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Original Research Article

Study of salivary gland cytopathological lesions and categorized according to Milan reporting system at tertiary care centre Rajkot

Disha Bipinbhai Patel[1]*, Shilpa H Gandhi[1], Gauravi H Dhruva[1]

[1]*Dept. of Pathology, PDU Medical College and Hospital, Rajkot, Gujarat, India*

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ABSTRACT

Aims and Objectives: Classification of salivary gland lesions into 6 diagnostic categories by using Milan Reporting System. Calculate risk of malignancy (ROM) of each category in present study and compare with other similar study.

Background: The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) developed in 2015, aims of MSRSGC to standardize the reporting of salivary gland cytology. It provides a uniform diagnostic terminology that enhances communication between pathologists and clinicians. Moreover, it facilitates the evaluation of data and ensures a precise cytologic and histologic correlation of cases. Ultimately, this system is designed to improve patient care by streamlining the diagnosis process and enabling more accurate treatment decisions.

Materials and Methods: Clinical history and cytology smears of salivary gland lesions, which were diagnosed from October 2022 to September 2023, were retrieved in a P.D.U. medical hospital in Rajkot, Gujarat. The cytology smears were all meticulously reviewed and subsequently classified into one of the six categories as prescribed by MSRSGC. With HPE considered the gold standard, the sensitivity, specificity, positive predictive value, and negative predictive value of FNAC for detecting malignant lesions were meticulously calculated.

Results: A total of 59 salivary gland lesions underwent examination, of which 38 (64.4%) were found in males, and 21 (35.6%) were identified in females. The patients had a median age of 45 years, with ages ranging from 10 to 80 years. It was revealed through statistical analysis that the sensitivity, specificity, positive predictive value, and negative predictive value were determined to be 80%, 100%, 100%, and 88%, respectively.

Conclusion: MSRSGC serves as an effective framework for the categorization of salivary gland tumors, be they benign or malignant. Our findings reflect the positive contribution of the MSRSGC towards accurately identifying the malignant lesions and thus further helping the clinicians regarding the specific management decisions.

1. Introduction

Fine-needle aspiration cytology (FNAC) has been widely accepted as the primary diagnostic test in the management of salivary gland lesions. This acceptance came about due to its effectiveness and reliability in diagnosing various conditions affecting the salivary glands. An international consortium of experienced health care professionals has developed a reporting system for salivary gland cytology specimens, which is known as The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).[1,2]

In the head and neck tumors, salivary gland neoplasms represent less than 3% of all cases. Various factors such as infections, inflammation, cystic lesions, degenerative

* *Corresponding author*.
E-mail address: pateldisha1323@gmail.com (D. B. Patel).

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processes, obstructions, or benign/malignant neoplasms can cause nodules or diffuse enlargement in the salivary glands. To address these issues systematically, The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was established. It includes six categories: non-diagnostic (category I), non-neoplastic (category II), atypia of undetermined significance (category III), benign neoplasm (category IVa), salivary gland neoplasm of uncertain malignant potential (SUMP) (category IVb), suspicious for malignancy (category V), and malignant (category VI). Additionally, MSRSGC provides an estimation of the risk of malignancy (ROM) and clinical management recommendations for each category, aiming to streamline patient care and decision-making processes.[3]

The study was conducted with the objective of classifying salivary gland lesions according to the Milan System in order to ascertain the rate of malignancy and to evaluate the diagnostic accuracy in the vicinity of our institute. This was achieved by correlating the cyto-histopathological diagnoses wherever possible, thereby providing a comprehensive analysis of the effectiveness of the Milan System in accurately diagnosing salivary gland lesions.[4]

2. Materials and Methods

A retrospective study was carried out in the cytopathology department of P.D.U. medical hospital, located in Rajkot, Gujarat, spanning from October 2022 to September 2023. During this period, detailed clinical histories of cases along with cytology smears of salivary gland lesions were retrieved. It was noted that the cytology smears of salivary gland lesions encompassed both major and minor salivary glands. These smears were then categorized into one of the six categories defined by MSRSGC. A comparison was made between the cytological diagnosis and the histological reports, wherever these were available.

