Original Research Article

Diagnostic Accuracy and Risk Stratification of Salivary Gland Lesions Using the Milan System: A Retrospective Study from Western India

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Abstract

Background: Salivary gland lesions form a small but significant proportion of head and neck pathologies. Fine needle aspiration cytology (FNAC) is a crucial diagnostic tool due to its minimally invasive nature and high diagnostic yield. However, due to the heterogeneity of salivary gland lesions, diagnostic challenges remain. To streamline reporting and enhance diagnostic accuracy, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was introduced. This study aims to analyze the applicability and accuracy of MSRSGC in a tertiary care hospital setting in Western India.
Materials and Methods: This is a retrospective study conducted from January 2017 to December 2022 in the Department of Pathology, SBKS MI & RC, Vadodara, Gujarat. A total of 120 FNACs of salivary gland lesions were included. Cytological smears were stained using Hematoxylin and Eosin (H&E), Papanicolaou, and May-Grunwald Giemsa (MGG) stains. Histopathological correlation was available in 50 cases. Risk of malignancy (ROM) was calculated for each MSRSGC category.
Results: Most lesions were classified under Category IVa (Benign neoplasms), with pleomorphic adenoma being the most common diagnosis. The sensitivity, specificity, PPV (Positive predictive Value), NPV (Negative predictive Value), and diagnostic accuracy for malignant lesions were calculated. The ROM for each MSRSGC category was compared with existing literature.

Conclusion: MSRSGC is an effective classification system that provides consistency and clarity in reporting salivary gland cytopathology. It enables better clinical correlation and management of patients.

Key words

Salivary gland, FNAC, Milan system, MSRSGC, Cytopathology, Histopathology.

Introduction

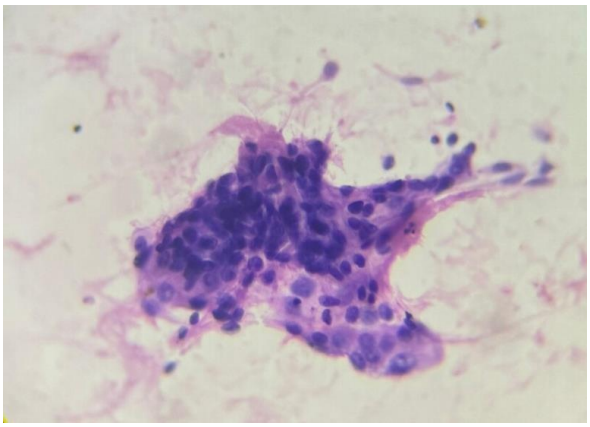
Salivary gland lesions encompass a diverse group of pathologies ranging from inflammatory and reactive conditions to benign and malignant neoplasms. These lesions, although constituting only about 3% to 9% of all head and neck neoplasms, present significant diagnostic challenges due to their overlapping morphological features and varied clinical presentations [1]. Among the major salivary glands, the parotid gland is most frequently involved, followed by the submandibular and sublingual glands. Minor salivary glands, scattered throughout the mucosa of the upper aerodigestive tract, are less commonly affected [2]. Fine Needle Aspiration Cytology (FNAC) has become a valuable initial diagnostic tool for evaluating salivary gland lesions. FNAC provides critical information for preoperative planning, potentially sparing patients from unnecessary surgical interventions in cases of benign or non-neoplastic lesions [3, 4]. However, the diagnostic accuracy of FNAC may be compromised by the heterogeneity of salivary gland tumors, morphological similarities between tumor types, and technical limitations such as poor cellularity and cystic degeneration. To address these diagnostic challenges and standardize cytopathology reporting, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was introduced in 2015. Sponsored by the American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC), the MSRSGC classifies salivary gland FNAC results into six diagnostic categories: Non-diagnostic, Non-neoplastic, Atypia of Undetermined Significance (AUS), Neoplasm (further subdivided into Benign and Salivary Gland Neoplasm of Uncertain Malignant Potential - SUMP), Suspicious for Malignancy, and Malignant. Each category is associated with an implied risk of malignancy (ROM) and provides recommended clinical management guidelines. This study aims to apply the MSRSGC framework to a series of salivary gland FNACs conducted at a tertiary care hospital in Western India. By correlating cytological findings with histopathological outcomes, the study evaluates the diagnostic accuracy, sensitivity, specificity, and predictive values of FNAC. Furthermore, it seeks to estimate the ROM for each MSRSGC category and identify the potential pitfalls in cytological interpretation. The results are compared with existing literature to assess the utility and reproducibility of the MSRSGC in routine clinical practice. This research contributes to the growing body of evidence supporting the implementation of standardized reporting systems in cytopathology to improve diagnostic precision and patient care.

