10%)
61-70	12 (16.44%)	10 (13.69%)	2(2.75%)
71-80	2 (2.75%)	1 (1.37%)	1(1.37%)
TOTAL	73(100%)	47 (64.38%)	26(35.62%)

Table 2. Distribution of lesions based on salivary gland involved, cytology diagnosis and categorization according to MILAN system (n=73)

Diagnostic categories of MILAN System	FNAC Diagnosis	Parotid (%)	Submandibular (%)	Minor (%)	Total (%)
I.Non-diagnostic(4.11%)	Inadequate cellularity	1	0	0	1 (1.37%)
	Acinar cells only	0	1	0	1 (1.37%)

	Cystic lesion	0	0	1	1 (1.37%)
II.Non-neoplastic (42.46%)	Sialadenosis	4	3	0	7 (9.60%)
	Acute Sialadenitis	4	6	0	10 (13.69%)
	Chronic Sialadenitis	5	2	0	7 (9.60%)
	Suppurative sialadenitis	1	2	0	3 (4.11%)
	Lymphoepithelial cyst	1	0	1	2 (2.74%)
	Retention cyst	0	0	2	2 (2.74%)
III. Atypia of undetermined significance [AUS] (1.37%)	Paucicellular with myxoid stroma	0	1	0	1 (1.37%)
IV. Neoplasm - A. Benign (39.72%)	Pleomorphic adenoma	19	6	0	25 (34.23%)
	Warthin's tumour	3	1	0	4 (5.48%)
IV. Neoplasm – B. Salivary gland neoplasm of uncertain malignant potential (SUMP) (1.37%)	SUMP with basaloid features	0	0	1	1 (1.37%)
V. Suspicious for malignancy (4.11%)	Possibility of Malignant epithelial lesion	2	0	0	2 (2.74%)
	Possibility of Metastatic deposits	1	0	0	1 (1.37%)
VI.Malignant (6.85%)	Mucoepidermoid Carcinoma	0	3	0	3 (4.11%)

	Adenoid cystic carcinoma	2	0	0	2 (2.74%)
	TOTAL	43 (59%)	25 (34%)	5 (7%)	73 (100%)

Table 3. Comparison of FNAC with histopathology (19 cases)

No. of cases in Milan category	FNAC Diagnosis	No. of cases	No. of HPE cases	HPE Finding	Risk of Malignancy (%)
I. 3	Inadequate cellularity	1	1	Pleomorphic adenoma	0 %
	Acinar cells only	1	1	Sialadenosis	
	Cystic lesion	1	0		
II. 31	Sialadenosis	7	0		0%
	Chronic sialadenitis	7	2	Chronic sialadenitis	
	Acute sialadenitis	10	0		
	Suppurative sialadenitis	3	0		
	Lymphoepithelial cyst	2	1	Warthin's tumour	
	Retention cyst	2	1	Retention cyst	
III. 1	Paucicellular with myxoid stroma	1	1	Pleomorphic adenoma	0%
IV a. 29	Pleomorphic adenoma	25	6	Pleomorphic adenoma	0%
	Warthin tumour	4	2	Warthin tumour	
IV b . 1	SUMP with basaloid features	1	1	Adenoid cystic carcinoma	100%

V. 3	Possibility of Malignant epithelial lesion	2	1	Acinic cell carcinoma	66.6%
	Possibility of Metastatic deposits	1	1	Mucoepidermoid carcinoma	
VI. 5	Mucoepidermoid carcinoma	3	1	Mucoepidermoid carcinoma	20%
	Adenoid cystic carcinoma	2	0		