For each defined category, the risk of malignancy (ROM) was assessed. This assessment of ROM involved the division of the number of malignant cases identified through histopathology in each category by the total number of patients examined cytologically in that specific category. For the purposes of statistical analysis, the cytological diagnoses were classified into two groups: positive (indicating malignancy) and negative (indicating benign conditions).

The sensitivity, specificity, positive predictive value, and negative predictive value of Fine Needle Aspiration Cytology (FNAC) in detecting malignant lesions were then calculated. These calculations were performed by considering the histopathology examination as the gold standard.

3. Results

During the study period, a total of 59 salivary gland lesions were examined. Of these, males constituted 38 (64.4%), and females made up 21 (35.6%), resulting in a male to female ratio of 1.8:1 (Figure 1). The median age of our study population was 45 years, with an age range of 10-80 years. The parotid gland was identified as the most frequent site of involvement, accounting for 74.5% of cases, followed by the submandibular gland, which accounted for 23.7%. The minor salivary gland was affected in only 1.8% of cases. All cases were reviewed and were categorized according to the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) into six categories, as presented in Table 1. The distribution of cases showed that the majority were identified as neoplasm benign, making up 59.72% of the cases, followed by non-neoplastic lesions, which comprised 22.03%. Non-diagnostic cases represented 6.70%, while malignant cases accounted for 5.08%. Cases of atypia of undetermined significance were identified in 3.30% of instances, and both SUMP [Salivary gland neoplasm of uncertain malignant potential] and cases suspicious of malignancy each accounted for 1.60%.

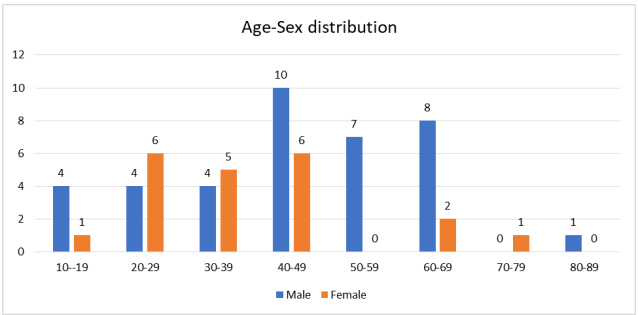

Figure 1: Age–sex distribution (X-axis: Age group, Y-axis: Case count)

The distribution of the cases across the categories of the Milan System and their cytohistopathological correlation are depicted in Tables 1 and 2 respectively. In Category I, which consists of 4 cases, 2 cases were initially diagnosed with a cystic lesion cytologically and were later reported as benign cystic lesions upon histopathological examination. The cytological features of the normal salivary gland structures were reported in two cases through fine-needle aspiration cytology (FNAC), with no follow-up histopathological report being available. The risk of malignancy (ROM) for Category I was found to be 0%.

In category II of the MSRSGC, which included 6 cases, chronic sialadenitis was identified as the most common lesion. Histopathological follow-up was conducted for 3 cases, all of which confirmed the initial diagnosis of chronic sialadenitis. However, one case that was initially diagnosed with granulomatous inflammation cytologically was later identified as chronic sialadenitis upon histopathological

Table 1: Distribution of all cases according to the Milan category

MILAN Category		Number (N=59)	Percentage (%)
I	Non-Diagnostic	04	06.70
II	Non-Neoplastic	13	22.03
III	Atypia of undetermined significance	02	03.30
IVa	Neoplasm Benign	35	59.72
IVb	SUMP (Salivary gland neoplasm of uncertain malignant potential)	01	01.60
V	Suspicious of malignancy	01	01.60
VI	Malignant	03	05.08

examination, marking a discordant case. The ROM for Category II was determined to be 0%.

Category III contained 2 cases, with one being diagnosed with squamous metaplasia through FNAC and later identified as metastatic squamous cell carcinoma (SCC) upon histopathological follow-up. The other case was cytologically reported as a mucinous cyst, with no histopathological follow-up being reported. The ROM for Category III was calculated at 50%.

