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Original Research

Assessing Salivary Gland Lesions Through the Milan Grading System: A Cytological Approach

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Abstract

Background: Salivary gland lesions encompass a wide spectrum of benign and malignant conditions, necessitating accurate classification for appropriate clinical management. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) provides a standardized framework to improve diagnostic accuracy and communication between clinicians and pathologists.

Aim: To classify salivary gland lesions according to the Milan System and evaluate the prevalence and risk of malignancy in different categories.

Methods: This observational study included 72 patients with salivary gland swellings who underwent fine-needle aspiration cytology (FNA) at a tertiary care hospital from 2022 to 2024. Cytological findings were categorized using the Milan System into six diagnostic groups. Demographic data, lesion distribution, and malignancy risk were analyzed using SPSS version 23.0, with a significance level set at $p < 0.05$.

Results: Among 72 cases, 40 (55.6%) were neoplastic, with pleomorphic adenoma being the most common benign tumor (33.3%). Non-neoplastic lesions accounted for 10 cases (13.9%), while 5 cases (6.9%) were nondiagnostic. Suspicious for malignancy (SFM) and malignant categories comprised 9 (12.5%) and 11 (15.3%) cases, respectively, including mucoepidermoid carcinoma and carcinoma ex pleomorphic adenoma. The parotid gland was most frequently affected (55.6%), with a higher incidence of malignancy in the submandibular and minor salivary glands.

Conclusion: The Milan System provides a systematic approach to stratifying salivary gland lesions, facilitating early diagnosis and clinical decision-making. However, diagnostic uncertainty in SUMP and AUS categories highlights the need for histopathological confirmation.

Recommendations: Further studies with larger sample sizes and the use of ancillary techniques such as immunocytochemistry and molecular testing are recommended to improve diagnostic accuracy. Continuous training in the Milan System can enhance consistency in reporting.

Keywords: Salivary gland lesions, Milan System, FNAC, pleomorphic adenoma, cytopathology

Introduction

Salivary gland lesions encompass a diverse array of pathologies, ranging from benign neoplasms to malignant tumors and non-neoplastic conditions. Accurate diagnosis of these lesions is crucial for determining appropriate clinical management strategies. (FNAC) has emerged as a minimally invasive, cost-effective, and reliable diagnostic tool for evaluating salivary gland masses. However, the absence of a standardized reporting system historically led to variability in FNAC interpretations, potentially causing miscommunication between cytopathologists and clinicians. To address this issue, the (MSRSGC) was introduced, providing a uniform framework for the assessment and reporting of salivary gland cytology specimens.

The MSRSGC was created in 2018 and divides salivary gland FNAC results into six diagnostic categories: malignant, suspicious for malignancy, neoplasm (including benign neoplasms and salivary gland neoplasms of uncertain malignant potential [SUMP]), atypia of undetermined significance (AUS), nondiagnostic, and non-neoplastic. Every group has a related clinical care advice and an implied risk of

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malignancy (ROM). For example, the malignant category has a ROM of around 90%, indicating the necessity for surgical intervention, whereas the nondiagnostic category has a ROM of about 25%, indicating the need for clinical and radiologic correlation or repeat FNAC [1].

The implementation of the MSRSGC has significantly enhanced the clarity and consistency of salivary gland cytology reporting. By standardizing diagnostic terminology and correlating each category with specific ROMs and management guidelines, the MSRSGC facilitates effective communication between cytopathologists and clinicians, ultimately improving patient care. A study by Rossi et al. (2019) demonstrated that the application of the MSRSGC led to more precise risk stratification and management decisions, thereby reducing unnecessary surgeries and associated morbidities [2].

Recent studies have validated the diagnostic accuracy and clinical utility of the MSRSGC across diverse populations and clinical settings. A comprehensive meta-analysis by Wei et al. (2020) encompassing over 4,000 salivary gland FNAC cases reported that the MSRSGC effectively stratifies lesions based on their malignancy risk, with ROMs aligning closely with the system's proposed estimates [3]. Furthermore, the MSRSGC's structured approach aids in identifying cases that may benefit from ancillary testing, such as immunocytochemistry or molecular studies, to refine diagnoses and guide therapeutic decisions [4].

