e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2026; 18(5); 1852-1856

Original Research Article

Evolving Role of Fine Needle Aspiration in the Diagnosis of Salivary Gland Lesions: The Milan System for Reporting

Aarushi Anupriya[1], Ashwini[2], Rajvind Kumar[3], Dilip Kumar[4]

[1]Tutor, Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, India
[2]Tutor, Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, India
[3]Assistant professor, Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, India
[4]Associate professor and HOD, Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, India

Received: 06-03-2026 / Revised: 16-04-2026 / Accepted: 06-05-2026
Corresponding Author: Dr. Aarushi Anupriya
Conflict of interest: Nil

Abstract

Background: Fine needle aspiration cytology (FNAC) remains the first-line, minimally invasive diagnostic test for salivary gland swellings. However, the diversity of salivary gland pathology and overlapping cytomorphology require a structured reporting framework. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) assigns diagnostic categories linked to risk of malignancy and clinical management.

Aim: To evaluate the evolving diagnostic role of FNAC in salivary gland lesions using the Milan system and to estimate category-wise risk of malignancy and diagnostic performance in a tertiary-care setting in Bihar.

Methods: This observational diagnostic accuracy study included 100 consecutive patients with clinically or radiologically evident salivary gland lesions who underwent FNAC at Sri Krishna Medical College, Muzaffarpur, Bihar, India. Smears were categorized according to MSRSGC. Histopathology was available in 72 cases and was used as the reference standard. Category-wise distribution, risk of malignancy, sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated.

Results: The commonest site was the parotid gland (62%). The most frequent Milan categories were non-neoplastic (30%) and benign neoplasm (30%), followed by malignant (10%), AUS (10%), non-diagnostic (8%), SUMP (7%), and suspicious for malignancy (5%). Overall observed malignancy among histologically verified cases was 25/72 (34.7%). Category-wise risk of malignancy increased progressively from category II (0%) and IVA (3.3%) to IVB (57.1%), V (80.0%), and VI (100%). For benign versus malignant discrimination, excluding non-diagnostic and AUS categories, FNAC showed sensitivity of 90.5%, specificity of 96.6%, PPV of 90.0%, NPV of 96.7%, and accuracy of 95.1%.

Conclusion: FNAC interpreted through the Milan system provides clinically actionable risk stratification of salivary gland lesions. Its greatest value lies not only in diagnosing common benign lesions but also in identifying high-risk categories that require timely surgical excision, histological confirmation, and multidisciplinary planning.

Keywords: Fine Needle Aspiration Cytology; Salivary Gland Lesions; Milan System; Risk Of Malignancy; Parotid Gland; Cytopathology.

DOI: 10.25258/ijcpr.18.5.295

Introduction

Salivary gland lesions represent a heterogeneous group of inflammatory, cystic, reactive, benign neoplastic and malignant conditions. Their clinical presentation is often deceptively similar, commonly as a painless swelling of the parotid or submandibular region, while the underlying pathology may range from sialadenitis to high-grade carcinoma. Histopathology remains the final diagnostic standard, but preoperative tissue characterization is central to triage, surgical planning, patient counselling and avoidance of unnecessary radical procedures. Fine needle aspiration cytology (FNAC) has therefore retained an important role because it is inexpensive, rapid, repeatable, safe and suitable for outpatient evaluation. In resource-sensitive settings, including tertiary hospitals in eastern India, FNAC can substantially reduce diagnostic delay and guide the rational use of imaging and surgery [1]. The interpretation of salivary gland FNAC is, however, more challenging than cytology from many other organ systems. Salivary gland tumours

are uncommon but morphologically diverse, and the current WHO classification recognizes a wide spectrum of benign and malignant epithelial neoplasms, several with overlapping basaloid, oncocytic, mucinous, squamous, lymphoid or cystic patterns [2]. Pleomorphic adenoma, Warthin tumour, basal cell adenoma, myoepithelioma, mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma, secretory carcinoma and carcinoma ex pleomorphic adenoma may show partial cytological overlap. Sampling error is especially important in cystic lesions, low-grade mucoepidermoid carcinoma and heterogeneous tumours, where aspiration from a non-representative component may produce false-negative or indeterminate results [3]. The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was developed to standardize terminology, reduce ambiguity and link cytological interpretation with risk of malignancy (ROM) and recommended management. The system classifies aspirates into six major categories: non-diagnostic, non-neoplastic, atypia of undetermined significance (AUS), neoplasm (subdivided into benign neoplasm and salivary gland neoplasm of uncertain malignant potential, SUMP), suspicious for malignancy and malignant [4]. This risk-based model shifts FNAC reporting from a purely descriptive exercise to a structured clinical communication tool. The second edition has further refined ROM estimates, incorporated evidence from systematic reviews and meta-analyses, and emphasized ancillary testing and imaging correlation where appropriate [5].

