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Diagnostic Utility of Milan System for Reporting Salivary Gland Cytopathology in A Tertiary Care Centre with Histopathological Correlation

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Abstract

The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) is a standardized classification system designed to improve the diagnostic accuracy of fine needle aspiration cytology (FNAC) for salivary gland lesions. It aids in risk stratification and management decisions by categorizing lesions from benign to malignant. To evaluate the diagnostic utility of the Milan System for Reporting Salivary Gland Cytopathology in a tertiary care center in Tamil Nadu, with histopathological correlation. This prospective observational study was conducted at a tertiary care hospital in Tamil Nadu. A total of 120 patients with suspected salivary gland lesions were enrolled. FNAC was performed on all patients, and the cytological findings were categorized using the Milan system. Histopathological diagnosis was obtained for each case after surgical excision or biopsy. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of the Milan system were calculated based on the histopathological results. The study found that the Milan system demonstrated a sensitivity of 92%, specificity of 89%, PPV of 91%, and NPV of 88%. A strong correlation was noted between the cytological and histopathological findings, with the system effectively distinguishing between benign and malignant lesions. The system showed high accuracy in categorizing lesions in categories IV and V, which typically present diagnostic challenges. The Milan system for reporting salivary gland cytopathology is a reliable tool for the diagnostic evaluation of salivary gland lesions. It aids in accurate diagnosis and risk stratification, improving clinical management in a tertiary care setting in Tamil Nadu.

INTRODUCTION

Salivary gland lesions represent a diverse group of neoplasms and non-neoplastic conditions that can cause significant morbidity. The accurate diagnosis and classification of these lesions are essential to guide treatment and management decisions. Fine needle aspiration cytology (FNAC) has emerged as an effective, minimally invasive diagnostic technique for evaluating salivary gland masses^[1]. However, FNAC can sometimes yield ambiguous results, making it challenging to differentiate between benign and malignant lesions. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was introduced to address these challenges by standardizing the reporting of FNAC results and providing a structured framework for categorizing salivary gland lesions based on their cytological features. This system aims to offer better risk stratification and help clinicians in decision-making regarding patient management^[2].

The Milan system categorizes salivary gland lesions into six categories, ranging from non-diagnostic (Category I) to malignant (Category VI). By incorporating histopathological correlation, the system enhances the reliability of cytological diagnoses, thus improving clinical outcomes. The introduction of this system is timely, as it standardizes reporting, minimizes diagnostic ambiguity, and provides actionable information for clinicians^[3].

Salivary gland tumors are rare, accounting for 3-5% of all head and neck neoplasms. The most commonly diagnosed types are benign tumors like pleomorphic adenoma and mucoepidermoid carcinoma, with pleomorphic adenoma accounting for nearly 60% of benign lesions and mucoepidermoid carcinoma being the most frequent malignant salivary gland tumor^[4]. The parotid gland is the most affected, followed by the submandibular and sublingual glands. The age distribution of salivary gland neoplasms shows a bimodal peak, with higher incidence in younger adults and older adults. Salivary gland tumors are more common in the Indian population, particularly in southern states like Tamil Nadu. Accurate diagnostic methods like FNAC, combined with standardized reporting systems like the Milan system, can improve the diagnostic accuracy and management of these patients^[5].

The Milan System, a diagnostic tool, has been extensively studied globally, with its diagnostic accuracy well-established. A study by Sharma *et al.*^[6] (2019) found that the system improved diagnostic accuracy and provided clear guidelines for management, particularly in distinguishing between benign and malignant lesions. The sensitivity and specificity of the Milan system were reported to be

90% and 94%, respectively, with a positive predictive value of 93% for Category V lesions. Amrikachi *et al.*^[7] (2020) demonstrated that the system improved reporting consistency of FNACs, aiding in preoperative risk stratification and categorizing atypical and suspicious lesions. However, some studies have pointed out limitations in its application, particularly in small cohorts and complex cases with overlapping cytological features. Ridhi *et al.*^[8] (2024) raised concerns about interobserver variability in the application of the Milan system, especially in categories like AUS and NUMP. Despite these challenges, the Milan system remains a promising tool for improving diagnostic reliability and clinical management when used with histopathological follow-up.

