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Original Research Article

Implentation of Milans System for Reporting Salivary Gland Cytopathology in Our Institute

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ABSTRACT

Background
Fine needle aspiration cytology of salivary glands (FNAC) has become a most accepted method of evaluating salivary gland tumors preoperatively. It has many pitfalls, to overcome this the Milan System for reporting Salivary gland Cytopathology (MSRGC) was introduced. The Milan System for reporting Salivary gland Cytopathology (MSRGC) represents a standardized, evidence based reporting system for salivary gland lesions. The present study was undertaken to study and categorize various salivary gland lesion according to MSRSGC and do histological correlation.

Methods
Present study is a retrospective study done over a period of four year duration. Cytological slides were retrieved and reviewed and categorised into six categories according to MSRGC. Histopathological correlation was done wherever possible.

Results
A total of 273 cases were studied, males were commonly affected compared to females. Percentage of cases in each category as follows: nondiagnostic-2.93%, Nonneoplastic-58.6%, AUS-0%, benign 34.4%, suspicious of uncertain malignant potential-0.73%, suspicious of malignancy-1.46% and malignant in 1.83% cases. Surgical follow up was available in 85 cases, out of which 96.5% (82 cases) showed concordance and 3 cases showed discordance. Sensitivity, specificity, positive predictive value and negative predictive value of salivary gland lesions with the application of Milan system was 66.7%,100%, 100% and 96.25%. ROM was calculated for each category which is category I-0, category II- 56%, category III- 0, category Iva- 2.63%, category IVb-50%, category V & VI-100%.

Conclusion
MSRSGC on FNA of salivary gland lesion has standardized the reporting method to classify the lesions, facilitating risk stratification and deciding the treatment protocol.

Keywords: The Milan System for reporting Salivary gland Cytopathology (MSRGC), Risk of malignancy (ROM), salivary gland.

INTRODUCTION
Salivary gland lesions are frequently encountered in cytopathology practice and fine needle aspiration cytology (FNAC) is a simple diagnostic method utilised for evaluating salivary gland tumors.[1,2] Superficial location of the salivary gland lesions makes FNAC a preferred first line

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modality for investigating salivary gland lesions along with radiology. FNAC is an easily acceptable procedure for the patients owing to its low cost, minimal invasion and rapid diagnosis.[1,3,4]

Salivary gland lesions have been classified as infections, inflammations, benign lesions and malignant lesions. Many of these lesions have similar clinical presentations. FNAC plays a vital role in differentiating these lesions and guiding treatment.[2] However salivary gland FNAs can be challenging due to the diverse morphology of salivary gland tumors which includes tumor heterogeneity and overlapping of morphologic features between different tumor subtypes.[5-7] Secondary changes in the lesions and improper sampling can also contribute to this problem. At times it might be difficult to distinguish between non neoplastic and neoplastic lesions.[3] Clinical management of patients is profoundly dependent on the cytopathology reports. Lack of uniform reporting system has made it difficult for reporting pathologists as well as treating clinicians in management of these lesions.[4,6]

The American society of cytopathology and International Academy of cytology proposed an internationally accepted, standardized classification for salivary gland FNA-The Milan System for reporting Salivary gland Cytopathology (MSRGC) was introduced to address these problem. MSRGC represents a standardized, evidence based reporting system for salivary gland lesions.[3] It is aimed at cytology and histopathology correlation, promote enhanced sharing of data between institutions and better communication between clinicians and pathologists as it gives implied risk of malignancy (ROM) and recommended clinical management.[8-10]

The present study was undertaken to study feasibility of implementing MSRGC in our institution.

AIMS AND OBJECTIVES

To study the cytological spectrum of lesions presenting in salivary gland, categorise the lesions according to the MSRSGC, assess risk of malignancy and do histological correlation wherever available.

MATERIALS AND METHODS

The present study is a retrospective study of four year duration from 2016 to 2019 conducted in the Department of Pathology, Hassan Institute of Medical Sciences. Ethical approval was taken from Institutional Ethical committee prior to the commencement of study. All cases of salivary gland lesions presented to the cytopathology section during the study period, irrespective of age or gender were included in the study. Routine FNAC was done after obtaining informed consent from the patient. 22-23guage needle is attached to 10ml syringe to perform FNAC. Multiple passes were done to obtain satisfactory number of smears. Air dried smears were stained with giemsa stain and alcohol fixed smears were pap stained. FNAC smears of lesions affecting both the major as well as minor salivary glands were included in this study. Demographic data and radiological findings were obtained from case records. All the archived smears were retrieved. Cases where cytology smears were unavailable were excluded from the study. All the slides were reviewed separately by two pathologists and categorised according to MSRSGC into six categories.

