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Application of the Milan System for Reporting Salivary Gland Cytopathology with Histopathological Correlation

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ABSTRACT

Background: Fine-needle aspiration (FNA) is widely accepted as an efficient first line diagnostic of salivary gland lesions. Intratumoral heterogeneity and morphological overlap existing between salivary gland tumors makes it rigorous and challenging in the diagnosis by FNA. The Milan System for Reporting Salivary Gland Cytopathology (TMSRSGC) is a tiered risk-stratification scheme designed to standardize reporting and facilitate decision making.

Method: A prospective study of salivary gland cytology was performed over a 1-year period at Department of Pathology BPKIHS. Cases were categorized as per the MSRSGC and histopathological correlation was obtained. The risk of malignancy were calculated for all diagnostic categories.

Result: A total of 30 salivary gland cytology with histopathological follow up were evaluated. FNA had a sensitivity, specificity, diagnostic accuracy, PPV and NPV of 72.7%, 100%, 88.88%, 100% and 84.2% respectively. Good agreement was seen between cytological and histopathological diagnosis.

Conclusion: The Milan System for Reporting Salivary Gland Cytopathology provides an effective standardized diagnostic framework which aids in better clinicopathological communication and improves the quality, clarity as well as reproducibility of cytological diagnosis of salivary gland lesions.

Key words: TMSRSGC; salivary gland cytology; histopathology.

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INTRODUCTION

Fine-needle aspiration (FNA) has been widely accepted as an efficient first line diagnostic in the management of salivary gland lesions.[1] Diagnosis of salivary gland lesions by fine-needle aspiration (FNA) cytology is a challenging and rigorous area in cytopathology [2] because of the diversity of salivary gland tumors.[3] Intratumoral heterogeneity as well as morphological overlap exist between many salivary gland tumors.[1] For the development of standardized terminology for reporting salivary gland cytopathology, the American Society of Cytopathology and the International Academy of Cytology initiated a project to propose an international classification system, The Milan System for Reporting Salivary Gland Cytopathology(TMSRSGC) for reporting salivary gland FNA which is based on the experience of experts and on evidence from the literatures.[1] The objectives of this study is to evaluate the efficacy of The Milan system for reporting salivary gland cytopathology with histopathological correlation and also to study the cytological spectrum of salivary gland lesion.

METHODS

A comparative cross sectional study of FNAC and histopathology from salivary gland lesion was carried out at Department of Pathology, BP Koirala Institute of Health Sciences (BPKIHS) for duration of 1 year. Ethical Clearance was obtained from Institutional Review Committee, BPKIHS (Ref no. IRC/1321/018). Descriptive Statistics which includes percentage, proportion, mean, and standard deviation were derieved and graphical and tabular presentations were made. Cohen's Kappa test was used for inferential statistic and for diagnostic measurement sensitivity, specificity, positive predictive value, negative predictive value were calculated. Probability of significance was set at 5% level.

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RESULTS

Among around 70 cases with salivary gland cytopathological analysis, 30 cases which had histopathology follow up were enrolled in the study. There was equal gender distribution with 15 cases in each category with Male : Female ratio of 1:1. Parotid swelling was the commonest site of clinical presentation owing 57% followed by 43% in submandibular gland. The 73.3% of patient presented with chief complain of asymptomatic lump, followed by painful lump in 13.3%, with pain only in 10% and 3.3%, i.e. 1 case presented with complain of facial palsy. In cytology, Pleomorphic adenoma (PA) was the commonest benign lesion (46.6%) and Mucoepidermoid carcinoma (MEC) was the commonest malignant lesion, (13.33%). In histopathology similar to cytology, pleomorphic adenoma accounted for 46.6% cases and was commonest benign lesion and mucoepidermoid carcinoma comprised of 23.33% being commonest malignant lesion. In comparisons of cytological diagnoses (TMSRSGC) with histopathology, there were 24 concordant and 6 discordant results on cytology - histology correlation as presented in table 1. One case categorized as atypia of undetermined significance (AUS) turned out to be cellular pleomorphic adenoma, which was considered a concordant diagnosis owing to its benign nature.