Materials and Methods

A retrospective study was conducted for the duration of 5 years from January 2017 - December 2022 at Department of Pathology, SBKS MI & RC, Vadodara, Gujarat. A total of 120 salivary gland lesions were studied. Out of this, Histopathological examination was available in 50 cases. The Ethical Committee permission was obtained before starting the study. Demographic data and Clinical history of patients and other relevant information were retrieved. Fine needle aspiration cytology was performed and two ethanol fixed smears were stained by Hematoxylin & Eosin stain and Papanicolaou stain. One air dried smear stained by May Grunwald Giemsa stain. These slides were then examined under a light microscope for a cytological and histological diagnosis.

Cytomorphological and Histopathological evaluation of smears and reporting were done. The smears classified according to Milan classification of Salivary Gland Cytopathology into following categories : Category I: Non diagnostic (ND) Category II: Non Neoplastic (NN) Category III: Atypia of undetermined significance (AUS) Category IVa: Benign Neoplasm Category IVb: Salivary gland neoplasm of undetermined significance (SUMP) Category V: Suspicious for malignancy (SFM) Category VI: Malignant (MAL) All cases reclassified according to Milan classification (**Figure - 1, 2, 3, 4, 5**) and Histopathological correlation was done, wherever available. Wilcoxon signed rank test applied to this paired data and sensitivity, specificity, PPV, NPV, ROM and Diagnostic accuracy measured.

Figure - 1: Atypia Of Undetermined significance -The smears are scanty cellular showing cystic fluid and few clusters of atypical cells. The cells are having mild pleomorphism and prominent nucleoli (40X, H & E stain).



Results

A total of 120 salivary gland FNAC cases were analysed over a five-year period, with histopathological correlation available in 50 cases. The cohort included 65 male and 55 female patients, with an age range from 12 to 85 years. The most commonly affected age group was 41–60 years, and the parotid gland was the most frequently involved site (approximately 70% of cases), followed by the submandibular and minor salivary glands (**Table - 1**).

Figure - 2: Non Diagnostic: Cystic fluid: Macrophages only (40X, H & E stain).

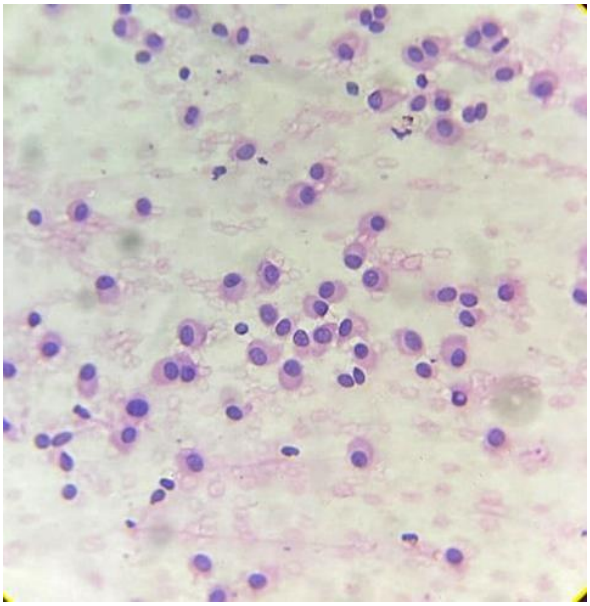
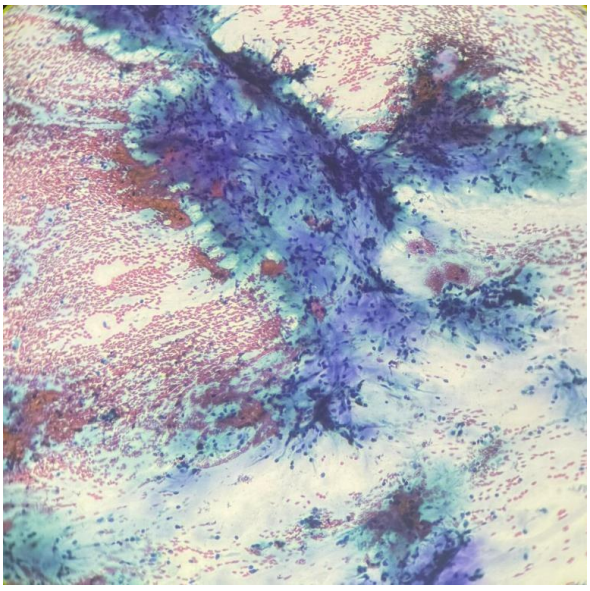


Figure – 3: Benign Neoplasm: Pleomorphic adenoma – The smears are showing fibriller chondromyxoid stroma stained as magenta colour (10X, PAP stain).