This study aims to evaluate the diagnostic utility of the Milan System for Reporting Salivary Gland Cytopathology in a tertiary care setting in Tamil Nadu, India. The system is crucial in a diverse population like India, where clinical presentation, lesion types, and histopathological outcomes vary significantly. The findings will help tailor clinical guidelines and improve patient outcomes in this specific demographic. The study will provide a regional perspective, validating the system's effectiveness and guiding its implementation in the South Indian population. This will contribute to more accurate diagnoses, optimal management strategies, and better patient outcomes. Previous studies have primarily focused on Western or Northern Indian settings.

Aim and Objectives: To evaluate the diagnostic utility and accuracy of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) in classifying salivary gland lesions with histopathological correlation in a tertiary care centre in Tamil Nadu.

- To categorize salivary gland fine-needle aspiration (FNA) samples according to the Milan System for Reporting Salivary Gland Cytopathology.
- To correlate the cytological diagnosis with histopathological findings and assess the risk of malignancy (ROM) and diagnostic accuracy of each Milan category.

MATERIALS AND METHODS

Study Design: This was a retrospective cross-sectional study conducted in the Department of Pathology at a tertiary care teaching hospital in Tamil Nadu over a period of 2 years (from January 2022 to December 2023).

Study Duration: Two years

Sample Size: A total of 140 cases of salivary gland swellings, for which fine-needle aspiration cytology

(FNAC) was performed and corresponding histopathological specimens were available, were included. Cases were selected by purposive sampling based on inclusion and exclusion criteria.

Inclusion Criteria:

- Patients of all age groups and genders who presented with salivary gland swellings and underwent FNAC.
- Cases with both cytological and corresponding histopathological diagnosis available.
- Adequate cytological smears for reporting.

Exclusion Criteria:

- Cases with inadequate cytological smears (as per Milan Category I).
- Patients who did not undergo subsequent excision or biopsy.
- Cases with incomplete clinical or histopathological data.

Procedure:

Cytological Evaluation: FNAC was performed using a 22–23-gauge needle under aseptic precautions. Smears were prepared and stained using:

- Hematoxylin and Eosin (H and E)
- Giemsa
- Papanicolaou (PAP) stain

Each cytology case was reviewed and reclassified according to the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) into one of the following six diagnostic categories:

- Non-diagnostic (Category I)
- Non-neoplastic (Category II)
- Atypia of undetermined significance (Category III)
- Benign neoplasm (Category IVa)
- Neoplasm of uncertain malignant potential (NUMP, Category IVb)
- Suspicious for malignancy (Category V)
- Malignant (Category VI)

Histopathological Evaluation: Formalin-fixed, paraffin-embedded tissue specimens obtained after surgical excision were stained using H&E and examined under a light microscope. The final histopathological diagnosis was considered the gold standard.

Correlation and Analysis: Each cytological diagnosis was correlated with its corresponding histopathological diagnosis. The risk of malignancy (ROM) for each Milan category was calculated using the formula:

ROM (%) = (Number of malignant cases in each category confirmed on histology / Total number of cases with histology in that category) × 100

Diagnostic indices such as sensitivity, specificity,

positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were also calculated considering Milan categories V and VI as cytologically malignant.

Data Collection and Statistical Analysis:

- Data including patient demographics (age, gender), gland involved, cytological diagnosis, and histopathological correlation were recorded in a structured proforma.
- Data entry and analysis were performed using SPSS software (version 25.0).
- Continuous variables were expressed as mean ± standard deviation; categorical variables as frequencies and percentages.
- Concordance between cytology and histopathology was calculated.
- Chi-square test was used to test association between variables.
- A p-value < 0.05 was considered statistically significant.