The second edition of the MSRSGC, published in 2023, incorporates updates based on accumulated evidence and user feedback since its initial release. This edition refines ROM estimates for each diagnostic category, integrates advancements in ancillary testing methodologies, and emphasizes the role of multidisciplinary collaboration in managing salivary gland lesions [5]. These updates aim to further enhance the system's diagnostic precision and clinical applicability.

In conclusion, the MSRSGC represents a pivotal advancement in the field of cytopathology, offering a standardized, evidence-based framework for reporting salivary gland FNAC findings. Its widespread adoption has improved diagnostic accuracy, facilitated effective communication among healthcare providers, and informed clinical management strategies, ultimately benefiting patient outcomes. Ongoing research and periodic updates to the system ensure that it remains aligned with emerging scientific evidence and evolving clinical practices. This study aims to assess salivary gland lesions using the Milan Grading System, categorize them based on cytological findings, and determine the prevalence of benign, malignant, and inflammatory conditions among patients at GMC Rajouri.

Methodology

Study Design

This study is a hospital-based observational study.

Study Setting

The study was conducted at Government Medical College (GMC) Rajouri, a tertiary care hospital in India. The research was carried out over a period of two years, from 2022 to 2024.

Participants

A total of **72 patients** with salivary gland lesions were included in this study. The cases were classified according to the **Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)**, providing a structured approach to categorize salivary gland cytology into six diagnostic categories. Each category represents a different risk of malignancy (ROM) and guides subsequent management.

Inclusion Criteria

- Patients presenting with salivary gland swellings undergoing FNAC.
- Individuals of all age groups and genders.
- Patients willing to participate and provide informed consent.

Exclusion Criteria

- Patients with recurrent salivary gland tumors post-surgery.
- Inadequate or unsatisfactory FNAC samples.
- Patients with a history of radiation therapy to the head and neck region.

Bias

To minimize selection bias, consecutive patients meeting the inclusion criteria were enrolled. Observer bias was reduced by involving multiple pathologists in the cytological assessment. Additionally, the FNAC slides were reviewed by an independent pathologist to ensure consistency in grading.

Data Collection

The patients' FNAC reports, clinical histories, and demographic information were gathered. Using Milan's Grading System, the lesions were divided into three categories: benign, malignant, and non-neoplastic. When required, immunocytochemistry and special stains were employed for additional classification.

Procedure

(FNAC) was performed using a 22–24 gauge needle with a 10 mL syringe. The aspirated material was smeared onto slides, air-dried, and stained using Giemsa and Papanicolaou stains. The lesions were classified as follows:

1. Sialadenosis
2. Acute sialadenitis
3. Chronic sialadenitis
4. Granulomatous sialadenitis
5. Retention cysts
6. Cystic lesion
7. Pleomorphic adenoma

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8. Warthin's tumor
9. Low-grade mucoepidermoid carcinoma
10. Suspicious of malignancy

Statistical Analysis

Microsoft Excel was used to enter all of the obtained data, and SPSS version 23.0 was used for analysis. Data were summarized using descriptive statistics, such as frequency distributions, mean, and standard deviation. A significance level of $p < 0.05$ was established for the chi-square test, which was used to evaluate relationships between categorical variables.

Results

A total of **72 patients** with **salivary gland lesions** were included in this study. The cases consisted of a range of cytological diagnoses, categorized according to the **Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)**. The lesions were classified into six diagnostic categories, from **nondiagnostic** to **malignant**, to systematically assess their clinical significance and risk of malignancy.

The classification was based on histopathological and cytological features observed in **fine-needle aspiration (FNA)** samples.