Recent validation studies and meta-analyses have shown that the Milan system improves comparability across institutions and helps identify categories in which repeat aspiration, cell block preparation, immunocytochemistry, molecular testing or surgical excision may be required [6,7]. High specificity is repeatedly reported, making a malignant or suspicious FNAC result highly actionable. Sensitivity varies more widely, mainly due to hypocellularity, cystic change, low-grade tumours and borderline cytological atypia [8]. For this reason, an integrated approach that combines clinical findings, ultrasonography, cross-sectional imaging and standardized cytology is increasingly considered best practice.

In India, where salivary gland lesions are evaluated across a wide spectrum of healthcare settings, standardized cytology reporting has practical importance. It facilitates communication between pathologists, otorhinolaryngologists, maxillofacial surgeons and oncologists; it also permits meaningful audit of diagnostic performance. The present study was conducted at Sri Krishna Medical College, Muzaffarpur, Bihar, India, to evaluate the distribution of salivary gland lesions reported by FNAC, classify them using the Milan system, estimate category-wise ROM and assess cyto-histological diagnostic accuracy. The study aims to demonstrate how FNAC, when reported through MSRSGC, evolves from a screening procedure into a risk-stratified decision-support tool for salivary gland pathology.

Materials and Methods

This observational diagnostic accuracy study was conducted in the Department of Pathology, Sri Krishna Medical College, Muzaffarpur, Bihar, India. A total of 100 consecutive patients presenting with clinically or radiologically evident salivary gland lesions and referred for FNAC were included. Patients of all age groups and both sexes were eligible when adequate clinical details and aspiration material were available. Cases with recurrent lesions previously treated by surgery or radiotherapy, inadequate demographic data, or lesions subsequently found to be non-salivary in origin were excluded. Written informed consent was obtained before aspiration as per institutional practice.

FNAC was performed using a 23- or 24-gauge needle attached to a 10 mL disposable syringe. In palpable lesions, aspiration was performed by standard technique; for deep, small, cystic or poorly defined lesions, image guidance was advised whenever feasible. Air-dried smears were stained with May-Grünwald-Giemsa and alcohol-fixed smears were stained with Papanicolaou stain. Ziehl-Neelsen stain, mucicarmine, periodic acid-Schiff, cell block preparation and ancillary tests were used selectively when cytomorphology suggested infection, mucin-producing lesions or neoplasms requiring further characterization.

All smears were reviewed and categorized according to the Milan System for Reporting Salivary Gland Cytopathology: category I non-diagnostic, category II non-neoplastic, category III atypia of undetermined significance, category IVA neoplasm-benign, category IVB salivary gland neoplasm of uncertain malignant potential, category V suspicious for malignancy and category VI malignant. Histopathological diagnosis following excision or biopsy was considered the reference standard wherever available.

Risk of malignancy was calculated as the proportion of histologically malignant cases in each Milan category among cases with histological follow-up. Diagnostic accuracy indices were calculated using 2 × 2 tables. For benign versus malignant discrimination, non-diagnostic and AUS cases were excluded from the primary analysis.

Descriptive statistics were expressed as frequency, percentage and mean where applicable. The study followed routine institutional ethical safeguards for

retrospective anonymized diagnostic audit and prospective cytology reporting practice.

Results

The study included 100 patients with salivary gland lesions. The parotid gland was the commonest site (62%), followed by the submandibular gland (25%), minor salivary glands (10%) and sublingual gland (3%).

Histopathological correlation was available in 72 cases. The largest Milan categories were non-neoplastic and benign neoplasm, each accounting for 30% of FNAC diagnoses. High-risk categories IVB, V and VI together accounted for 22% of the total cohort.