Applying the Milan System, cases were distributed among the six diagnostic categories as follows: Non-diagnostic (5 cases, 4.2%), Non-neoplastic (15 cases, 12.5%), AUS (6 cases, 5%), Neoplasm - Benign (60 cases, 50%), SUMP (8 cases, 6.7%), Suspicious for Malignancy (10 cases, 8.3%), and Malignant (16 cases, 13.3%).The most common benign neoplasm was pleomorphic adenoma, followed by Warthin

tumor and oncocytoma. Among malignant lesions, mucoepidermoid carcinoma, adenoid cystic carcinoma, and salivary duct carcinoma was predominant (**Table - 2**).

Figure - 4: SUMP: Cellular Oncocytic/ Oncocytoid Neoplasm – The cellular smears show oncocytoid cells with absence of stroma (40X, H & E stain).

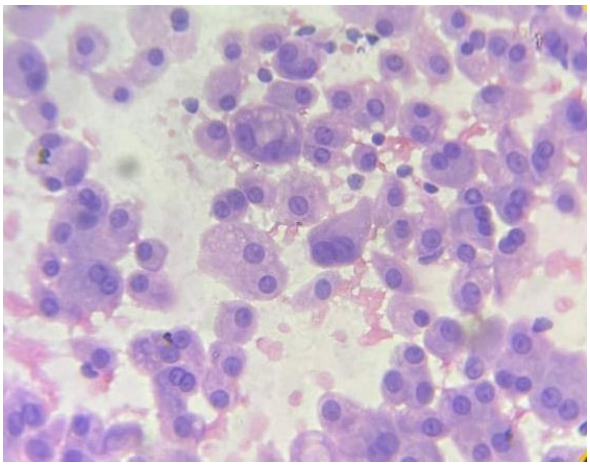


Figure - 5: Malignant: Mucoepidermoid Carcinoma – The smears show mucinophages, intermediate cells with dirty background (10X, H & E stain).

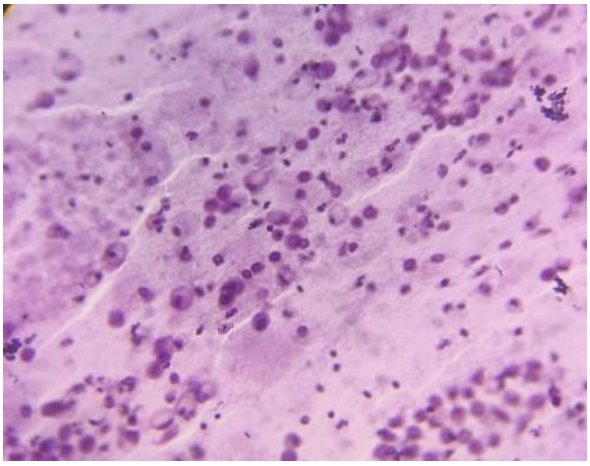


Table – 1: Age wise Distribution of cases.

Age Group (Years)	Number of Cases
0-20	4
21-40	35
41-60	50
61-80	25
81+	6

Table – 2: Distribution of Cases Milan classification and Risk malignancy (ROM).

MSRSGC Category	Number of Cases	ROM (%)
Non-diagnostic	5	20
Non-neoplastic	15	6.7
Atypia of Undetermined Significance (AUS)	6	33.3
Benign Neoplasm	60	1.7
SUMP	8	37.5
Suspicious for Malignancy	10	80
Malignant	16	93.7

Table – 3: Cytological vs Histological Correlation.

Diagnosis	Cytology (n)	Histology (n)	Correlation (%)
Pleomorphic Adenoma	30	28	93.3
Warthin Tumor	10	9	90
Mucoepidermoid Carcinoma	5	4	80
Adenoid Cystic Carcinoma	3	3	100
Oncocytoma	2	2	100

Table – 4: Diagnostic Metrics for Malignant Lesions.

Metric	Value (%)
Sensitivity	92
Specificity	95
Positive Predictive Value	90
Negative Predictive Value	96
Overall Diagnostic Accuracy	94

Histopathological correlation confirmed the cytological diagnoses in the majority of cases. Pleomorphic adenomas showed a 93.3% concordance rate between cytology and histology, while mucoepidermoid carcinomas and adenoid cystic carcinomas demonstrated accuracies of 80% and 100%, respectively. The ROMs were calculated for each MSRSGC category, showing a gradient of risk that aligned with the original system's recommendations: Non-diagnostic (20%), Non-neoplastic (6.7%),

AUS (33.3%), Benign (1.7%), SUMP (37.5%), Suspicious for Malignancy (80%), and Malignant (93.7%) (**Table - 3**).