Salivary gland cytological and histopathological statistical analysis

Considering concordant histological diagnosis and Risk of malignancy (ROM), the categories of non neoplastic, AUS and benign were collectively termed benign. Similarly SUMP, suspicious of malignancy and malignant categories were termed malignant. Non diagnostic category was not kept in the statistical analysis. Sensitivity and specificity of FNAC for salivary gland lesions on detection of malignant from benign lesion as per application of MSRSGC was 72.7% and 100% respectively. Positive predictive value and negative predictive value were 100% and 84.2% respectively. The diagnostic accuracy of MSRSCG was found to be 88.88%. Cytology was considered test. Histology was the gold standard (true).

Table 1. Comparisons of cytological diagnoses (MSRSGC) with histopathology. (n=30)

FNA Diagnosis	Histopathology Diagnosis		
	No. of Cases	Concordant	Discordant (specific diagnosis)
Non diagnostic	3	0	3(2-PA, 1-Lymphoepithelial cyst)
Non neoplastic	1	1	-
Atypia of undetermined significance(AUS)	1	1	0(1-cellular PA)
Benign			
Pleomorphic adenoma (PA)	14	11	3(2-MEC, 1-Adenoid cystic carcinoma(AdCC)
Warthin's Tumor	3	3	-
Salivary gland neoplasm of uncertain malignant potential(SUMP)	1	1	-
Suspicious for malignancy	2	2	0 (1-MEC, 1-AdCC)
Malignant			
Mucoepidermoid carcinoma(MEC)	4	4	-
Adenoid cystic carcinoma (Ad CC)	1	1	-

Cohen's Kappa test was performed which provided value of 0.760 which shows good agreement between cytopathological and histopathological diagnosis.

DISCUSSION

MSRSGC is followed by cytopathologists globally and are validating it with positive results which are shown in various studies. Due to lack of tier categories and heterogeneity of the salivary gland neoplasm, it was tedious to report few indefinite cases, which now could be kept in category of AUS/SUMP. Similarly, the other diagnostic categories criteria help for better evaluation of the salivary gland cytology. This study was conducted to evaluate the utility of MSRSGC and validate its importance with histological correlation. The mean and median age of presentation was 43.87 and 47 with peak age group being 20-39 years followed by 40-59 years accounting 36.7% and 33.3% respectively which is in concordance with the studies conducted by Shrestha S et al[4], Rohilla et al[1] and Gupta M et al. [5]

In our study gender distribution was equal (50% each) with ratio of 1:1. Studies conducted by Rohilla et al[1], Gupta M et al[5], Pujani M et al[6] and Kakoty S et al[7] have shown slight male preponderance whereas study conducted by Viswanathan K et al[8] showed slight female preponderance with male to female ratio of

1:1.2. The most common clinical presentation with salivary gland lesion, either benign or malignant, was asymptomatic lump/swelling followed by painful lump, with pain only and a single case presented with facial palsy similar to other study.[9,10] This finding is in accordance with the study done by To VSH et al[11] and Sood S et al[12] Parotid was the commonest site for salivary gland lesions owing for 57% in this study followed by 43% of submandibular gland. Similar findings were seen in other various studies by Katta R et al[9], Karuna V et al[10], Mazzola et al[13] and Thiryayi SR et al.[14] For histopathological and cytopathological correlation, the non-neoplastic and benign categories were merged as benign in histopathology. Hence, The MSRSGC categories of non-neoplastic, atypia of uncertain malignant potential and benign neoplasm were grouped in benign category. AUS was also kept in benign, owing to the fact of its low ROM in various studies. Similarly the categories of SUMP, suspicious of malignancy and malignant were grouped together as malignant, as these groups had higher ROM. This shows that cytological diagnosis was sensitive and specific while distinguishing between benign and malignant lesions. Current study had sensitivity of 72.7%, specificity of 100%, positive predictive value (PPV) of 100% and negative predictive value (NPV) of 84.2% which is in accordance with previous studies as in Table 2.

Table 2. Comparision of strength of our study with various studies.

