

Diagnostic Utility of the Milan System for Reporting Salivary Gland Cytology in a Tertiary Hospital of Western Nepal

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ABSTRACT

Introduction: Salivary gland Fine Needle Aspiration Cytology is a well-established pre-operative diagnostic tool done routinely worldwide. Heterogeneity of salivary gland lesions makes Aspiration cytology diagnosis challenging for most cytopathologists. Milan system for reporting salivary gland cytology is a six tier reporting system developed to minimize inter-observer variability, thus to enhance reproducibility of cyto-diagnosis. **Aims:** To study diagnostic utility of Milan System for Reporting Salivary Gland Cytology. **Methods:** This is a one-year hospital based study done at Department of Pathology, Nepalgunj Medical College Teaching Hospital. It included 46 cases of salivary gland Cytology. Biopsy was available for 22 of them. Fine Needle Aspiration Cytology cases were reported as per the Milan System and subsequently correlated with gold standard histopathology. **Results:** Age of patients ranged from 8-79 years with submandibular and parotid gland being the commonly involved ones. Most cases were in Category II (Non Neoplastic) according to Milan System for Reporting Salivary Gland Cytology (48%) followed by Category IVa (Neoplasm- Benign) accounting for 37%. Pleomorphic Adenoma was the commonest Benign Neoplasm. Malignancy (Category VI) accounted for 11% of FNAC while suspicious for Malignancy (Category V) were 6% case. Diagnostic accuracy of the Milan System was calculated as 88.88%. Cohen Kappa test value 0.81 showed strong agreement between cytology reporting by Milan System and biopsy. **Conclusion:** The Milan System for Reporting Salivary Gland Cytology should be applied for standardization of salivary gland cytology reporting as there is a good correlation between it and Histopathology, hence are complementary to each other.

Keywords: Fine Needle Aspiration Cytology, Histopathology, Milan System, Salivary Gland

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INTRODUCTION

Salivary gland neoplasms account for 5-6% of head and neck Tumors subjected to Fine Needle Aspiration Cytology (FNAC) procedure.¹ Salivary gland FNAC is a well-established diagnostic modality done routinely almost in all settings across the globe. Heterogeneity of lesions has made FNA diagnosis of salivary gland challenging to most of the cytopathologists.^{2,3} Owing to the lack of a Tier system for cyto-diagnosis of Salivary Gland FNA, subtyping of salivary gland lesions, particularly those with overlapping features was at times subjective, with inter observer variability.⁴ This limited the overall efficacy of the test and caused confusions to treating clinicians. In order to create uniformity and inter-observer reproducibility, cytopathologists from 15 countries, in 2015 developed this

Tier system at Milan, Italy and named it "The Milan System for Reporting Salivary Gland Cytology" (MSRSGC).³⁻⁵ It is an evidence based diagnostic system designed to enhance better communication between clinician and cytopathologist and to provide better guidelines for treatment planning and ultimately improve patient care.^{1,5} MSRSCG contains six categories of diagnostic schemes, including a description, risk of malignancy (ROM), and management plan for each category.³ This study was conducted to categorize salivary gland FNA results as per MSRSGC and correlate FNA findings with Histopathology in order to establish the diagnostic accuracy.

METHODS

This is a hospital based study conducted over a period of one

year starting from April 2022 to March 2023 in department of Pathology, Nepalgunj Medical College (NGMC) - Kohalpur. Ethical clearance was obtained from IRC, NGMC. Patients visiting ENT OPD for Salivary Gland swelling and undergoing routine FNA procedure were included in the study after receiving a verbal consent. A total of 46 cases of salivary gland FNA were studied. Histopathology follow up was available for 22 of them. Patients of all age and both sexes were included in the study. Slides both air dried and alcohol fixed were stained for Giemsa and PAP as per standard staining protocols. Clinical and Radiological correlation were done in available cases. Slides were reviewed and reporting done as per MSRSGC.