34 cases were included in MSRSGC Category IVa, with pleomorphic adenoma (Figures 2 and 3) being the most frequently diagnosed tumor. Of the 22 cases that had available histopathological follow-up, 15 were confirmed as pleomorphic adenomas, matching their initial FNAC diagnosis. Additionally, 10 cases initially reported as Warthin's tumor (Figures 4 and 5) through FNAC had 6 cases confirmed through histopathology. One case initially diagnosed with Basal cell Adenoma and another with Oncocytoma through FNAC were followed up histologically, with the latter receiving no follow-up. The ROM for Category IVa was reported as 0%.

Category IVb of the MSRSGC comprised two cases; one was initially reported as a salivary gland neoplasm through FNAC and later confirmed as mucoepidermoid carcinoma upon histopathological follow-up. The other case, initially diagnosed with a cellular neoplasm with oncocytic feature through FNAC, was later identified as a Warthin tumor upon histopathological evaluation. The ROM for Category IVb was found to be 50%.

A solitary case in MSRSGC Category V was initially diagnosed as a malignant epithelial lesion through FNAC and was later confirmed to be metastatic squamous cell carcinoma upon histopathological follow-up, resulting in a ROM of 100% for Category V.

Category VI saw 3 cases, with one being diagnosed as Adenocytic carcinoma (Figures 6 and 7) through FNAC and confirmed upon histopathology. The other two cases, initially diagnosed as high-grade mucoepidermoid carcinoma via FNAC, were also confirmed as mucoepidermoid carcinoma (Figure 8) upon histopathological examination. The ROM for Category VI was therefore 100%.

The analysis of the statistical data revealed the sensitivity, specificity, positive predictive value, and negative predictive value as 80%, 100%, 100%, and 88% respectively. The comparison of these statistical values with those from other published series is presented in Table 3.

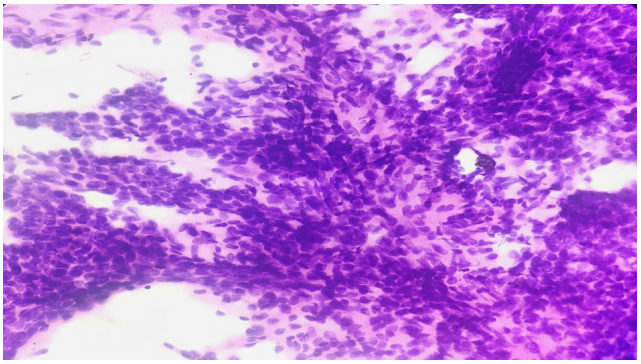

Figure 2: Pleomorphic adenoma: Pleomorphic adenomais characterized by myoepithelial cells having abundant pale cytoplasm and bland nuclei, and fibromyxoid stroma containing scattered spindle cells

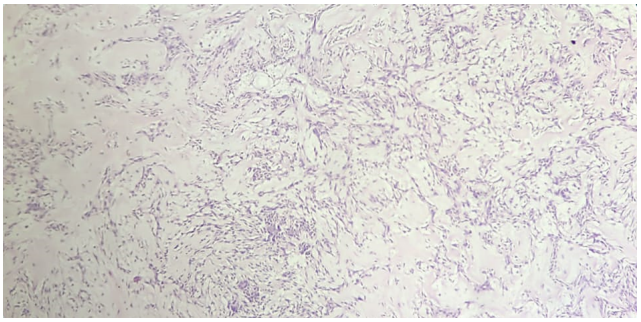

Figure 3: Pleomorphic adenoma: A triphasic tumor composed of ductal (epithelial), myoepithelial, and stromal components is described, with the stromal component being typically chondromyxoid

4. Discussion

59 salivary gland lesions were reclassified using the MILAN system, with histopathological correlation available for 37

Table 2: Categorization of FNAC cases according to Milan system and correlation with histopathological findings

