

Original Article

The Milan System for Reporting Salivary Gland Cytopathology: A 3-year Retrospective Analysis in Patan Hospital

Dipti Gautam¹, Rojin Thapa¹

¹Department of Pathology, Patan Academy of Health Sciences (PAHS), Lalitpur, Nepal

ABSTRACT

Introduction: The characteristics of salivary gland lesions identified by fine-needle aspiration cytology are varied and may overlap, which makes diagnosis difficult for cytopathologists. To provide consistency in the reporting of salivary gland cytology and to enhance clinic-pathologic communication, the "Milan system for reporting salivary gland cytopathology" has been introduced, which offers guidelines for diagnosis and treatment based on various categories of malignancy risk.

Material and Methods: In this retrospective study, Fine needle aspiration cytology was done for all salivary gland lesions for three years and were retrieved from the Department of pathology, Patan hospital. All the cases were recategorized according to the Milan system for reporting salivary gland cytology with histopathology follow-up wherever available. Consistency of the two different types of assessment techniques (Milan category and primary cytology diagnosis) were assessed and the kappa score was calculated

Results: A total of 58 cases were included in the study of which histological follow-up was available in 27 cases. Out of 58 cases, maximum cases 32 (55.1%) were classified under IVA followed by 15.5% cases classified under II, 8.6% of cases under Category IVB), 6.8% under category V and 5.1% cases under category VI. Kappa's score was 0.58 which represents a moderate agreement.

Conclusion: Milan system for reporting salivary gland cytopathology is a recently proposed six-category scheme, which places salivary gland fine needle aspiration cytology into well-defined categories that limit the possibilities of false negative and false positive cases.

Keywords: Fine needle aspiration cytology; Milan System; Salivary Gland

Correspondence:

Dr. Dipti Gautam, MD
Department of Pathology,
Patan Academy of Health Sciences (PAHS), Lalitpur,
Nepal
ORCID ID: 0000-0003-0887-0775
Email: gdipsy@gmail.com

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INTRODUCTION

Salivary gland (SG) tumours account for approximately 6% of head and neck neoplasms and approximately 0.5% of all human malignancies.¹ Around the world, the annual incidence of all salivary gland tumours is 0.4–13.5 cases per 100,000 and 0.4–2.6 per 100,000 for malignant tumour.² Fine-needle aspiration cytology (FNAC) of salivary glands is a well-established procedure effectively used worldwide. It provides a minimally invasive, safe, cost-effective, and accurate technique. It has been reported to be a sensitive (54–98%) and specific (88–98%) modality for the diagnosis of salivary gland lesions for diagnosis

and management of salivary gland lesions.³⁻⁵

Salivary gland tumours are one of the most heterogeneous groups of neoplasm with overlapping cytopathological and complex histopathological features making it difficult for accurate subtyping of the neoplasms.^{6,7} Proper reporting format has been a controversial issue among cytopathologists for many years, influenced by strong personal preferences and often by their training.

The lack of a tiered diagnostic framework for salivary gland FNAC limits the overall effectiveness of the test. To overcome this challenge, the American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC) collectively proposed a tiered classification system called the “Milan System for Reporting Salivary Gland Cytopathology” (MSRSGC), to ensure uniform reporting and to provide relevant information to clinicians.^{8,9} The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) contains six categories of diagnostic schemes, including a description, implicit risk of malignant tumours (ROM), and a brief management plan for each diagnostic category.⁷ To date, only a few studies have shown the optimistic use of this system. (Table 1)

Table 1: The Milan system for reporting salivary gland cytopathology

Diagnostic category	% Risk of malignancy (ROM)
I. Non-diagnostic (ND)	25
II. Non-neoplastic (NN)	10
III. Atypia of Unknown Significance (AUS)	20
IV. Neoplasm	
IV a. Neoplasm: Benign (BN)	<5
IV b. Neoplasm: Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP)	35
V. Suspicious for malignancy	60
VI. Malignant	90

The current study was conducted retrospectively to recategorize salivary gland lesions from previous FNAC diagnoses and to assess the consistency of the two different types of assessment techniques.