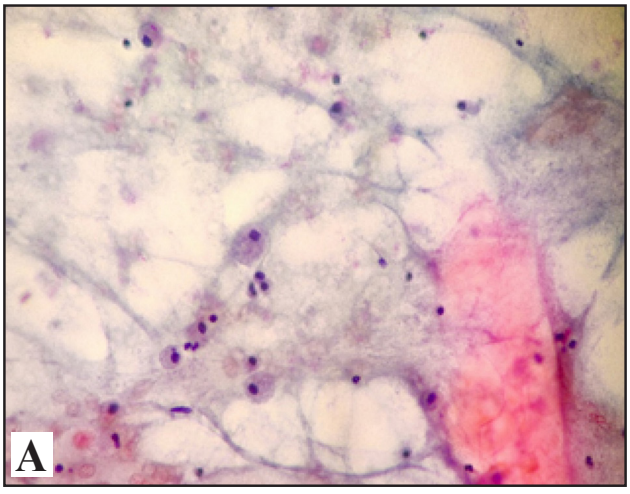
???	Sensitivity	Specificity	PPV	NPV
Current study	72.70%	100%	100%	84.20%
Karuna V et al[10]	85%	98.14%	94.44%	94.64%
Howard H Wu et al[15]	89%	99%	98%	96%
Kala C et al[16]	83.33%	98.91%	95.74%	92.80%
Katta R et al[9]	73.34%	95.56%	84.62%	91.49%
Pujani M et al[6]	81.80%	100%	100%	96.40%
Vishwanathan K et al[8]	79%	98%	94%	92%
Rohilla et al[1]	79.40%	98.30%	96.40%	89.20%

Diagnostic Accuracy: In the current study, diagnostic accuracy of salivary gland cytology (excluding the non-diagnostic category) was 88.88% which is in agreement with the various studies as depicted in table 3. This discerns the utility of salivary cytology as per MSRSGC and the high accuracy correlates well with its valuable importance.

Table 3. Comparison of diagnostic accuracy among various studies.

Study	Diagnostic Accuracy
Current study	88.80%
Rohilla et al[1]	91.40%
Pujani M et al[6]	96.90%
Katta R et al[9]	90%
Karuna V et al[10]	94.59%
Jaiswal P et al[17]	86.88%

Non diagnostic: Out of three cases of non diagnostic category, two cases turned out to be pleomorphic adenoma and one lymphoepithelial cyst. Our study showed similar result to the study by Katta R et al[9] in context to pleomorphic adenoma. One of the case in non-diagnostic category FNA revealed predominantly non mucinous cystic component with rare degenerated epithelial cells. However histology revealed solid component of lesion as pleomorphic adenoma with adjacent cystic change. This is the fact that FNAC should be done from the solid lesion. Similarly a case was reported as non-diagnostic cyst fluid only on MSRSGC which was done as non USG guided FNA. Histology of the same case revealed pleomorphic adenoma with large areas of myxoid and cystic changes. Thus a thorough radiological correlation is must especially in a cystic or a solid-cystic lesion so as not to miss any significant lesion on FNA. FNA done from the multiple sites avoid the area of tumor heterogeneity and lowers risk of sampling error (Figure 1A, 1B).



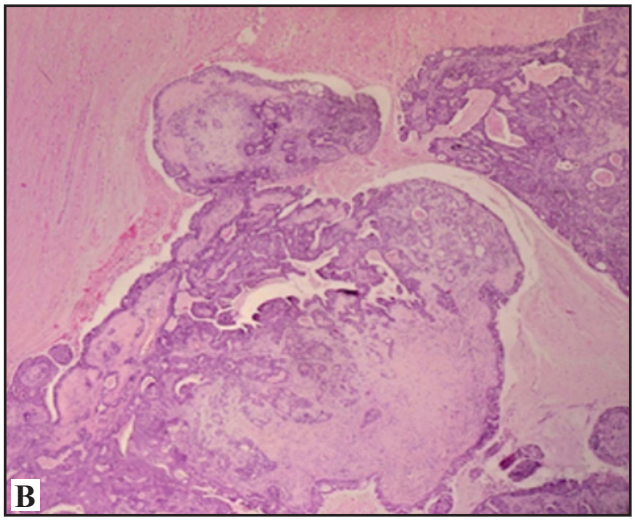


Figure 1. (Discordant case): A-(cyto) Non-Diagnostic: cyst fluid only (Pap,100x), B-(histo) Pleomorphic Adenoma with adjacent cystic component (H&E,100x).