Milan Category	No. of Cases	Primary FNAC Diagnosis	No. of Cases	No. of HPE Cases	HPE Finding	ROM (%)
I (Non-Diagnostic)	4	Normal Salivary Gland Structures	2			0
II (Non-Neoplastic)	13	Cystic Lesion	2	2	Benign Cystic Lesion	0
		Acute Sialadenitis	3	1	Acute Sialadenitis	
		Chronic Sialadenitis	6	3	Chronic Sialadenitis	
		Acute Supporative Lesion	1	1	Abscess formation.	
		Parotitis	1	0		
		Sialoadenosis	1	0		
		Granulomatous inflammation	1	1	Chronic sialadenitis	
III (AUS-Atypia of undetermined significance)	2	Squamous metaplasia	1	1	Metastatic SCC	50
		Mucinous Cyst	1	0		
IV- a (Benign Neoplasm)	34	Pleomorphic Adenoma	22	15	Pleomorphic Adenoma	0
		Warthin tumor	10	6	Warthin tumor	
		Oncocytoma	1	0		
		Basal cell Adenoma	1	1	Basal cell Adenoma	
IV- b (SUMP-Salivary gland neoplasm of uncertain malignant potential)	2	Salivary Gland Neoplasm	1	1	MEC	50
		Cellular neoplasm with oncocytic feature	1	1	Warthin tumor	
V (SM-Suspicious Malignancy)	1	Malignant Epithelial Lesion	1	1	Metastatic SCC	100
VI (Malignancy)	3	MEC	2	2	MEC	100
		Adenocytic carcinoma	1	1	Adenocytic carcinoma	

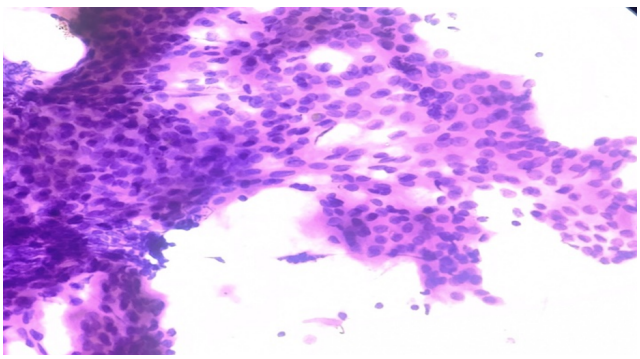

Figure 4: Warthin's tumor- large sheets of bland oncocytic cells arranged in monolayered sheets and occasional lymphocytes in background

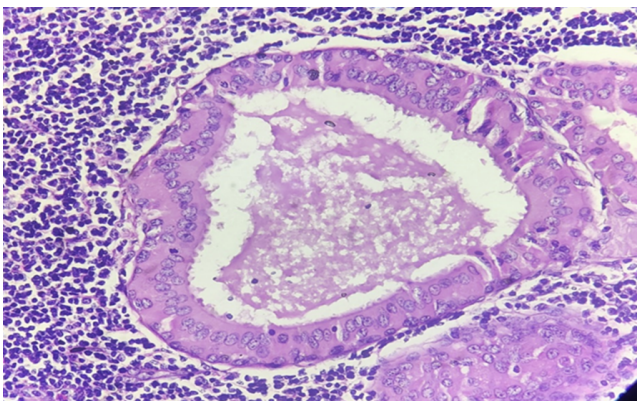

Figure 5: Warthin's tumor- Papillary cystic structure lined by double layered oncocytic epithelial cells and surrounding lymphoid stroma

cases was conducted in the pathology department of P.D.U. medical hospital in Rajkot, Gujarat, from October 2022 to September 2023.

There were 38 males (64.4%) and 21 females (35.6%) in our study, with a male-to-female ratio of 1.8:1. This is comparable with Kamna V et al,[5] Wu H et al[6] & Dubucs et

Table 3: Comparison of risk of malignancy (ROM) of present study with published literature

Authors	Risk of malignancy% of Milan Category						
	I	II	III	IVa	IVb	V	VI
Faquin et al[8]	25	10	20	<05	35	60	>90
Dubucs et al[7]	34.2	00	00	3.1	45.5	68.8	100.0
Kamna V et al[5]	00	00	50	2.44	33.33	100	93.33
Wu H et al[6]	15	00	40	9.5	13.3	50	100
Huang Yi-tien et al[9]	16.4	9.5	24.4	2.7	34.8	85.7	100
Viswanathan K et al[10]	6.7	7.1	38.9	05	34.2	92.9	92.3
Chen Y et al[11]	8.6	15.4	36.8	2.6	32.3	71.4	100
Datta B et al[12]	00	00	50	00	50	100	50
Present study	00	00	50	00	50	100	100