Table 1: Overall Distribution of Salivary Gland Lesions (Milan Categories)

Category	Number of Cases (n)	Percentage (%)	Risk of Malignancy (ROM)
I. Nondiagnostic	5	6.9	25
II. Non-neoplastic	10	13.9	10
III. Atypia of Undetermined Significance (AUS)	8	11.1	20
IV. Neoplasm	40	55.6	Variable
V. Suspicious for Malignancy (SFM)	9	12.5	60
VI. Malignant	11	15.3	90
Total	**72**	**100**	

1. Category I: Nondiagnostic (6.9%)

This category included **5 cases**, where cytological material was insufficient for a conclusive diagnosis.

Subtype	Number of Cases (n)	Example Conditions
Poor cellularity	2	Blood contamination, sparse cells
Cystic fluid without epithelium	3	Mucinous cysts, retention cysts
Total	**5**	

- Repeat FNAs or imaging-guided biopsies were recommended for all cases.

2. Category II: Non-neoplastic (13.9%)

10 cases were classified as non-neoplastic lesions. These are inflammatory or degenerative conditions often mimicking neoplasms clinically.

Subtype	Number of Cases (n)	Example Conditions
Sialadenosis	3	Non-inflammatory swelling
Acute / Chronic Sialadenitis	4	Long-standing inflammation
Cystic lesions/Retention cysts	2	Fluid-filled retention cysts
Granulomatous inflammation	1	Granulomatous response due to infection
Total	**10**	

- Conservative management or infection control was sufficient in most cases.

3. Category III: Atypia of Undetermined Significance (AUS) (11.1%)

8 cases presented with atypical features that did not conclusively indicate malignancy.

Findings	Number of Cases (n)	Cytological Features
Nuclear enlargement and pleomorphism	5	Mild pleomorphism with scant cells
Cytoplasmic vacuolization	2	Cytoplasmic changes with indeterminate features
Focal nuclear atypia	1	Few atypical cells not meeting malignant criteria
Total	**8**	

- Repeat FNA and imaging were recommended for further evaluation.

4. Category IV: Neoplasm (55.6%)

This was the largest category, with **40 cases**, further classified into benign and neoplasms of uncertain malignant potential (SUMP).

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Subtype	Number of Cases (n)	Common Diagnoses
IVA. Neoplasm: Benign	25	Pleomorphic Adenoma (24), Warthin's Tumor (1)
IVB. Neoplasm: SUMP	15	Indeterminate features of malignancy
Total	**40**	

- **Pleomorphic adenoma** was the most common benign tumor.
- SUMP cases required histopathological confirmation.

5. Category V: Suspicious for Malignancy (SFM) (12.5%)

9 cases were classified as suspicious for malignancy due to prominent atypia without definitive features.

Findings	Number of Cases (n)	Cytological Features
Prominent nucleoli	4	Enlarged nuclei with irregular contours
Nuclear pleomorphism	3	Severe pleomorphism without invasion
Increased nuclear-cytoplasmic ratio	2	High N/C ratio with mitotic activity
Total	**9**	

- Surgical excision or core biopsy was recommended for definitive diagnosis.

6. Category VI: Malignant (15.3%)

11 cases were classified as malignant, including common and rare malignancies.

Subtype	Number of Cases (n)	Common Diagnoses
Mucoepidermoid carcinoma (MEC)	3	Low-grade, cystic or solid appearance
Carcinoma ex Pleomorphic Adenoma (Ca ex PA)	4	Malignant transformation from PA
Other malignant tumors	4	Adenoid cystic carcinoma, others
Total	**11**	

- Malignant lesions presented with high-grade cytological features, including hyperchromasia and mitotic activity.

Table 7: Glandular Distribution of Lesions

Gland	Number of Cases (n)	Percentage (%)
Parotid gland	40	55.6
Submandibular gland	15	20.8
Minor salivary glands	12	16.7
Sublingual gland	5	6.9
Total	**72**	**100**

- The **parotid gland** was the most frequently affected.
- Minor salivary glands had a higher proportion of malignant lesions.

Key Findings:

- **Benign tumors**, particularly **pleomorphic adenoma**, were the most common lesion.
- **Non-neoplastic and AUS** categories required repeat FNAs due to diagnostic uncertainty.
- **SUMP and SFM** categories indicated diagnostic challenges, necessitating histopathological correlation.
- **Carcinoma ex Pleomorphic Adenoma** in the malignant category underscored the need for vigilant follow-up.