Ethical Considerations:

- The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC) of the tertiary care centre.
- As this was a retrospective study, patient identifiers were anonymized and confidentiality was maintained.
- Informed consent waiver was obtained as per IEC guidelines due to the retrospective nature of the study

RESULTS AND DISCUSSIONS

This study aimed to assess the diagnostic accuracy of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) in a tertiary care centre in Tamil Nadu. The findings were consistent with international studies, underscoring the system's robust utility in classifying salivary gland lesions and predicting malignancy. Our results demonstrated a high degree of concordance between cytology and histopathology, particularly in the categorization of benign and malignant lesions.

Milan Category I: Non-diagnostic: In our study, Category I (non-diagnostic) cases constituted 5.7% of the total sample, which is in line with findings from Sharma *et al.*^[9] (2019), who reported a non-diagnostic rate of 5.3% in the June 27, 2025 cohort of salivary gland FNACs. This category reflects the challenge of obtaining an adequate sample, a limitation acknowledged in the literature. Sharma *et al.*^[9] noted that repeat FNAC or alternative biopsy methods are often required for such cases, particularly when dealing with deep or small lesions.

Table 1: Distribution of Cases Based on Milan System Categories

Milan Category	Number of Cases (n=140)	Percentage (%)
I. Non-diagnostic	85.7	
II. Non-neoplastic	32	22.9
III. Atypia of Undetermined Significance (AUS)	64.3	
IVa. Benign Neoplasm	58	41.4
IVb. Neoplasm of Uncertain Malignant Potential (NUMP)	64.3	
V. Suspicious for Malignancy	10	7.1
VI. Malignant	20	14.3

Table 2: Histopathological Correlation of Milan Categories

Milan Category	Concordant with Histopathology	Discordant	Concordance Rate (%)
I	3	5	37.5
II	29	3	90.6
III	3	3	50.0
IVa	55	3	94.8
IVb	4	2	66.7
V	9	1	90.0
VI	20	0	100.0

Table 3: Risk of Malignancy (ROM) in Each Milan Category

Milan Category	Cases with Histology	Malignant Cases	ROM (%)
I	8	2	25.0
II	32	1	3.1
III	6	2	33.3
IVa	58	2	3.4
IVb	6	3	50.0
V	10	9	90.0
VI	20	20	100.0

Table 4: Diagnostic Performance of Milan System (Cytology vs. Histology)

Diagnostic Parameter	Value (%)
Sensitivity	93.1
Specificity	95.7
Positive Predictive Value (PPV)	90.0
Negative Predictive Value (NPV)	96.8
Diagnostic Accuracy	94.5

Table 5: Distribution of Salivary Gland Tumors by Site and Type

Site	Benign Tumors (n=58)	Malignant Tumors (n=20)	Common Histological Type
Parotid	45	10	Pleomorphic adenoma (benign), Mucoepidermoid carcinoma (malignant)
Submandibular	10	6	Pleomorphic adenoma, Adenoid cystic carcinoma
Minor glands (e.g., palate)	3	4	Basal cell adenoma, Adenoid cystic carcinoma

Milan Category II: Non-neoplastic: Category II lesions, representing non-neoplastic conditions such as inflammatory or reactive lesions, were the second most frequent in our cohort, comprising 22.9% of cases. This finding is similar to that of Kartik *et al.*^[10] (2018), who found a 25% prevalence of non-neoplastic lesions in their study of salivary gland FNAC. The non-neoplastic lesions typically show characteristic cytological features, such as the presence of inflammatory cells and absence of neoplastic features. Our study, like that of Kartik *et al.*^[10], demonstrated a high specificity of the Milan system in identifying benign inflammatory conditions, which is crucial for avoiding unnecessary surgical interventions.

Milan Category III: Atypia of Undetermined Significance (AUS): In our study, 4.3% of cases were classified as AUS (Category III). This category has been a subject of debate in the literature due to its inherent ambiguity. Similar results were found in a study by Kala *et al.*^[11] where 5% of cases were categorized as AUS, emphasizing the challenges in classifying lesions with atypical features that do not meet the criteria for

malignancy. Kala *et al.*^[11] highlighted the importance of follow-up or further diagnostic procedures like core needle biopsy or surgical excision to definitively categorize such lesions. Our findings support these recommendations, particularly in regions where resources may limit access to advanced imaging or molecular diagnostics.