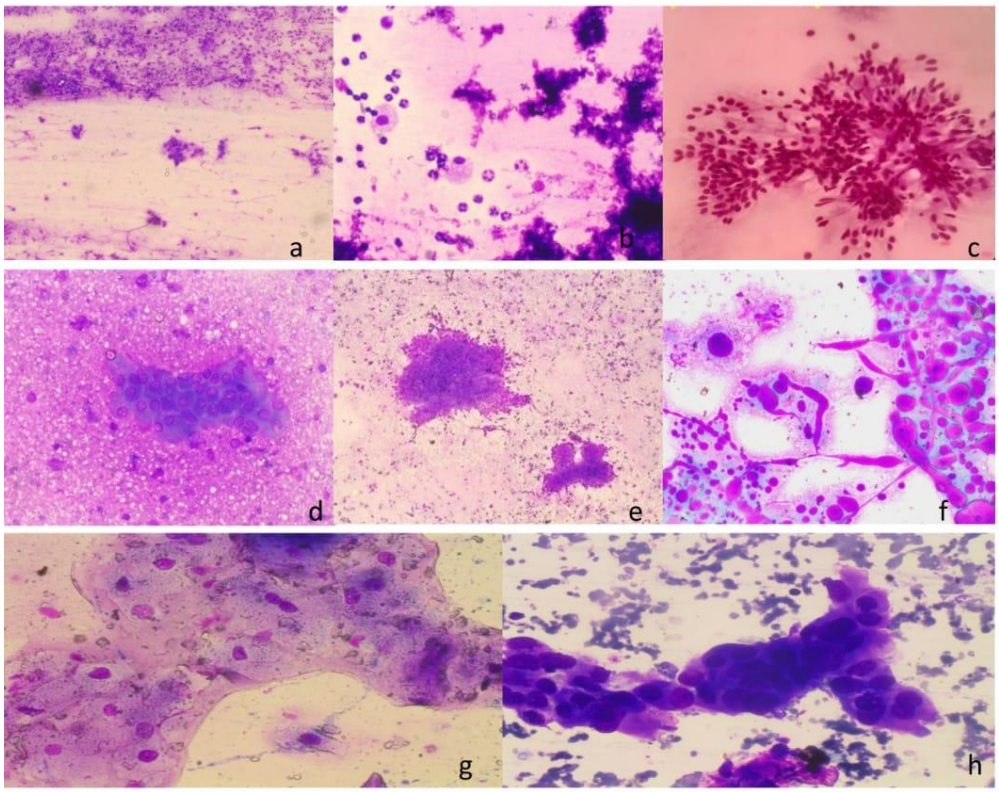

Figure 1: shows cytology of Acute sialadenitis (a) [MGG,10 X], Retention cyst (b) [MGG,40 X], Pleomorphic adenoma (c) [PAP,10 X], Warthin's tumor (d) [MGG,40 X], SUMP with basloid features (e) [MGG,10 X], Adenoid cystic carcinoma (f) [MGG,10 X], Possibility of Malignant epithelial lesion (g) [MGG,40 X], Mucoepidermoid carcinoma (h) [MGG,40 X].