1. Non-diagnostic
2. Non-neoplastic
3. Atypia of undetermined significance (AUS)
4. Neoplasm: benign neoplasm, and salivary gland neoplasm of undetermined significance (SUMP)
5. (V) Suspicious for malignancy (SFM)
6. Malignant neoplasm

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Cytological diagnosis was then compared with histopathological diagnosis wherever surgical follow up was available. Histopathologic examination was considered as gold standard, to know the diagnostic accuracy of malignant lesion by FNA. ROM (Risk of Malignancy) was determined by dividing number of malignant cases by a total number of histopathological follow up available in each particular category.

RESULTS

A total of 273 cases were studied over a period of four year duration in our institute from 2016 to 2019 of which 148 cases (54.2%) were males, 125 cases (45.7%) were females with male to female ratio of 1.1:1. The maximum number of patients were in 5th decade of life, constituting 23.4% of cases. In the present study, youngest patient was 3yr old and oldest patient was 88year old.

Among the 273 cases, parotid gland (163 cases,59.7%) was most commonly affected salivary gland followed by submandibular salivary gland (94 cases,34.4%) and minor salivary gland (16 cases,5.9%). Left sided glands (140 cases) were involved more. Bilateral salivary glands were involved only in 11 cases. All cytological slides were retrieved, reviewed and categorised as per MSRGSC into six categories(Table 1).

Surgical follow up was available in 85 cases in the present study. Out of these 96.5% (82 cases) were concordant and 3 cases showed discordance. In the first discordant case of low grade of mucoepidermoid carcinoma was diagnosed as retention cyst on FNA (category II). In the second case metastatic adenocarcinoma to salivary gland was reported as Pleomorphic adenoma on cytology (category IV). In the last case category IV B SUMP turned out to be pleomorphic adenoma which was cellular and few atypical cells were present.

CATEGORY	NO. OF CASES	Percentage %
I	08	2.93
II	160	58.6
III	0	0
IV A	94	34.4
IV B	2	0.72
V	4	1.46
VI	5	1.83

Table 1: Categorization of FNA cases according to Milan system

In the present study, utilizing MSRGC for diagnosing malignant lesion by FNAC, overall sensitivity rate was 66.7%, specificity was 100%. Positive predictive value was 100% and Negative predictive value was 96.25%. Diagnostic accuracy was 96.5% in the present study. The risk of malignancy for each category is depicted in table II.

Category	Cytological diagnosis	Cytology no of cases(273)	ROM	Histopathology (85 cases)	Specific HPE Diagnosis
I	Non diagnostic	08	0	01	Sialadenitis
II	Sialadenosis Sialadenitis Retention cyst/benign cyst	12 109 30 01 03	2.56	25 12	Sialadenitis(25) Mucocele (11) Low-grade MEC(1)

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	Granulomatous inflammation Suppurative lesion Lymphoepithelial lesions	05		02	Lymphoepithelial cyst(2)
III	AUS	00		00	
IV A	PA Monomorphic adenoma/basal cell adenoma Warthins tumor Myoepithelioma	85 05 03 01	2.63	35 01 02	PA(35) Metastasis (1) Warthin (2)
IV B	Salivary gland neoplasm of uncertain malignant potential.	02	50	01 01	PA(1) MEC
V	Mucoepidermoid Carcinoma SFM	01 03	100	01	MEC(1)
VI	Mucoepidermoid Carcinoma Adenoid cystic carcinoma Acinic cell carcinoma Poorly differentiated carcinoma	02 01 01 01	100	04	MEC(2) AdCC (1) ACC (1)

Table 2: Categorization of FNA cases according to Milan system and correlation with histopathological findings