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FIG 1: Cystic lesions

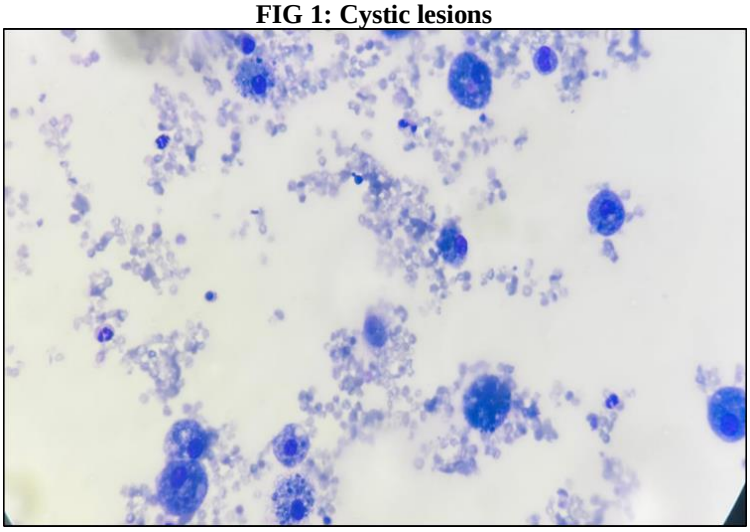

FIG 2: Granulomatous sialadenitis

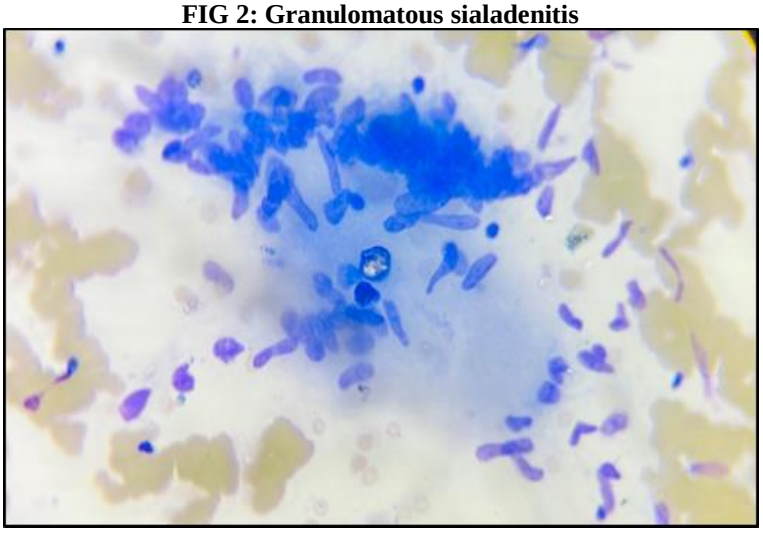

FIG 3: Pleomorphic Adenoma

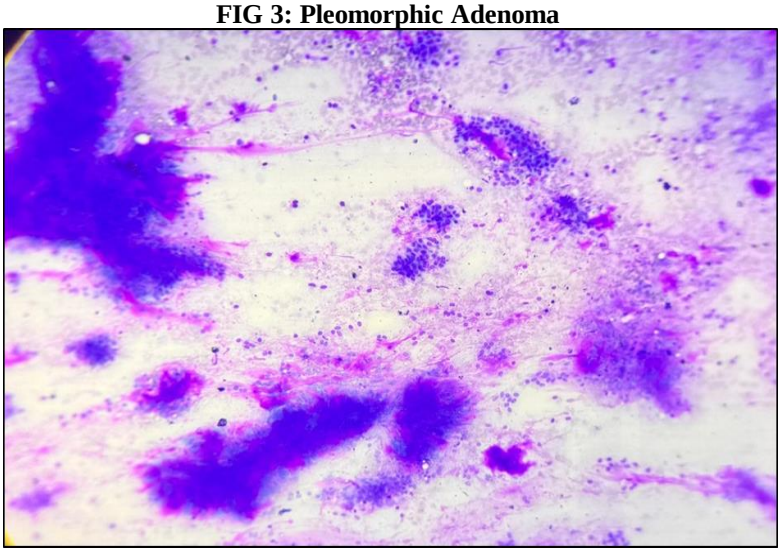

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FIG 4: Low grade mucoepidermoid carcinoma