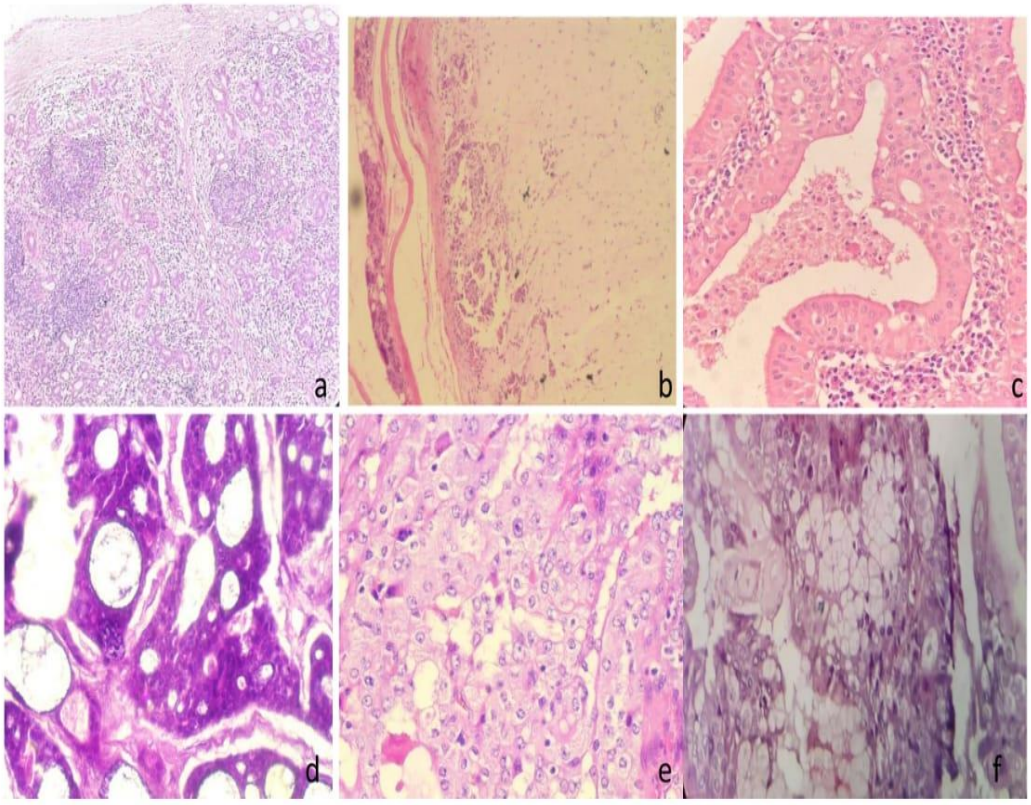

Figure 2: Shows histopathology of Chronic sialadenitis [H and E,10 X], Pleomorphic adenoma (b) [H and E,40 X], Warthin's tumor (c) [H and E,40 X], Adenoid cystic carcinoma (d) [H and E,40 X], Acinic cell carcinoma (e) [H and E,40 X], Mucoepidermoid carcinoma (f) [H and E ,40 X].

DISCUSSION:

Salivary gland lesions can be classified into non-neoplastic, benign and malignant and show wide variation in clinical features and morphological pattern. FNAC aims at distinguishing these lesions and further subtyping wherever possible thus aiding the clinician to plan better management for the patient and avoid unnecessary surgery. Present study includes 73 cases of salivary gland lesions. The mean age in our study was 43.15 years which was almost similar to Rohilla M et al[7] (43.7 years), Naz et al[11] (42 years) and Ghartimagar et al[12] (40.01 years). However in studies by Balmiki Datta et al[16] and Vaidya S et al[17]mean age was 35 years and 38 years respectively. There were 47 males and 26 females with male to female ratio of 1.8:1 similar to Ambedkar et al[13](1.7:1) and Rohilla M et al[7] (1.7:1). However in study by Ghartimagar et al[12] females were affected more than males with male to female ratio of 1:1.36, whereas Naz et al[11] showed equal distribution in both males and females (1:1). Most frequent gland involved in our study was parotid gland (59%) followed by submandibular gland (34%) and minor salivary glands (7%). Ghartimagar et al[12], Vaidya S et al[17], Koirala S et al[18] and Balmiki Datta et al[16] showed similar findings. Literature also shows that Parotid gland is the most common gland affected by salivary gland neoplasms.[19]

According to MSRSGC Category I (Non-diagnostic) consists of lesions which have insufficient cellular material that is less than 60 lesional cells, non-neoplastic acinar cells only, non-mucinous cyst fluid only and poorly prepared slides with artifacts (air drying, obscuring blood, poor staining etc). Our study showed 4.11% non-diagnostic cases which is similar to Naz et al[11] (4.3%). Studies by Tochtermann et al[14], Balmiki Datta et al[16]and Sandhu V K et al[15] showed 8%, 8.7% and 11.7% non-diagnostic cases respectively.

Category II (Non-neoplastic) constitutes highest 42.46% lesions in our study which is similar to studies by Ambedkar et al[13] (45.5%) and Sandhu VK et al[15]. (41.17%). Acute sialadenitis [Fig.1.a] was the commonest among them. This may be because it presents with pain and fever for which patient seeks early medical consultation . Retention cyst was the least common [Fig.1.b].Out of the 7 cases of Chronic sialadenitis on cytology , histopathology was received for 2 cases which had similar diagnosis[Fig.2.a] .