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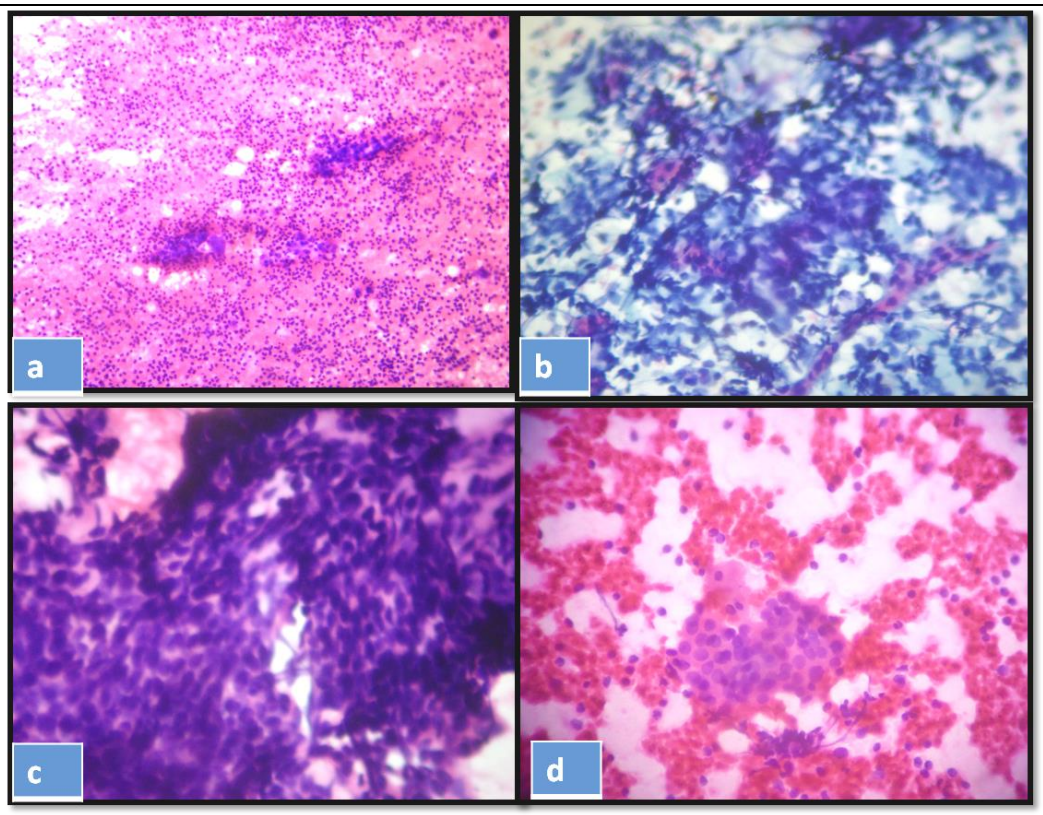

Figure 1: a. Chronic sialadenitis, b. Pleomorphic adenoma, c. Monomorphic adenoma and d.warthins tumor

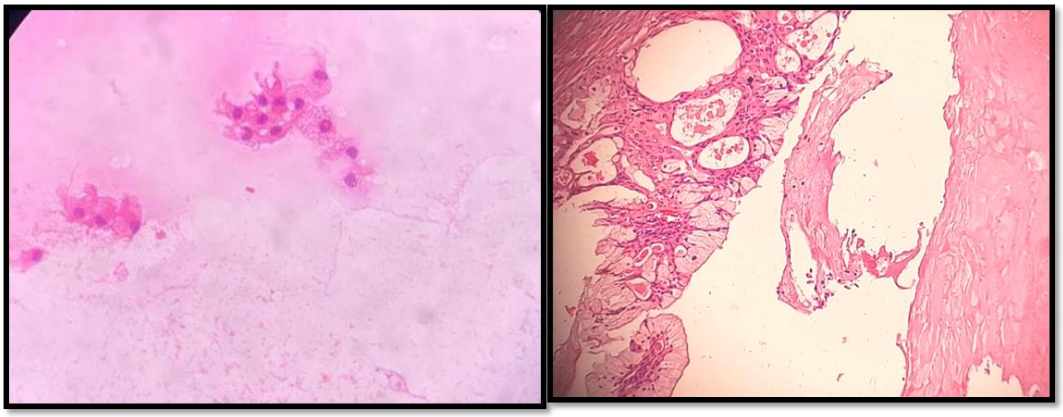

Figure 2: Smears shows and mucin and bland looking cells which was reported as retention cyst(H &E X100)on histopathology of same case shows features of mucoepidermoid carcinoma(H &E X100)