MATERIAL AND METHODS

This is a three-year retrospective study conducted on all cases of salivary gland lesions submitted to the Department of Pathology, Patan hospital over a period from April 2019 to February 2022. Total 58 cases of major and minor salivary gland FNAC were retrieved. After taking proper consent, both major and minor salivary gland masses were aspirated directly through the transdermal or intraoral route using a 10 ml syringe with a 22 or 23-gauge needle, with or without ultrasound guidance as needed. Depending on the size and complexity of the lesion, one to two needle passes were undertaken from a different region. All the prepared smears were air dried for May Grünwald Giemsa stain and wet-fixed in 95% ethyl alcohol for Pap stain. Patient of all age group and both genders were included in the study. Salivary gland lesions were reclassified using the MSRSGC category. Comparison of histological reports and clinical follow-up, wherever available were compared. At the end of the study, the consistency of the two different types of assessment techniques was evaluated by comparing the agreement between them by using Cohen’s kappa statistics (k score). The data was entered in an MS Excel spreadsheet and analysis was performed using Statistical Package for Social Sciences (SPSS) version 26.0. Retrieved slides were re-evaluated for cytomorphology, and were reclassified according to MSRSGC as follows. Consistency of the two different types of assessment techniques (Milan category and primary cytology diagnosis) were assessed and the k score was calculated.

RESULTS

The present study included a total of 58 cases. The age of patients ranged from 11–77 years with the mean age being 43.8± 18.6 years. The youngest patient was 11 years old and the oldest was 77 years old. Of the total of 58 cases, 36 (62.0%) were male and 22 (37.9%) were female with a male: female ratio of 1.6:1. Maximum number of the patient were grouped between 16-30 years, 31-45 years, and more than 61 year (Table 2)

Table 2: Distribution of cases according to age

Age (years)	Frequency
<15	2 (3.4%)
16-30	15 (25.8%)
31-45	15 (25.8%)
46-60	11 (18.9%)
>60	15 (25.8%)

The most commonly involved gland was parotid 32 (55.1%) followed by submandibular gland 17 (29.3%) and minor salivary gland 9 (15.5%) (fig.1).

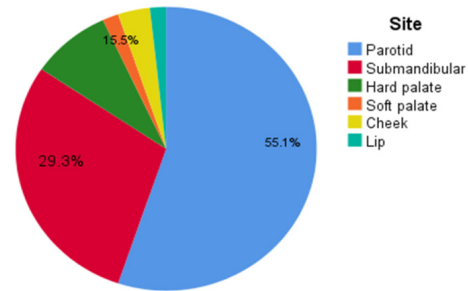


Figure 1: Pie chart with site distribution

All the cytology cases were recategorized according to the Milan system for reporting salivary gland cytopathology (MSRSGC) in six categories (Table 3). Out of 58 cases, maximum cases 32 (55.1%) were classified under IVa, i.e., benign neoplasm followed by 5 (8.6%) cases under IVb, i.e., SUMP. There were 4 (6.8%) cases in VI, i.e., malignant, and 3 (5.1%) cases each in III, i.e., AUS and V, i.e., suspicious for malignancy. Histopathology follow-ups were available in 28 cases highest (12) being in category IVa and the lowest (1) in category II.

Table 3: Distribution of cases according to Milan category

Milan category	n (%)	Histopathology follow up
Category I (Nondiagnostic)	3 (5.1%)	2
Category II (nonneoplastic)	9 (15.5%)	1
Category III (AUS)	3 (5.1%)	2
Category Iva (neoplasm benign)	32 (55.1%)	12
Category IVb (SUMP)	5 (8.6%)	4
Category V (suspicious for malignancy)	3 (5.1%)	2
Category VI (malignant)	4 (6.8%)	4
Total	58	26

Consistency of the two different types of assessment techniques (Milan category and primary cytology diagnosis) were assessed and the k score was calculated as 0.57, which represents a moderate agreement. However, the p-value was insignificant.