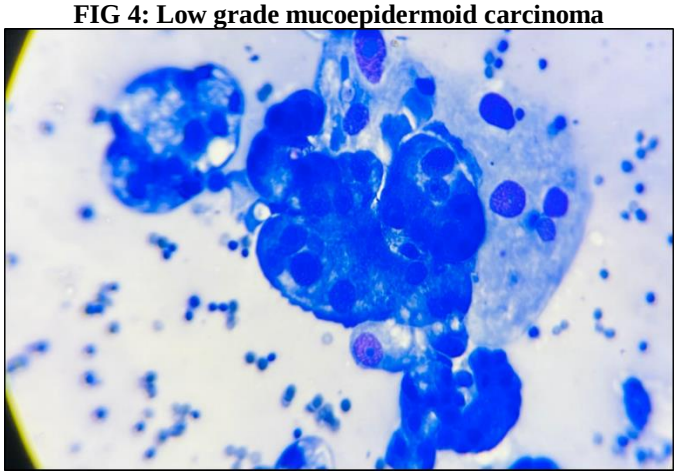


FIG 5: Retention cyst

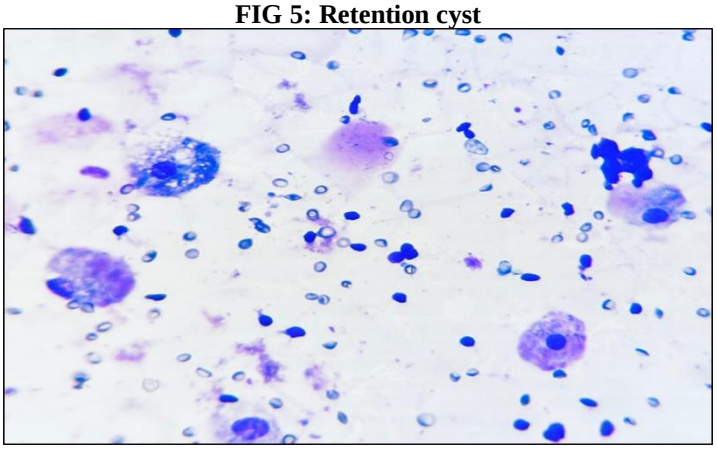
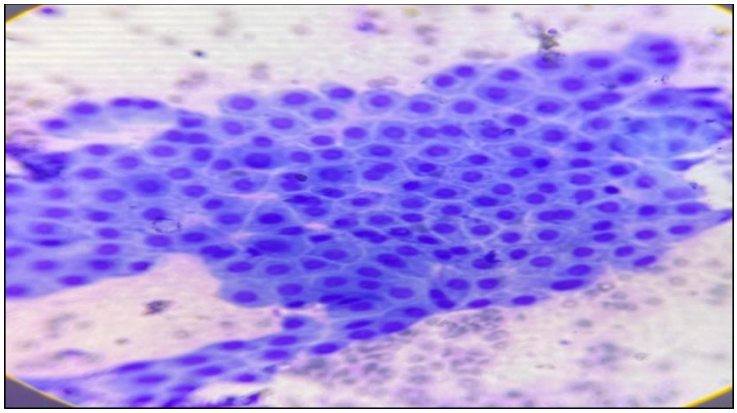


FIG 6: Warthin Tumour



Discussion

This study included 72 patients with salivary gland lesions. The majority of the cases fell under the neoplasm category (55.6%), reflecting the high prevalence of tumors in salivary gland pathologies. Within this group, pleomorphic adenoma (PA) emerged as the most common benign neoplasm, accounting for 24 cases, while Warthin's tumor was identified in one case. Additionally, 15 cases were categorized as (SUMP), highlighting the diagnostic challenges in differentiating between benign and low-grade malignant lesions based on cytology alone.