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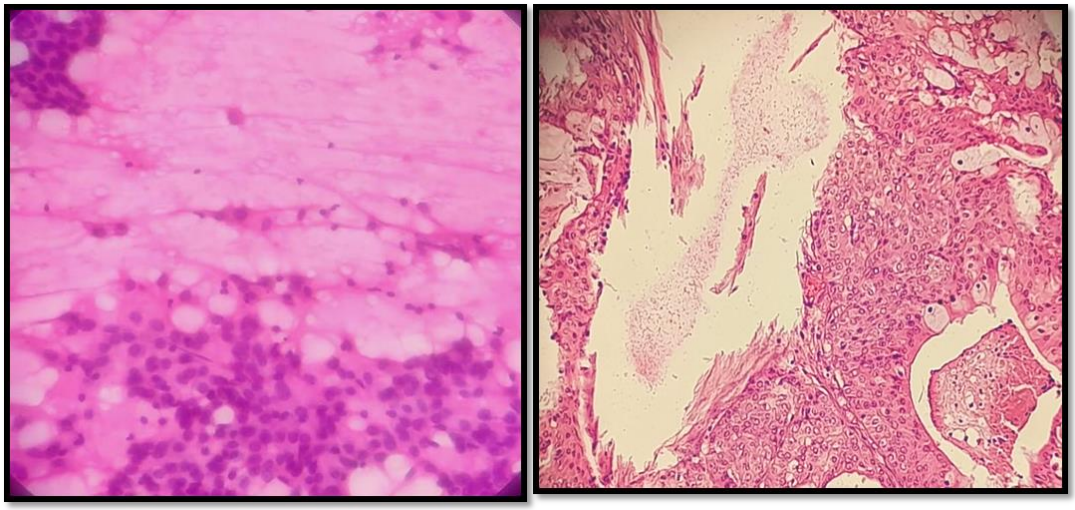

Figure 3: Smears shows and mucin and atypical cells in sheets which was reported as SUMP(H &E X100) on histopathology showed features of Mucoepidermoid carcinoma(H &E X100)

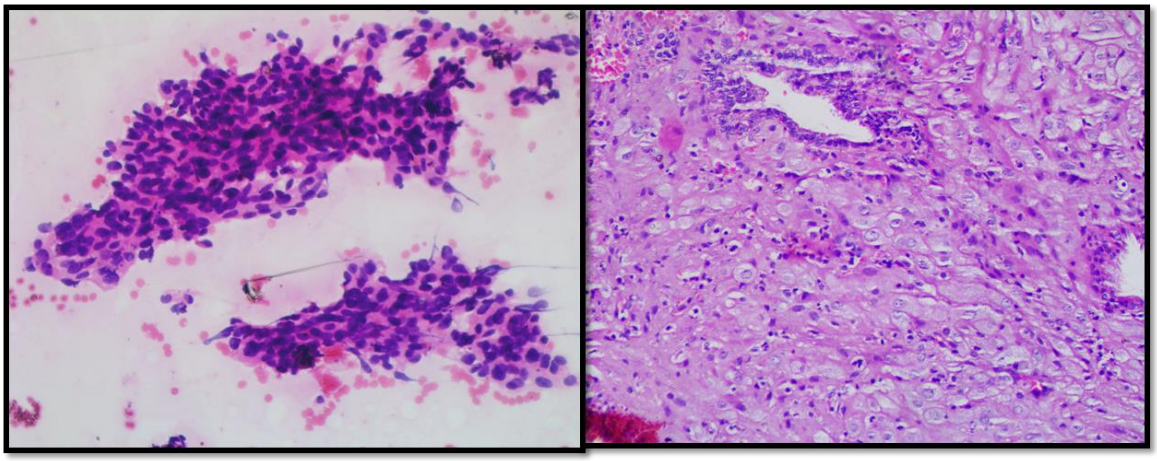

Figure 4: Smear was reported as pleomorphic adenoma(H &E X100) on histopathology of same case showed features of Metastatic adenocarcinoma(H &E X100)

DISCUSSION

Salivary gland neoplasms are prevalent in the head and neck region. FNAC of salivary gland lesions has gained widespread popularity due to its cost effectiveness, safety, minimal invasiveness with high sensitivity, specificity, and acceptance.[6,11] However, diagnosing salivary gland tumours through FNAC is challenging due to its significant morphological overlap and intratumoral heterogeneity. To overcome this challenges many risk based classifications were proposed.[12,13]

The development of MSRSGC is a concerted effort to standardize and bring uniformity to the reporting of salivary gland lesions. This initiative aims to prevent diagnostic confusion among treating clinician treating clinician in difficult cases.[11,14,15]

In our study, most common age group affected is 5th decade of life which was similar to study done by Meenai FJet al.[16] The predominant site involved was the Parotid gland(59.7%) followed by submandibular gland(34.4%) and minor salivary gland(5.9%). This distribution is consistent

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with studies done by Kala C et al [5] Karuna et al [4] and Rohilla et al[17] where Parotid gland was the commonest site of involvement (57.7%), followed by the submandibular gland(27.3%) and minor salivary gland(15%).