Category III (Atypia of undetermined significance) involves lesions with limited cellular atypia which lacks qualitative and quantitative features for diagnosing a neoplasm. The percentage of this category in our study was 1.37% which is similar to study done by Ambedkar et al[13] (1.29%). FNAC yielded myxoid stroma only which later on in histopathology was diagnosed as Pleomorphic adenoma [Fig.2.b].

The percentage of Category IVa (Benign neoplasm) was 39.72% in our study. Pleomorphic adenoma (34.24%) was the commonest [Fig.1.c] followed by Warthin's tumour (5.48%)[Fig.1.d]. Similar findings were noted in many other studies.[11-13] [15-18] Literature also states that pleomorphic adenoma is the most common benign salivary gland neoplasm followed by Warthin's.[19]

Out of 29 cases in IVa category histopathology was received for 8 cases and all were in concordance with cytopathological findings i.e 6 Pleomorphic adenoma and 2 Warthin's tumour [Fig.2.c].

Category IV b (Salivary gland neoplasm of uncertain malignant potential) includes cases with cytomorphologic features diagnostic of neoplasm but indefinite for a specific tumour type to distinguish it between benign and malignant. In our study we received only 1 case of SUMP on cytology which showed basaloid features[Fig.1.e] which on histopathology was reported as Adenoid cystic carcinoma[Fig.2.d] .

Category V(Suspicious for malignancy) shows features that are highly suggestive of but not unequivocal for malignancy.The percentage of this category in our study was 4.11% while Balmiki Datta et al[16] showed 1.80% and Ambedkar et al[13] showed 1.29% such cases in their study. On cytology 2 cases were reported as Possibility of malignant epithelial lesion [Fig.1.g] and Possibility of metastatic deposits which later on histopathology were reported as Acinic cell carcinoma [Fig.2.e] and Mucoepidermoid carcinoma[Fig.2.f] respectively.

In Category VI,we received 5 Malignant cases (6.85%) on cytopathology with Mucoepidermoid carcinoma [Fig.1.h] being the commonest (3;4.11%). Similar findings were seen in study conducted by Ambedkar et al[12] (3.8%), Koirala S et al[18] (7.46%) and Ghartimagar et al[11] (62.5%). Literature also states Mucoepidermoid carcinoma to be most common salivary gland malignant neoplasm.[19] Out of the 3 cases, histopathology was done for only 1 which showed concordance with FNAC diagnosis. The other malignancy on cytology was Adenoid cystic carcinoma [Fig.1.f] for which no histopathology was received. The risk of malignancy for each category (I,II,III,IVa,IVb,V,VI) in our study was calculated to be 0,0,0,0,100,66.6 and 20 % respectively which showed wide variation from MILAN and studies by Ambedkar et al[13] and Balmiki et al[16]. The reason for this is the very less number of cases received for histopathology during the study period as our hospital was converted into COVID hospital for the region.

The Sensitivity, Specificity, Positive predictive value, Negative predictive value and Diagnostic accuracy in our case was 75% ,100%, 100% , 93.75% and 94.73% respectively which was nearly similar to Rohilla M et al[7] (79.4%,98.3%,96.4%,89.2% and 91.4% respectively), Balmiki Datta et al[16] (75%, 100 %, 100%,95% and 95.65% respectively) and Vaidya S et al[17] (81.82%, 100 %, 100%, 95.9% and 96.55% respectively). The slight variation from other studies may be due to variation in the number of cases.

LIMITATIONS:

Factors affecting final diagnosis such as aspiration site (as in solid cystic tumors), smearing and staining quality. Immunohistochemistry and molecular studies were not available. Histopathology was not available for maximum cases because surgeries were withheld during COVID period.

CONCLUSION:

FNAC is a simple and cost-effective procedure and has high sensitivity ,specificity and accuracy which makes it a reliable diagnostic tool for rapid and early diagnosis of salivary gland lesions, especially for developing countries. However, due to heterogeneity and diversity of these lesions ,a standard and uniform reporting system called Milan system is helpful which provides universal reporting protocol and better understanding of lesion in relation to risk stratification and their clinical management. This also reduces descriptive reports and false positives on FNAC.

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Conflict of interest- None declared

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