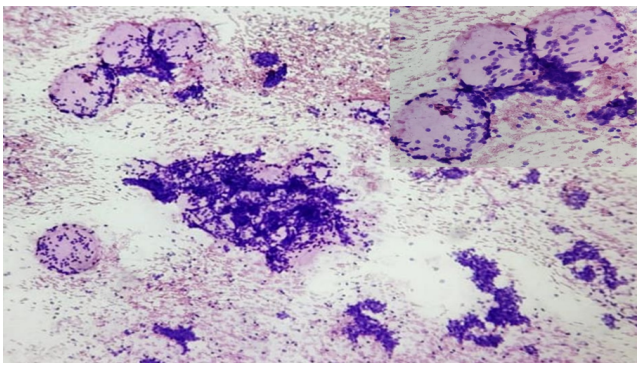

Figure 6: Adenocytic Carcinoma-Small uniform epithelial cells with hyperchromatic nuclei and coarse chromatin, adhering to a large hyaline stromal globule

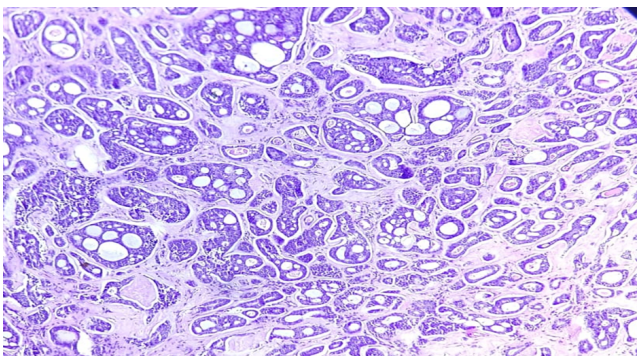

Figure 7: Adenocytic Carcinoma- Cribriform pattern: islands of epithelioid basal cells, cystic spaces contain mucoid or hyalinized material, uniform small cuboidal tumor cells

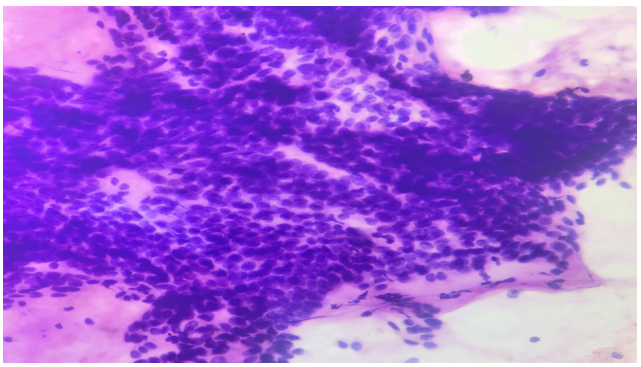

Figure 8: Mucoepidermoid Carcinoma- Dirty appearance of mucus, debris, inflammatory cells and macrophages & poorly cohesive epithelial cells with intermediate cells, bland nuclei and prominent nucleoli

al[7] study.

The most frequent site of involvement in our study was the parotid gland (74.5%), followed by the submandibular gland (23.7%). The minor salivary gland was affected only in 1.8% of cases. Datta B et al[12] had recorded similar findings. The percentage of non-diagnostic category cases in our study was 6.7%. The non-diagnostic criteria include; Insufficient cellular material (<60 lesional cells) for cytologic diagnosis, only nonneoplastic acinar cells present in clinically defined nodules, Presence of nonmucinous cyst fluid, poorly prepared slides, Air drying artifacts, obscuring blood, and poor staining.[13]