DISCUSSION

Salivary gland tumours account for approximately 6% of head and neck neoplasms and approximately 0.5% of all human malignancies.¹In addition to providing the clinician with important data, such as ROM, MSRSGC strives to provide a clear diagnostic category for salivary gland lesion cytology.¹⁰In this study, MSRSGC was used to reclassify FNA cases from a single center and compare the results to those from histopathology follow up.

In the present study, the highest incidence of salivary gland lesion was observed in the 3rd and 4th decades of life with the mean age being 43, this is in concurrence with other studies.¹¹⁻¹⁴ with a male to female ratio of 1.6:1 which is comparable to Rohilla et al., Kala et al.^{11,14}The majority of the cases in our study were from the parotid (55.1%) followed by the submandibular gland (29.3%), this distribution was in concurrence with Kala et al and most of the other studies in literature.^{11,13, 14, 15, 16, 17, 18, 19, 20, 21}

In the present study, there were 3 cases (5.1%) in category I (ND), out of these 2 histopathologies follow up were available, which was similar to the majority of the study conducted in India.^{12, 13, 14, 20, 21} However, Chen et al., Thiryayi et al., Maleki et al., and Vallenthaiel et al. found a higher proportion of non-diagnostic cases (18.4%, 21.3%, 21.4%, and 23%, respectively).^{18, 19, 22, 23} According to Chen et al., strict sufficiency criteria application results in an increase in non-diagnostic cases but a decrease in false-negative cases of malignancy.¹⁸ Fluid aspirate from a cystic lesion was the most frequent cause of the insufficiency (fig. 2A). In two cases where histopathology follow-up data was available, one case turned out to be pleomorphic adenoma and another was identified as metastatic squamous cell carcinoma. Insufficient sampling or cystic alterations in squamous cell carcinoma could be the causes of the discrepancy in diagnosis.

Category II (NN) was the second most prevalent in our analysis and accounted for 15.5 percent of all cases. Sialadenitis was the most prevalent lesion in this category, as noted similarly by Karuna et al., Chen et al., Song et al., and Wu et al.^{13, 18,20, 24,25} followed by reactive lymphadenitis. Histopathology follow-up was available for the only case of sialadenitis. Malignant cases were not identified in the NN category.(fig. 2B).

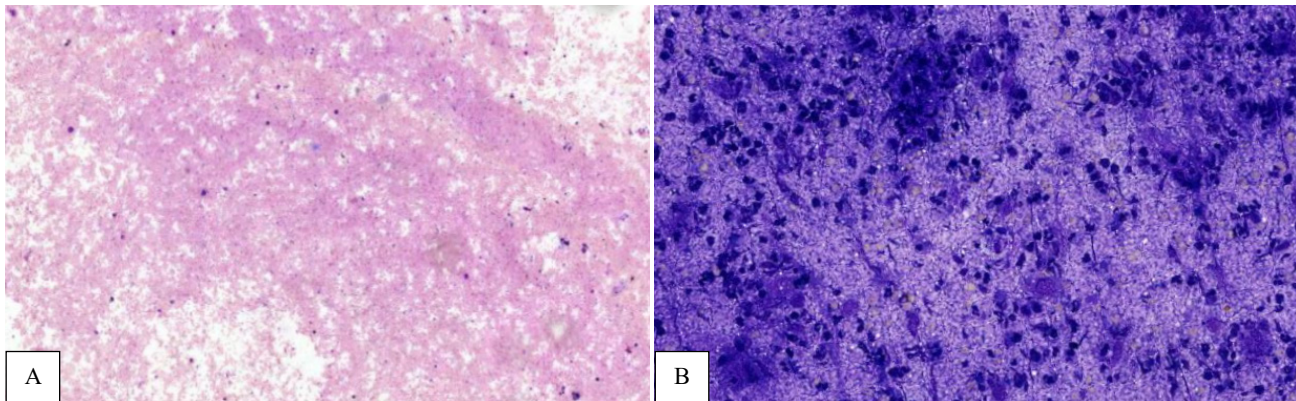


Figure 2: Cytological and histopathological salivary gland lesions. A; nondiagnostic, acellular cystic fluid B; nonneoplastic, acute suppurative sialadenitis. (40x100)