The nondiagnostic category (6.9%) consisted of 5 cases, where inadequate cellularity or cystic fluid hindered conclusive diagnosis. Such cases emphasize the importance of repeat (FNA) or advanced imaging techniques for accurate evaluation. Meanwhile, the non-neoplastic category (13.9%), with 10 cases, included inflammatory conditions like chronic sialadenitis, sialadenosis, and retention cysts. These lesions often mimic neoplasms clinically but can be managed conservatively once diagnosed.

Cases classified as (AUS) represented 11.1% of the total, indicating the presence of cytological atypia insufficient for a definitive diagnosis. Repeat FNAs or

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close clinical monitoring were recommended to avoid overtreatment.

The (SFM) category (12.5%) had 9 cases where prominent atypia raised concern but lacked unequivocal malignant features. Histopathological correlation through excisional biopsy was necessary for definitive diagnosis, underscoring the limitations of cytology in such ambiguous cases.

In the malignant category (15.3%), 11 cases were identified, including mucoepidermoid carcinoma (3 cases) and carcinoma ex pleomorphic adenoma (4 cases). The latter highlights the potential for malignant transformation in long-standing benign tumors, particularly PA. These findings reflect the critical need for vigilant follow-up and early intervention.

Glandular distribution analysis revealed that the parotid gland (55.6%) was the most commonly affected site, consistent with its higher propensity for both benign and malignant neoplasms. The submandibular gland (20.8%) and minor salivary glands (16.7%) showed a relatively higher frequency of malignant lesions, in line with previous literature.

Overall, the results demonstrate the utility of the Milan grading system in categorizing salivary gland lesions and guiding clinical management. However, the significant number of cases in the SUMP and SFM categories reflects the inherent limitations of cytology in certain scenarios, emphasizing the importance of histopathological correlation and multidisciplinary evaluation.

A retrospective study by Prakash et al. (2023) analyzed 151 salivary gland cases using the Milan system and found that it demonstrated high sensitivity (94.2%) and specificity (96%) when compared to histopathology, making it a reliable tool for diagnosing malignancy [6]. Similarly, Mishra et al. (2019) conducted a prospective study evaluating the Milan system's effectiveness in grading salivary gland lesions. They found that the risk of malignancy (ROM) was highest (93.3%) in category 6 (malignant lesions) and lowest (3.0%) in the non-neoplastic category, highlighting the system's reliability in patient management [7].

Another study by Manucha et al. (2020) assessed the Milan system in a real-time clinical setting over two years and found that strict adherence to its diagnostic criteria enabled accurate malignancy risk assessment, with ROM reaching 100% in categories 5 (suspicious for malignancy) and 6 (malignant) [8]. MukundaPai et al. (2019) conducted a four-year study in a tertiary cancer center and reported a high correlation between Milan classifications and histopathological diagnoses, with ROM varying from 96% to 100% in malignant cases, reinforcing its role in guiding clinical decisions [9].

Bhushan et al. (2023) prospectively classified 100 salivary gland FNAC cases according to the Milan system and found that the most common lesion was pleomorphic adenoma, categorized under benign neoplasms. The study concluded that the Milan system facilitated better communication between cytopathologists and clinicians, ensuring more effective patient management [10]. Additionally, a study by Torres et al. (2024) highlighted the Milan system's utility in minor salivary gland lesions, emphasizing the need for further refinement in atypical classifications due to differences in lesion distribution compared to major salivary glands [11].

Conclusion

The Milan System effectively classifies salivary gland lesions, guiding diagnosis and treatment. Pleomorphic adenoma was the most common benign lesion, with carcinoma ex pleomorphic adenoma highlighting the risk of malignant transformation. Diagnostic uncertainty in SUMP and AUS categories underscores the need for histopathological confirmation. Despite its limitations in borderline cases, the Milan system improves diagnostic accuracy and clinical management.

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