The percentage of the non-neoplastic category in our study is 22.03%, which is similar to studies done by Wu H7] Chronic sialadenitis was the commonest lesion diagnosed on cytology.[8] Histopathological follow up was available on three cases, of which three had a concordant diagnosis of chronic sialadenitis. One discordant case had a cytological diagnosis of Granulomatous inflammation, but histopathological follow-up was reported as chronic sialadenitis. Scant cellular content, and a few epithelioid cells, might be a possible reason for discordant diagnosis.[14]

Atypia of undetermined significance (AUS) was lesions that limited cellular atypia is observed, Qualitative or quantitative features for diagnosing a neoplasm are lacking.[15] The percentage of the AUS category in our study was 3.30% which is similar to studies done by Huang Yi-tien et al.[9] One case was reported as mucinous cysts on FNAC, but no histopathological follow up was available. One case reported suspicious-looking squamous cells on cytology led to categorization as AUS on FNAC. On histopathological follow-up, it was later reported as

metastatic squamous cell carcinoma.

The percentage of benign category IV a in our study was the highest, 59.72%. Similar findings were noted Datta B et al[12] study. Pleomorphic adenoma was the commonest salivary gland neoplasm followed by Warthin tumor. Histopathological follow up was available in 23 cases. 15 cases reported as pleomorphic adenoma and 6 case reported as Warthin tumor on FNAC had a concordant diagnosis on histopathology. One case reported as oncocytoma on FNAC no histological follow up obtained.

The diagnosis of salivary gland neoplasm of uncertain malignant potential (SUMP) for those salivary gland FNAs where the cytomorphologic features diagnostic of a neoplasm are identified but remain indefinite for distinguishing a specific tumor type as either benign or malignant.[13] One case report identified the case as salivary gland neoplasm, and histopathological follow-up reported it as Mucoepidermoid carcinoma. Another case revealed oncocytic cells, reactive lymphocytes, few squamous cells, and cellular debris on FNAC. The report identified it as a differential diagnosis of low-grade mucoepidermoid carcinoma versus Warthin tumour on FNAC and categorized it as SUMP based on MSRSGC. On histopathological follow-up, reported as Warthin tumour.

The diagnosis of suspicious for malignancy suspicious of malignancy (SM) category is features highly suggestive of but not unequivocally indicating malignancy.[13] The percentage of cases of SM category in our study is 1.60% which is similar to Chen Y et al[11] study.

The MSRSGC Category V reported only one case as a malignant epithelial lesion on FNAC, and on histopathological follow-up, it reported metastatic squamous cell carcinoma. The malignant category in MSRSGC includes salivary gland FNA showing diagnostic features of malignancy either alone or in combination with ancillary studies.

The percentage of cases of malignant category in our study is 5.08% which is similar to studies done by Chen Y et al.[11] MSRSGC Category VI had 3 cases. One case was reported as Adenocytic carcinoma on FNAC, concordance with histopathological diagnosis. We reported another two cases as high-grade mucoepidermoid carcinoma on FNAC. Histopathology confirmed mucoepidermoid carcinoma in these cases. In our study, we reported a malignancy risk of 0%, 0%, 50%, 0%, 50%, 100% and 100%, respectively for each category. Our results compare favourably with those provided in the MSRSGC and recent other studies.[5–13]

The sensitivity, specificity, positive, and negative predictive values in our study for malignant diagnosis were 80%, 100%, 100% and 88% respectively. These figures align well with other studies. Our study findings demonstrate the MSRSGC's positive contribution to accurately identifying malignant lesions and assisting clinicians in making specific management decisions.

5. Conclusion

An excellent reporting method for evaluating the risk of cancer in salivary gland tumors is provided by the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC). In the case of benign salivary gland tumors, the recommendation is for the maintenance of long-term follow-up. This follow-up may include re-biopsy or surgical therapy as measures to minimize the risk of misdiagnosis or the possibility of malignant transformation. It is crucial to acknowledge that the MSRSGC serves as an effective framework for the categorization of salivary gland tumors, be they benign or malignant. Nonetheless, the definitive diagnosis is to be established by a collaborative team. This team should be comprised of pathologists, radiologists, and surgeons who collectively consider the clinical presentation, imaging characteristics, and medical history of the patient in their deliberation.[9]