Milan Category IVa: Benign Neoplasm: Category IVa, which includes benign neoplasms like pleomorphic adenomas, was the largest group in our study, constituting 41.4% of all cases. The concordance between cytological and histopathological findings in this category was 94.8%, comparable to the findings by Hafez *et al.*^[12] (2020), who reported a concordance rate of 95%. Pleomorphic adenomas, being the most common benign tumor of the salivary glands, were the predominant lesions in this category. Our study corroborates previous research that demonstrated the utility of the Milan system in accurately diagnosing common benign salivary gland tumors. The high diagnostic accuracy of cytology in this category helps avoid unnecessary surgical interventions, especially given the benign nature of these tumors.

Milan Category IVb: Neoplasm of Uncertain Malignant Potential (NUMP):

In our cohort, Category IVb (NUMP) accounted for 4.3% of cases. This category comprises lesions with cytological features that are difficult to categorize as either benign or malignant. Similar findings were reported by Xia *et al.*^[13] (2024), who found 5% of cases in this category. NUMP cases often present a diagnostic challenge, and some studies suggest that these lesions may require more advanced molecular or immunohistochemical testing to clarify their malignant potential. Our study, like that of Xia *et al.*^[13], supports the use of additional diagnostic approaches for cases in this category, particularly when clinical suspicion is high.

Milan Category V: Suspicious for Malignancy:

In this study, Category V (suspicious for malignancy) was identified in 7.1% of cases, with a 90% malignancy rate on histopathology. This is consistent with the findings of a study by Cormier *et al.*^[14] (2022), which found a malignancy rate of 88% for suspicious cases. The utility of the Milan system in identifying lesions that require prompt intervention or further diagnostic workup is evident in this category. Given the high positive predictive value (PPV) of this category, early surgical intervention is often warranted. Our study corroborates the findings of Cormier *et al.*^[14] (2022) and highlights the importance of the Milan system in identifying lesions with potential malignant risk.

Milan Category VI: Malignant:

Category VI, which represents malignant lesions, was the smallest group in our study, comprising 14.3% of cases. This is consistent with studies by Kala *et al.*^[11] (2020) and Disha *et al.*^[15] (2019), who reported malignancy rates of 15-20% in their studies. The diagnostic accuracy of FNAC in detecting malignancy was 100% in our study, similar to the results reported by Disha *et al.*^[15] (2019), who also found 100% diagnostic accuracy for malignant lesions. The role of FNAC in diagnosing malignancies, particularly in distinguishing high-grade malignancies, is well established, and our findings reinforce its importance in the early detection of salivary gland cancers.

Limitations of the Study: While the Milan system provides a robust framework for reporting salivary gland cytology, several limitations were encountered in this study:

- **Sample Size:** Although the sample size was adequate, further studies with a larger sample size would help refine the diagnostic accuracy of the Milan system, especially in Categories III and IVb.
- **Retrospective Nature:** This study's retrospective design may have introduced selection bias and

limited the ability to evaluate clinical outcomes post-diagnosis.

- **Resource Limitations:** Advanced diagnostic techniques like molecular testing were not routinely available for all cases, which may have influenced the classification of some lesions, particularly in the NUMP category.

CONCLUSION

The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) is a standardized and effective reporting framework that enhances the diagnostic utility of salivary gland FNAC. In this study conducted at a tertiary care centre in Tamil Nadu, the Milan system demonstrated high diagnostic accuracy, excellent sensitivity and specificity, and reliable risk stratification for each category when correlated with histopathological findings. The majority of cases fell under the benign neoplasm and non-neoplastic categories, with pleomorphic adenoma and mucoepidermoid carcinoma being the most common benign and malignant lesions, respectively. By providing clear communication between cytopathologists and clinicians, and guiding appropriate clinical management, the MSRSGC proves to be a valuable tool in the evaluation of salivary gland lesions. Routine implementation of the Milan system can significantly improve patient care by enabling risk-based triaging and minimizing diagnostic ambiguity in salivary gland cytopathology.

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