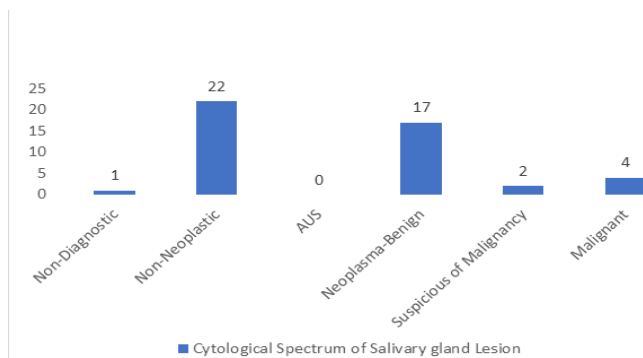


Figure 1: Cytological Spectrum of Salivary gland Lesion

Diagnostic category	ROM (%)	Management
I. Non-Diagnostic	25	Clinical and radiologic correlation/repeat FNA
II. Non-Neoplastic	10	Clinical follow-up and radiologic correlation
III. Atypia of undetermined significance (AUS)	20	Repeat FNA or surgery
IV. Neoplasm	<5	Surgery or clinical follow-up
A. Neoplasm: Benign		
B. Neoplasm: Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)	35	Surgery
V. Suspicious for malignancy (SM)	60	Surgery
VI. Malignant	90	Surgery

Table 1: The Milan System for Reporting Salivary Gland Cytology

Histopathology samples were processed as per standard protocols and stained with Hematoxylin and Eosin stains.

Data were analyzed using Microsoft excel 2010 and standard statistical software SPSS 20.0.

RESULTS

A total of 46 FNA cases were included in the study. Age of the patients ranged from 8-79 years, with the maximum number of patients falling in the age range 21-30 years. 21 of the patients were male (45%) and 25 were female (55%). The most commonly involved gland was submandibular gland 26 (56%) followed by Parotid gland 16(36%) and minor salivary gland- Four (8%). FNA diagnosis were made under the MSRSGC criteria in six categories. Our study showed the maximum number of cases of MSRSGC category II i.e Non Neoplastic -22 (48%), followed by Category IVa i.e Neoplasm- Benign 17 (37%). (Figure 1)

Chronic Sialadenitis was the commonest diagnosis accounting for Nine cases (40%) of the MSRSGC Category II diagnosis followed by mucocele- Six cases (26%) and sialadenitis- Four cases (18%). Of the benign Neoplasm, Pleomorphic Adenoma was the commonest entity diagnosed -13 cases(84%), followed by Warthin’s Tumor- two cases (11%) and a single case each of hemangioma and Schwannoma (5%). Two cases were classified as MSRSGC category V (suspicious for Malignancy) for which no histological follow up was obtained. Four cases were classified as malignant of which two were diagnosed as Muco-Epidermoid Carcinoma (MEC), one as Carcinoma Ex Pleomorphic Adenomam(Ca Ex-PA) and one as Adenoid Cystic Carcinoma (ACC). Histopathology follow up was obtained for 22 cases. Majority of cases in histology diagnosis were those of Pleomorphic Adenoma- Eight (36%) followed by chronic sialadenitis- Four (18%), mucocele –three (14%), Warthin’s Tumor- two (10%), MEC- two(10%) and others. A single case each of Hemangiopericytoma, Adenoid Cystic Carcinoma and Schwannoma were among the other entities diagnosed by histopathology. (Figure 2)

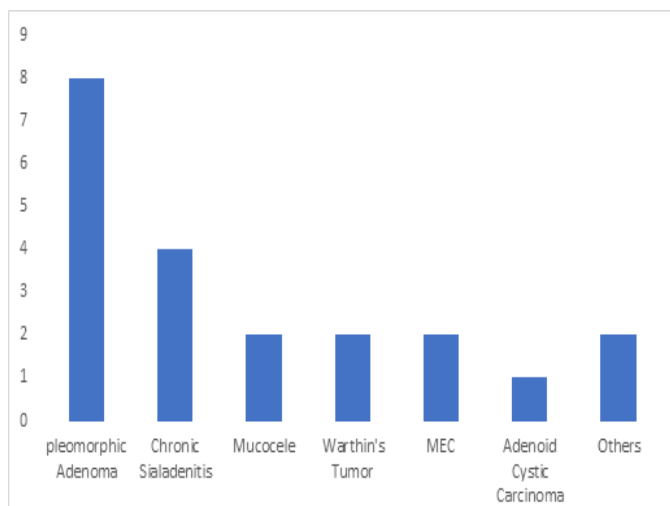


Figure 2: Histological Spectrum of Salivary Gland Lesion

Comparison was done between FNA diagnosis according to MSRSGC with the final histopathology diagnosis in available cases. Of the 46 FNA cases, 22 cases had follow-up histological examination and diagnosis. There were 18 concordant and four discordant results on cytology – histology correlation as

presented in table II. Out of four discordant results, one was categorized as non-diagnostic in cytology which turned out to be Chronic Sialadenitis in histopathology. One case categorized as benign in cytology as pleomorphic adenoma turned out to be Schwannoma in histology. One case categorized as benign vascular tumor on histopathology turned out to be Hemangiopericytoma. A single case which was categorized as malignant (Carcinoma Ex Pleomorphic Adenoma) in cytology, upon histopathology follow up turned out to be MEC.