Statistical analysis of the FNAC results, taking histopathological outcomes as the gold standard, yielded a sensitivity of 92% and specificity of 95% for detecting malignancy. The positive predictive value (PPV) was 90%, the negative predictive value (NPV) was 96%, and the overall diagnostic accuracy was 94% (**Table - 4**).

These results validate the effectiveness of the MSRSGC in stratifying salivary gland lesions and guiding clinical management. The few discordant cases were primarily due to overlapping cytomorphologic features or suboptimal sample quality, which underscores the importance of operator expertise and sample adequacy. The study confirms that MSRSGC serves as a reliable framework for cytopathological evaluation and enhances communication between pathologists and clinicians in managing salivary gland lesions.

Discussion

The implementation of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) has brought much-needed clarity and consistency to the diagnosis and management of salivary gland lesions. The findings of this study corroborate the effectiveness of the MSRSGC in real-world settings, particularly in resource-limited tertiary care institutions. The distribution of cases among MSRSGC categories in our study closely aligns with patterns reported in previous literature. The predominance of benign neoplasms, particularly pleomorphic adenoma, echoes findings by Maleki, et al. [5] and Rossi, et al. [3], who also reported high rates of benign diagnoses within FNAC samples. Similarly, the rates of malignant lesions, especially mucoepidermoid carcinoma and adenoid cystic carcinoma, reflect the known epidemiological distribution of salivary gland tumors in the Indian population [6, 7, 8].

Our study demonstrates a high overall diagnostic accuracy of 94%, with sensitivity and specificity of 92% and 95%, respectively, for malignant lesions. These results are comparable to the data published in studies by Faquin, et al. [1], who reported sensitivities ranging from 86% to 95% and specificities between 89% and 98%. This confirms the Milan System's utility in accurately stratifying lesions and guiding clinical decision-making. The calculated ROMs across MSRSGC categories followed the expected gradient, with benign categories showing low ROMs (Non-neoplastic: 6.7%; Benign: 1.7%) and malignant categories demonstrating high ROMs (Suspicious for Malignancy: 80%; Malignant: 93.7%). These values are consistent with those found in large-scale meta-analyses and support the validity of the MSRSGC as a risk-based stratification tool [4].

The category of AUS poses a notable diagnostic challenge. Although intended to capture equivocal or borderline findings, its use should be limited to no more than 10% of cases. In our study, the AUS rate was 5%, aligning with MSRSGC recommendations. The ROM for AUS (33.3%) was within the expected range but also highlights the importance of close clinical and radiological correlation, repeat FNACs, and possible surgical follow-up for definitive diagnosis [2, 9, 10]. The SUMP category is another area requiring careful interpretation. In our cohort, it constituted 6.7% of cases, with a ROM of 37.5%. This category encapsulates neoplasms with uncertain behavior, which can lead to either overtreatment or underdiagnosis. As emphasized by Rossi and Faquin [1, 3], the integration of ancillary studies, including immunocytochemistry and molecular diagnostics, can assist in clarifying indeterminate cases.

Discordant cases in our study primarily stemmed from low cellularity, cystic change, or overlapping features between benign and malignant neoplasms. These limitations are not unique and have been well-documented in other MSRSGC-based studies [2, 7, 8]. The findings

reiterate the need for adequate sampling techniques and the importance of correlating cytologic findings with clinical and radiological inputs [11, 12, 13]. An important strength of the Milan System is its ability to bridge communication between cytopathologists and clinicians. By associating each diagnostic category with a management algorithm and ROM, the system transforms cytologic interpretations into actionable clinical strategies. This attribute has been highly beneficial in streamlining decision-making, especially in multidisciplinary tumor boards and preoperative consultations [1, 2]. From a global perspective, the standardization of salivary gland cytopathology has facilitated multi-centric research, data pooling, and comparative analyses. Countries that have adopted the MSRSGC, including the USA, UK, Japan, and several European and Asian nations, report similar diagnostic patterns and performance metrics. This supports the Milan System's reproducibility across geographic and institutional contexts [14, 15, 16]. Despite its advantages, MSRSGC is not devoid of challenges. There remains a learning curve in adapting the classification, especially among institutions new to salivary gland cytology. Continuous training, updates to diagnostic criteria, and incorporation of digital pathology tools may enhance diagnostic consistency and accuracy further [15, 17, 18].

Conclusion

This study reaffirms that the Milan System is a robust and reliable reporting framework for salivary gland cytopathology. Its integration into routine practice significantly improves diagnostic precision, enhances communication between clinicians and pathologists, and supports informed clinical decision-making. Further studies involving larger cohorts and long-term follow-up are warranted to refine risk stratification and evaluate the impact on patient outcomes.

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