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Rossi ED, Faquin WC, Baloch Z, Barkan GA, Foschini MP, Pusztaszeri M, et al. The Milan System for Reporting Salivary Gland Cytopathology. *Cancer Cytopathol*. 2017;125(10):757–66.
2. Baloch Z, Faquin W, Layfield L. Is it time to develop a tiered classification scheme for salivary gland fine- needle aspiration specimens. *Diagn Cytopathol*. 2016;45(4):285–6.
3. Gaikwad VP, Anupriya C, Naik LP. Milan System for Reporting Salivary Gland Cytopathology– An Experience from Western Indian Population. *J Cytol*. 2020;37(2):93–8.
4. Bharti JN, Elhence P, Rao M, Nalwa A, Khera S. Risk stratification by application of Milan system for reporting salivary gland cytopathology: A tertiary care experience. *Cytojournal*. 2021;18:19.
5. Karuna V, Gupta P, Rathi M, Grover K, Nigam JD, Verma N. Effectuation to Cognize malignancy risk and accuracy of fine needle aspiration cytology in salivary gland using "Milan System for Reporting Salivary Gland Cytopathology": A 2 years retrospective study in academic institution. *Indian J Pathol Microbiol*. 2019;62(1):11–6.
6. Wu HH, Alruwaii F, Zeng BR, Cramer HM, Lai C. Application of the Milan System for Reporting Salivary Gland Cytopathology: A Retrospective 12-Year Bi-institutional Study. *Am J Clin Pathol*. 2019;151(6):613–21.
7. Dubucs C, Basset C, D'aure D, Courtade-Saïdi M, Evrard SM. A 4-Year Retrospective Analysis of Salivary Gland Cytopathology Using the Milan System for Reporting Salivary Gland Cytology and Ancillary Studies. *Cancers (Basel)*. 1912;11(12):1912.
8. Faquin WC, Rossi ED, Baloch Z, Barkan GA, Foschini MP, Kurtycz DFI. The Milan System for Reporting Salivary Gland Cytopathology. 1st ed. Germany: Springer Nature; 2018.
9. Huang YT, Ho CY, Ou CY, Huang CC, Lee WT, Tsai SW, et al. Evaluation of Fine Needle Aspiration Cytopathology in Salivary Gland Tumors under Milan System: Challenges, Misdiagnosis Rates, and Clinical Recommendations. *Biomedicines*. 2023;11(7):1973.

10. Viswanathan K, Sung S, Scognamiglio T, Yang G, Siddiqui M, Rao R. The role of the Milan System for Reporting Salivary Gland Cytopathology: A 5-year institutional experience. *Cancer Cytopathol*. 2018;126(8):541–51.
11. Chen Y, Wu C, Yang C. Application of the Milan System for Reporting Salivary Gland Cytopathology: A retrospective study in a tertiary institute. *Diagn Cytopathol*. 2019;47(11):1160–7.
12. Datta B, Daimary M, Bordoloi K, Thakuria C. Cytopathological Spectrum of Salivary Gland Lesions According to Milan Reporting System: A Retrospective Study. *Asian Pac J Cancer Care*. 2023;8(3):465–70.
13. Lee JJL, Tan HM, Chua DYS, Chung JGK, Nga ME. The Milan system for reporting salivary gland cytology: A retrospective analysis of 1384 cases in a tertiary Southeast Asian institution. *Cancer Cytopathol*. 2020;128(5):348–58.
14. Mukundapai M, Sharma N, Patil A, Gopal C. Fine-Needle Aspiration Cytology of Salivary Gland Lesions: A Revised Classification Based on "Milan System"—4years Experience of Tertiary Care Cancer Center of South India. *J Cytol*. 2020;37(1):12–7.
15. Wong LQ, LiVolsi VA, Baloch ZW. Diagnosis of atypia/follicular lesion of undetermined significance: An institutional experience. *Cytojournal*. 2014;11:23.

Author biography

Disha Bipinbhai Patel, Resident

Shilpa H Gandhi, Professor

Gauravi H Dhruva, Professor and HOD

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