In the current study, 8 cases (2.993%) were classified as non diagnostic due to the absence of cellularity, aligning with Griffith et al[18] criteria where smears are considered adequate with the presence of epithelial cells in four high power field to maintain a non diagnostic rate below 10% as suggested by Milan. The ROM in this category is 0% which is same as studies done by Karuna et al[4], Pujani et al[11] and Amit et al[19].

The most prevalent lesions fell into category II, non neoplastic constituting 58.6% which is similar to study done by Rohilla et al.[17] Chronic sialadenitis was the common followed by acute sialadenitis, sialadenosis, retention cyst, lymphoepithelial lesion, suppurative lesion and granulomatous inflammation. Notably, a discordant case involved a retention cyst mistaken for histiocytes or mucus containing macrophages, later confirmed as low grade mucoepidermoid carcinoma on histopathology. ROM in category II is 2.56%which is concordant with other study.[19] No cases of atypia cells of undetermined significance were identified in our study, a heterogenous group where definitive distinction between reactive and neoplastic process is challenging.

Benign neoplastic lesions constituting 34.4% with pleomorphic adenoma being most common followed by, monomorphic adenoma/basal cell adenoma, warthins tumor and myoepithelioma. ROM for this category in the present study is 2.63% which is similar to Karuna et al[4] study,

Suspicious of Uncertain Malignant Potential category is reserved for cases where cytological features are diagnostic of neoplastic process but cannot distinguish between benign and malignant tumors. Two case of salivary neoplasm of uncertain malignant potential was reported in our study which had high cellularity which turned out as pleomorphic adenoma on histopathology. Other cases was confirmed as Mucoepidermoid carcinoma on histopathology Risk of malignancy reported was 50% which is similar to studies done by Pujani et al[11] and Rohilla et al.[17] The Suspicious category includes four cases in the present study. One case showed cytohistological correlation as mucoepidermoid carcinoma. The ROM was 100% which is similar to other studies.[4,11,19] In the current study malignancy was found in 1.83% of cases. Mucoepidermoid carcinoma being common followed by adenoid cystic carcinoma, acinic cell carcinoma and poorly differentiated carcinoma. ROM for this category was 100% which is similar to that proposed by MSRSGC and reported by Rossi et al[7], Pujani et al[11] and Amita et al.[19]

Author	Nondiagnostic	Nonneoplastic	Atypia	Benign	SUMP	SFM	Malignancy
Kumari M et al[20]	20	14.3	100	4.2	100	83.3	100
Karuna et al[4]	0	0	50	2.44	33.3	100	93.3
Pujani et al[11]	0	10	50	2.5	50	100	100
Rohilla et al[17]	70.4	17.4	100	7.3	50	96	96
Amit etal.[19]		6.25	100	00	25	100	100
Present study	0	2.56	0	2.63	50	100	100

Table 3: Risk of malignancy for individual Milan category in various studies

Our study showed 96.5% (82 cases) of concordance which is similar to study done by Pusztaszeri et al[21]. Sensitivity was 66.7%, specificity was 100%, Positive predictive value was 100%, Negative predictive value was 96.25% and diagnostic accuracy was 96.5%. This findings align with Kumar et al[22] and Jaiswal et al[23] studies.

Comparison of risk of malignancy with other studies is given in table III. However, calculating ROM in the present study presented a significant challenge due to limited surgical

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follow up of cases(31%).Our study had certain limitations which include its retrospective design and small sample size.

CONCLUSION

The implementation of the Milan System in this study has showed reporting of salivary gland lesions, resulting in a reduction of both false positive and false negative cases. Recommending its application across institution become crucial to minimize ambiguity, elevate the care and management of patient and also avoids unnecessary surgical interventions in benign cases.

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