Sensitivity and specificity of FNAC for salivary gland lesions on detection of malignant from benign lesion as per application of MSRSGC was 75% and 100% respectively. The diagnostic accuracy of MSRSC was found to be 88.88%. Cohen's Kappa test was applied where the Kappa test provided value of 0.81 which shows good agreement between cytopathological and histopathological diagnosis. P value was calculated at <0.005 (significant) establishing good correlation between cytopathology of salivary gland according to the Milan system for reporting salivary gland cytopathology (MSRSGC) and histopathology.

FNA Diagnosis	No. of Cases	Histopathology Diagnosis	
		Concordant	Discordant (Specific Diagnosis)
Non diagnostic	1	0	1(Chronic Sialadenitis)
Non neoplastic	6	6	
Benign			
Pleomorphic Adenoma	9	8	1(Schwannoma)
Warthin's Tumor	2	2	
Hemangioma	1	0	1(Hemangiopericytoma)
Salivary Gland Neoplasm of uncertain Malignant Potential	0	0	
Malignant			
Muco-epidermoid Carcinoma	1	1	
Carcinoma Ex Pleomorphic Adenoma (Ca Ex PA)	1	0	1 (MEC)
Adenoid Cystic Carcinoma	1	1	

Table II: Comparisons of Cytological Diagnoses (MSRSGC) With Histopathology (n=22)

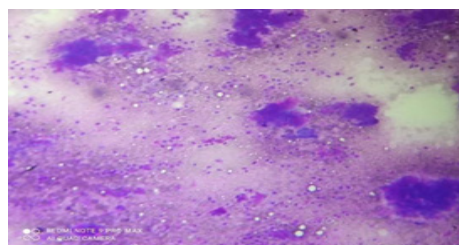
DISCUSSION

FNAC of salivary gland lesion is a simple, cost effective, minimally invasive OPD based procedure done on a routine basis. It provides a rapid preliminary diagnosis with a minimal risk for tumor seeding.⁶ The MSRSGC is the first step in standard-

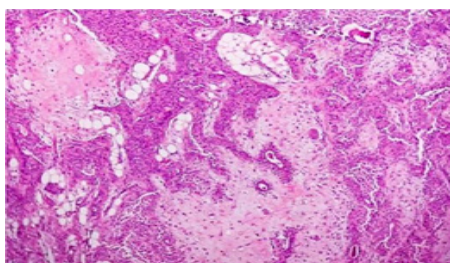
izing salivary gland cytology but contains some indeterminate diagnostic categories, including atypia of undetermined significance (AUS), salivary gland neoplasm of uncertain malignant potential (SUMP), and suspicious for malignancy. This study was carried out to evaluate the reproducibility of the MSRSGC in routine cytopathology practice.⁷

We studied a total of 46 FNA cases over a period of one year. Highest number of cases were in between the 3rd and 4th decade of age which is in concordance to other studies conducted by Rohilla M et al and Mishra S et al.⁸⁻⁹ Most studies show major salivary glands being the most involved ones. Parotid was the most commonly involved gland by both neoplastic as well as non neoplastic processes in most of the studies.^{9,10} However, Submandibular gland was the most commonly involved salivary gland in our study followed by parotid gland. FNA cases were classified as per the MSFRSGC. In the present study a single case (2.18%) was in category I (Non- diagnostic) for which histological follow up was available and was diagnosed as chronic sialadenitis. This is in concordance to studies conducted by Mishra et al, Rohilla M et al and Karuna V et al.⁸⁻¹¹ There are other studies which have a higher percentage of Category I cases. Strict sufficiency criteria application results in an increase in non-diagnostic cases but a decrease in false-negative cases of malignancy, as stated by a study done by Chen et al.¹²⁻¹³ FNA was non diagnostic as the lesion was fibrotic with loss of salivary gland ronic inflammation.