Category III (AUS) was of 5.1% cases with available histopathology for 2 cases, and none of the cases were reclassified as malignant. This was identical to the suggestion by MSRSGC (< 10%) and other literatures.^{10-15, 18- 23, 26, 27} One case of scant cell with atypia was histologically proven pleomorphic adenoma. However, Hollyfield et al. discovered that 11% of their cases belonged to AUS and noticed that interobserver reliability in the cases was fairly consistent.¹⁷

The most prevalent category in our analysis is category Iva (BN) represented 55.1 percent of all patients. Pleomorphic adenoma was the most common benign tumour (37.9%). This is in concurrence with the frequency that numerous researchers, like Karuna et al., have reported 51.3 % in the literature. Chen et al. reported 45.6 %, Wu et al. reported 37.2%, and Song et al. reported 34.9 %.^{13, 18, 24, 25} In contrary to Maleki et al. that only found 18.3% of their patients with the description of benign neoplasm.²²This

low number may be due to the non-neoplastic group being the most prevalent category and the fact that only submandibular gland lesions were included. Histopathological correlation was available in 12 cases. All of them were concordant with the diagnosis. There was one incidence of monomorphic adenoma found in an 11-year-old for which there was no histopathological follow-up. This was discordance with the study conducted by GA Mintz, et al where monomorphic adenoma mostly occurred at 32-87 years of age. This disparity could be due to limited aspiration content and the cellular area of the lesion.²⁸ However, in category IVa, Rohilla et al.¹¹ discovered two cases of MEC and one case of oncocytic carcinoma as false negatives. Six cases of carcinoma ex pleomorphic adenoma described as pleomorphic adenoma on FNA cytology were seen by Chen et al. in their study, and they came to the conclusion that sampling mistake was most likely to be responsible. (fig. 3A and 3B)

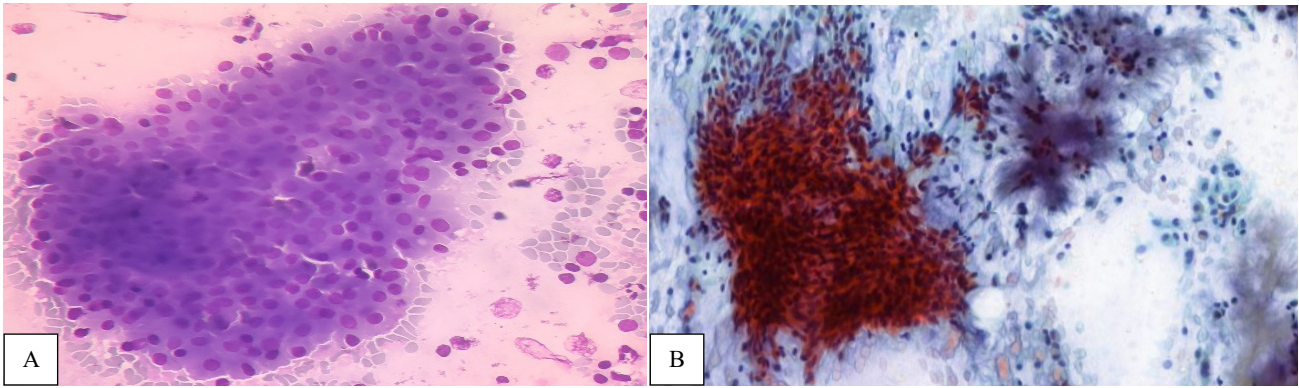


Figure 3: Cytological and histopathological salivary gland lesions C; benign neoplasm, Warthin tumour, D; benign neoplasm, pleomorphic adenoma. (Giemsa and Pap Staibn; X 400)