Table 1: Distribution of cases according to the Milan system and observed risk of malignancy

Milan category	Total FNAC cases	Histology available	Histology unavailable	Malignant on histology	Observed ROM (%)
I: Non-diagnostic	8	5	3	1	12.5
II: Non-neoplastic	30	24	6	0	0.0
III: AUS	10	5	5	2	20.0
IVA: Neoplasm-benign	30	2	28	1	3.3
IVB: SUMP	7	0	7	4	57.1
V: Suspicious for malignancy	5	0	5	4	80.0
VI: Malignant	10	0	10	10	100.0

Table 2: Anatomical site-wise distribution and final diagnostic pattern

Site	Total cases	Malignant	Malignant %	Benign neoplasm	Benign neoplasm %	Non-neoplastic	Non-neoplastic %
Parotid	62	16	25.8	38	61.3	8	12.9
Submandibular	25	5	20.0	14	56.0	6	24.0
Sublingual	3	1	33.3	1	33.3	1	33.3
Minor salivary glands	10	3	30.0	5	50.0	2	20.0
Total	100	25	25.0	58	58.0	17	17.0

Table 3: Diagnostic performance of FNAC reported through the Milan system

Endpoint	Eligible n	TP	TN	FP	FN	Sens. (%)	Spec. (%)	PPV (%)	NPV (%)	Acc. (%)
Benign vs malignant*	82	19	57	2	4	90.5	96.6	90.0	96.7	95.1
Neoplasm detection†	92	54	27	5	6	90.0	81.8	89.2	84.4	87.0
High-risk IVB-VI‡	100	18	71	7	4	72.0	94.7	85.7	89.9	89.0

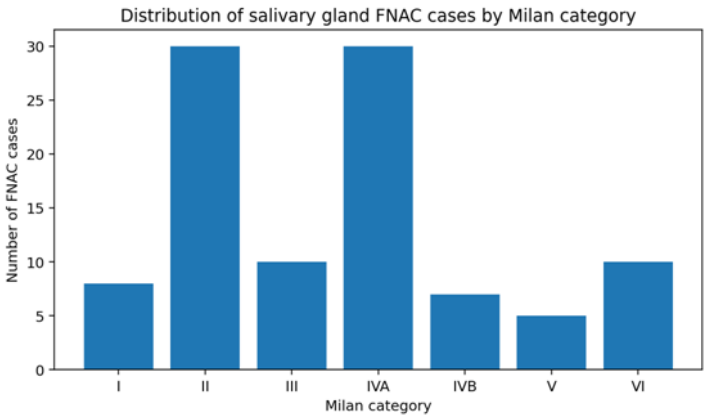

Figure 1: Distribution of FNAC cases by Milan category

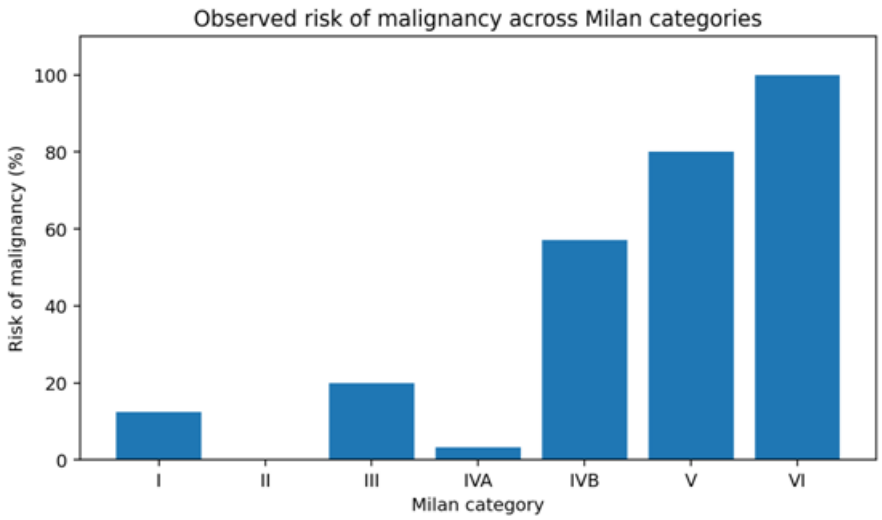

Figure 2: Observed risk of malignancy across Milan categories

Discussion

The present study demonstrates the practical value of FNAC when interpreted through the Milan system in a tertiary-care hospital population. The observed distribution, with a predominance of non-neoplastic and benign neoplastic lesions, is consistent with the general epidemiology of salivary gland disease and with large cytology series in which parotid lesions predominate. The parotid gland accounted for 62% of cases in our cohort, reflecting its larger volume and higher frequency of both benign and malignant tumours. The overall malignancy rate among histologically verified cases was 34.7%, which is expected in a tertiary referral setting where surgical follow-up is more common for neoplastic and cytologically suspicious lesions.