Benign: Three cases diagnosed as benign neoplasm category as per MSRSGC turned out to be malignant on histopathology. One case of Adenoid cystic carcinoma was misdiagnosed as pleomorphic adenoma on cytology. Studies by Howard et al[15] and Pujani et al[6] showed similar discordant result. Similarly other two cases diagnosed as pleomorphic adenoma in cytology were both confirmed as low grade mucoepidermoid carcinoma on histopathology. This finding is similar to the study done by Rohilla et al[1] and kala C et al.[16] False-negative results in cytology are mainly due to sampling errors, few observational errors, cystic lesions, and underassessment of low-grade tumors due to their bland cytological features

Other categories

AUS: A case was categorized in AUS category which on histology follow up revealed an ill circumscribed cellular lesion with biphasic proliferation of predominantly epithelial and few mesenchymal cells and was diagnosed as cellular pleomorphic adenoma. Similar findings were observed in the study by Karuna V et al.[10]

SUMP: A single case of SUMP presented in our study was categorized as so on the basis of cytological atypia of the epithelial cells along with presence of few hyaline globules and scattered lymphoid cells. Cytological findings could not effectively distinguish between a benign and malignant neoplasm in this case so it was kept in SUMP category. This case turned out to be lymphoepithelial carcinoma on histology.

In the SUMP category, use of ancillary techniques such as immunochemistry on cell blocks and fluorescence in situ hybridization can improve the diagnostic accuracy [1] (Figure 2. A, B).

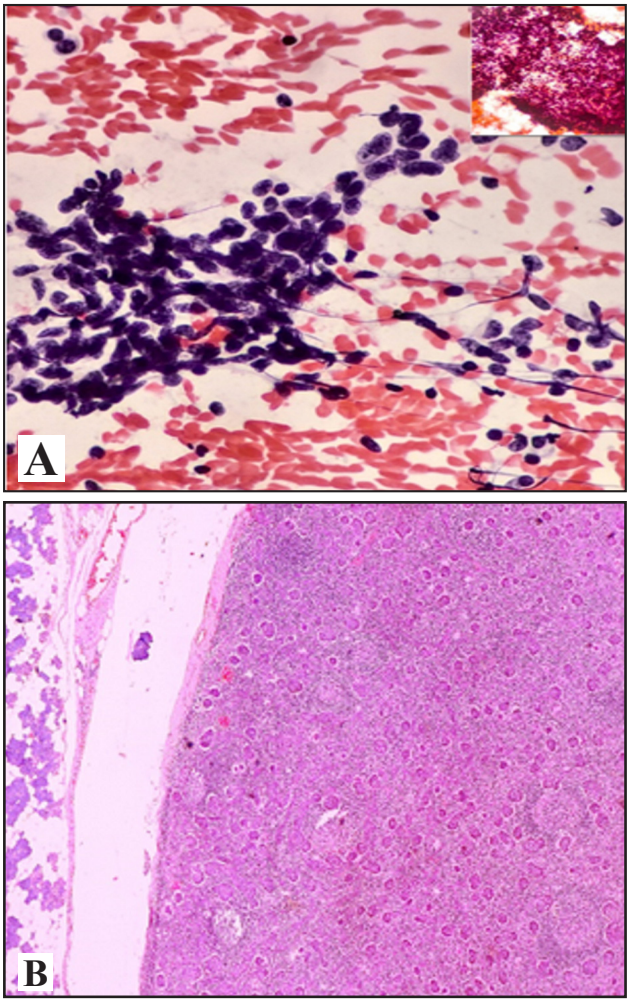


Figure 2. A: (Cyto) SUM: Presence of cellular atypia in form of nuclear hyperchromasia, irregularities and scattered lymphoid cells (Pap, 400x). B: (histo) Lymphoepithelial carcinoma (H & E, 100x)

Other cases categorized on cytology were in concordance with histology similar to other various literatures of Rohilla et al[1], Pujani et al[6], Jaiswal P et al[17], etc.

CONCLUSIONS

Application of The Milan System for Reporting Salivary Gland Cytopathology provides an easy template-based classification system and marginalizes diagnostic discrepancies to a minimum. This study

shows sensitivity, specificity and diagnostic accuracy of 72.7%, 100% and 88.88% respectively with a good agreement between cytology and histology. Thus implementation of this reporting system provides a standardized universal framework for diagnosis and improves the quality, clarity and reproducibility of cytological diagnosis of salivary gland lesions.

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Conflict of Interest: None

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