The neoplasm subcategory of IVb (SUMP) is adopted for SG FNAs in which the morphologic features are compatible with a neoplastic process, but a specific diagnosis cannot be made. In our study, 8.6% of cases involved SUMP which is less than 10% as described by the Milan system for reporting salivary gland cytopathology, Dubucs C et al. and Wei S, et al.^{29,30} Cases in the present study were recategorized as Warthin tumour with the differential of MEC and acute sialadenitis to rule out MEC and one case each of pleomorphic adenoma with the differential of adenoid cystic carcinoma and cellular pleomorphic adenoma. Histology follow-ups were available in 4 cases which confirmed one case of low-grade MEC, another being Warthin tumor. This smear displayed bland epithelial cells arranged against a dirty background of extensive myxoid, and sporadic mucinous cells. One case of adenoid cystic carcinoma showed a matrix-forming tumour with cells organized in globules of hyaline globules. Ancillary test for spindle cell neoplasm of intermediate malignant potential was not available.

A sample that is strongly indicative of a malignant tumour characterizes the cytomorphologic aspects of category V (SM), although they are not conclusive. In our study, SM was seldomly observed in 5.1% cases and Malignant (M) in 6.8% cases, which is consistent with the study done by Karuna et al, Singh G et al.^{13,32} where they reported 4.76% and 6.8% of cases under SM and M respectively. All of the suspicious cases were recategorized as MEC. Histopathology correlation was available for 2 cases which turned out to be MEC (fig. 3 E). In malignant cases, two were recognized as adenoid cystic carcinoma and two as MEC. Histopathology follow-up was available in all four cases, out of which one turned out to be Warthin tumour. This smear revealed abundant mucinophages, and a few clusters of metaplastic squamous cells in the dirty background of mucin.

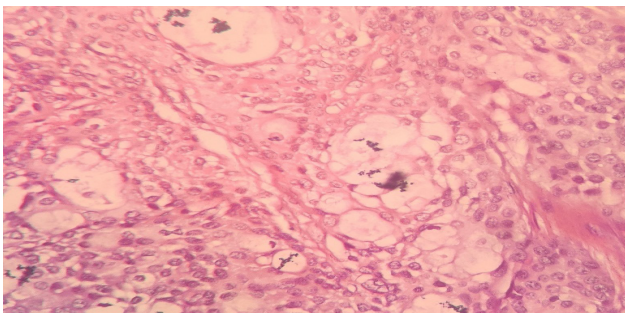


Figure 4: Cytological and histopathological salivary gland lesions (HE stain, X 400)

Variable studies have been conducted to determine the sensitivity, specificity, and ROM (risk of malignancy) for each of the 6 categories, correlate classification with outcomes and demonstrate the usefulness of this approach in everyday practice. However, the present study calculated the inter-assessment technique by using cohen's kappa statistics (k score) which was 0.58 which showed a moderate agreement for MSRSGC and can serve as a very useful tool for reporting salivary gland lesions.

The advantages of the standardized Milan System for Reporting Salivary Gland Cytology (MSRSGC) are, to clarify communication among cytopathologists and treating clinicians, develop tiers of diagnostic categories with corresponding ROM, for pertinent and useful for institutions with all degrees of salivary gland cytology competence and facilitates clinical audits and quality improvement reviews by establishing standards.

The drawback of the present study is that sensitivity, specificity, and accuracy was not been established due to the comparatively smaller sample size, and lack of all histopathology follow-up.

CONCLUSIONS

The study demonstrates consistent findings when compared to research conducted globally and advises the MSRSGC for the standardization of salivary gland FNA reporting. AUS and SUMP will effectively express the clinician's level of suspicion of cancer and will help to reduce the number of false-negative diagnoses. In order to manage discordant cases optimally without requiring a precise diagnosis, lesions might be categorized using MSRSGC along with calculating ROM for each group should be included to aid in patient triage. In light of this, we advise using the Milan system to report salivary gland cytopathology In order to effectively manage the patients.

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