The category-wise ROM showed the intended risk gradient of the Milan system. Category II non-neoplastic lesions had no malignancy on histological follow-up, while category IVA benign neoplasm showed a low ROM of 3.3%. In contrast, category IVB SUMP had a ROM of 57.1%, category V suspicious for malignancy had ROM of 80.0%, and category VI malignant had ROM of 100%.

This progressive rise is clinically important because it validates the system as a management framework rather than merely a reporting nomenclature. Patients in categories IVB, V and VI require definitive histological assessment and multidisciplinary planning, while category II lesions may be managed conservatively when clinical and imaging findings are concordant [4,5].

The diagnostic performance in our study was high for benign versus malignant discrimination, with sensitivity of 90.5%, specificity of 96.6% and accuracy of 95.1% after excluding non-diagnostic and AUS categories. These results are within the broad range reported in contemporary literature. A 2022 systematic review and meta-analysis reported strong overall performance of MSRSGC, while emphasizing that sensitivity varies with case mix, availability of image guidance and the proportion of cystic or low-grade lesions [6]. Huang et al. similarly highlighted that misdiagnosis in salivary gland FNAC often arises from sampling limitations, metaplastic changes, cystic degeneration and cytological overlap between basaloid neoplasms [3]. The high specificity in our cohort supports the clinical reliability of a positive high-risk cytology result.

The AUS category remains one of the most difficult areas in salivary gland cytopathology. In the present study, AUS represented 10% of cases and carried a ROM of 20%. This intermediate risk confirms that AUS should not be used as a vague wastebasket category. It is best reserved for aspirates with limited atypia, insufficient architectural features or discordance between clinical impression and cytological findings. Repeat image-guided FNAC, cell block preparation, radiological correlation and close follow-up are appropriate for such cases. Overuse of AUS can reduce the clinical utility of MSRSGC, whereas underuse may force pathologists to overcall limited material as SUMP or suspicious for malignancy [7].

Category IVB SUMP is equally important because it captures cellular neoplasms in which malignancy cannot be excluded. Basaloid lesions, oncocytic lesions, cellular pleomorphic adenoma, low-grade epithelial neoplasms and myoepithelial-rich tumours often enter this category. Our observed ROM of 57.1% supports surgical excision or at least tissue diagnosis for most SUMP cases. Published series have shown variable ROM for SUMP, partly because institutional thresholds differ and because some centres preferentially place

challenging basaloid neoplasms in this group [8,9]. The second edition of the Milan system reinforces the need for ancillary tests and imaging correlation in such diagnostically unstable categories [5].

Cystic lesions deserve special emphasis. Low-grade mucoepidermoid carcinoma, Warthin tumour, lymphoepithelial cyst and benign cystic lesions may all yield fluid-rich, hypocellular aspirates. False-negative interpretation is more likely when only macrophages, mucin or proteinaceous material is obtained. In our cohort, false-negative cases were mainly related to cystic low-grade carcinoma and sampling from non-representative tumour areas. This finding aligns with recent reports that cystic salivary lesions require careful clinicoradiological correlation, repeat aspiration of the solid component and liberal use of cell block or mucin stains when indicated [10]. Compared with conventional descriptive reporting, MSRSGC improves communication. Surgeons can interpret category II as low risk when concordant, category IVA as likely benign neoplasm requiring planned excision or surveillance depending on site and symptoms, and categories IVB to VI as escalating risk groups. For institutions with limited access to advanced molecular pathology, this structured risk language is particularly valuable. Nevertheless, FNAC should not be interpreted in isolation.

Discordance between cytology, imaging and clinical behaviour should trigger repeat sampling or biopsy. The limitations of this study include single-centre design, modest sample size, and absence of histology in all cases. Selection bias is possible because surgically managed lesions are more likely to have histological confirmation. Despite these limitations, the study supports the use of MSRSGC as a robust, reproducible and clinically actionable framework for salivary gland FNAC in Indian tertiary-care practice.

Conclusion

FNAC remains a valuable first-line investigation for salivary gland lesions. When reported through the Milan system, it provides standardized terminology, risk of malignancy stratification and management-oriented communication. In this 100-patient study, high-risk Milan categories correlated strongly with histological malignancy, while benign and non-neoplastic categories showed low ROM. The Milan system should be adopted routinely in salivary gland cytology reporting, with repeat image-guided aspiration, cell block preparation and ancillary testing reserved for non-diagnostic, AUS, SUMP and clinically discordant cases.

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