Category II (Non Neoplastic) was the most prevalent in our study accounting for 46% of cases. Chronic sialadenitis was the most prevalent lesion in this category and this finding is in concordance with the studies done by Karuna et al, Song et al, Wu et al and Gautam et al.^{2,11,14,15} Other cases in these Categories included Mucocele, Lymphoepithelial cyst and Reactive Lymphadenitis. Histopathology follow up was available for six of these cases and all show concordant results.¹⁶ Category IVa (Neoplasm-Benign) was the second most prevalent in our study accounting for 37% of cases. Pleomorphic Adenoma was the commonest of all benign neoplasm. This is in concordance to most of the studies done in salivary gland Cytopathology.¹⁷⁻¹⁹ Warthin tumor and Schwannoma of the Parotid gland were the other entities diagnosed in this category. Histopathology follow up was available for Eleven of these cases with two discordant cases. A case that was diagnosed as Pleomorphic Adenoma in FNA, on histopathology follow up was diagnosed as Schwannoma, both falling under the same Category IVa according to MSRSGC. Another case diagnosed as benign Vascular Tumor- Hemangioma upon histopathology was diagnosed as Hemangiopericytoma.

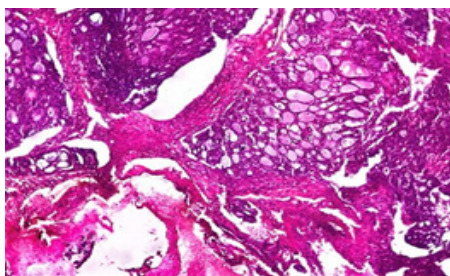


Picture 1: Pleomorphic Adenoma (FNA-Giemsa-100X)

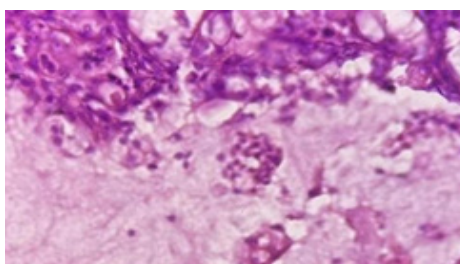


Picture 2: Pleomorphic Adenoma (Histology-100X)

No cases were reported as per MSRSGC into category IVb (Salivary Gland Neoplasm of Uncertain Malignant Potential – SUMP). Two cases were categorized into Category V (Suspicious for Malignancy). However biopsy follow up was not available in both of these cases. So a histopathological correlation was not available. This might be largely because of the fact that there is a dedicated cancer hospital in Banke district with the Government of Nepal (GoN) providing free treatment amounting to one lakh NRs to these cancer patients. Many of these patients need post-surgical chemo/radiotherapy. Due to the unavailability of these services in our institution these patients are referred to higher centers prior surgery as well. Category VI (Malignant) of the MSRSGC had four cases and three had biopsy follow up. One case each of MEC and Adenoid Cystic Carcinoma shows concordance in histopathology follow up. One case diagnosed as Ca ex PA upon histopathology follow up turned out to be MEC.²



Picture 3: Adenoid Cystic Carcinoma (Histo-100X)



Picture 4: MEC (Histo-100X)

In our study, the diagnostic accuracy of salivary gland cytology was 88.88% and this finding is in concordance to the studies done by Rohilla et al, Karuna et al, kata R et al, Jaiswal P et al.^{8,11,15,20} Our study calculated the inter-assessment technique by using cohen’s kappa statistics (k score) which was 0.81 which showed a strong agreement for MSRSGC and hence can serve as a very useful tool for reporting salivary gland lesions. The P value being <0.005 (statistically significant) rejected the null

hypothesis and hence established that there is no significant difference between cytopathology of salivary glands according to MSRSGC and histopathology.

LIMITATIONS

The most important limitation of our study is a small sample size. Our study did not have any cases in MSRSGC category III (AUS) and Cat IVb (Salivary Gland Neoplasm of Uncertain Malignant Potential). So their representation in the study could not be done. Also biopsy follow up for all the FNA cases were not available.

CONCLUSION

This study establishes the value of the Milan System for reporting Salivary gland Cytology as a standard reporting tool which can serve to reduce inter observer variability and enhance reproducibility of the cytopathology reports. Good correlation was established between the cytology diagnosis by MSRSGC and Histopathology. Hence, we can conclude that these two diagnostic modalities serve as complementary to one another, particularly helpful in cases with overlapping features.

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