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Risk Stratification of Milan System of Reporting Salivary Gland Cytology Along with Histological Correlation

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Abstract

OBJECTIVES: The objective of this study was to evaluate the diagnostic accuracy and clinical utility of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) by correlating cytological findings from FNAC with histopathological diagnoses, estimating the risk of malignancy for each category, and assessing the system's effectiveness in standardizing reporting and guiding patient management.

METHODS: FNAC was performed on all clinically palpable salivary gland swellings over 1.5 years using universal sampling. Smears were stained with MGG, Pap, and H&E. Resected specimens were processed and classified as per WHO guidelines. Cytological diagnoses were categorized using MSRSGC and correlated with histopathology. Risk of malignancy was calculated per category. Data were recorded on a proforma and analyzed using Microsoft Excel.

RESULTS : In this study of 100 salivary gland FNAC cases, histopathological correlation was available for 52. The majority were aged 41–60 years, with a male predominance. Parotid was the most involved gland. Category IVa (47%) was most common. Concordance with histology was 90.38%. ROM ranged from 0% (Categories I–III) to 100% (IVb, V). FNAC showed 55.56% sensitivity, 97.67% specificity, and 90.38% diagnostic accuracy using the MSRSGC.

CONCLUSION: The study validates the MSRSGC as an effective, reproducible system for salivary gland FNAC, ensuring accurate diagnosis, risk stratification, and improved clinical decisions, despite moderate sensitivity.

Keywords: FNAC(fine needle aspiration cytology), cytohistological correlation, MSRSGC(Milan system for reporting salivary gland cytopathology), histopathology, ROM(risk of maliganancy).

INTRODUCTION

Salivary gland lesions encompass a broad and heterogeneous group of pathologies that present unique diagnostic challenges due to their cytomorphologic diversity and the rarity of certain neoplasms. These lesions account for less than 5% of all head and neck tumors, with the parotid gland being the most commonly affected, followed by the submandibular, sublingual, and minor salivary glands.[1,2] Clinically, patients often present with a painless swelling, although symptoms such as facial nerve palsy, rapid growth, or fixation to deeper tissues may indicate malignancy.

Fine-needle aspiration cytology (FNAC) has emerged as the first-line diagnostic modality for evaluating salivary gland swellings. It is a minimally invasive, cost-effective procedure that provides rapid and reliable preliminary information, assisting in clinical decision-making and surgical planning. Despite its utility, the interpretation of salivary gland FNAC specimens can be difficult due to overlapping features among benign and malignant tumors, such as pleomorphic adenoma, Warthin tumor, mucoepidermoid carcinoma, and adenoid cystic carcinoma[3-5].

Historically, salivary gland cytology lacked a standardized reporting protocol, resulting in significant interobserver variability and inconsistent communication between pathologists and clinicians. This inconsistency compromised the

reliability of cytological assessments and often led to unnecessary surgeries or mismanagement. To overcome these issues, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) was introduced in 2018 under the joint efforts of the American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC)[6].

The MSRSGC provides a six-tiered classification system that assigns salivary gland FNAC specimens into well-defined diagnostic categories, each associated with an implied risk of malignancy (ROM) and management recommendations [7-9].This structured approach enhances diagnostic reproducibility and allows for meaningful risk stratification, thus improving communication and optimizing patient care.

Table 1. Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)

Category	Risk of Malignancy (ROM)	Definition
I. Non-Diagnostic	~25%	Insufficient sample for diagnosis.
II. Non-Neoplastic	<10%	Benign conditions like chronic sialadenitis or reactive lymph nodes.
III. Atypia of Undetermined Significance (AUS)	~20%	Limited atypia; not definitive for neoplasm.
IVa. Benign Neoplasm	<5%	Clear features of benign tumors (e.g., pleomorphic adenoma).
IVb. SUMP (Uncertain Malignant Potential)	~35%	Neoplasm suspected but unable to determine benign or malignant nature.
V. Suspicious for Malignancy	~60%	Features strongly suggest malignancy but not definitive.
VI. Malignant	~90%	Clear cytological features of malignancy.

Multiple retrospective and prospective studies have validated the effectiveness and reproducibility of the MSRSGC. A meta-analysis by Wang et al. demonstrated consistent ROM values across diverse institutions, confirming the system's global applicability[10]. Studies by Rohilla, Kala, and AksoyAltinboga further affirmed the system's strong correlation with histopathological outcomes and its role in guiding appropriate clinical management.
In day-to-day practice, FNAC plays a pivotal role in the work-up of salivary gland lesions. It helps to determine:

- Whether the lesion is neoplastic or non-neoplastic.
- If neoplastic, whether it is benign or malignant, and if malignant, whether it is low-grade or high-grade.
- The cell of origin, assisting in tumor typing.

FNAC is typically performed from multiple sites to maximize cellular yield. In cystic lesions, fluid is first aspirated and then the solid component is sampled to ensure adequacy. A standard FNAC report should include a diagnostic category based on MSRSGC and, when possible, a specific cytological diagnosis. For instance:

- Evaluation Status: Satisfactory for evaluation
- Interpretation: Neoplasm, Benign
- Diagnosis: Pleomorphic Adenoma

It is important to recognize that the ROM associated with each category is based on cases with surgical follow-up and may be overestimated due to selection bias, institutional referral patterns, and patient demographics.
Understanding the normal anatomy, histology, and embryology of salivary glands is crucial for accurate cytologic diagnosis. The three major salivary glands—parotid, submandibular, and sublingual—and numerous minor glands secrete saliva essential for lubrication, digestion, and antimicrobial activity. Histologically, glands consist of serous and mucous acini, myoepithelial cells, and a complex ductal system[11-13]. The parotid gland is purely serous, the submandibular is mixed, and the sublingual is predominantly mucous-secreting.

The introduction of the MSRSGC has transformed the diagnostic landscape of salivary gland cytology by promoting standardization, improving interobserver agreement, and enhancing clinician-pathologist communication. The system enables accurate stratification of malignancy risk and provides a roadmap for further diagnostic and therapeutic steps.

The MSRSGC serves as a cornerstone in the reporting of salivary gland FNAC. Its integration with knowledge of salivary gland structure, development, and disease behaviour allows for better patient outcomes. Ongoing research is needed to refine the criteria further, explore ancillary testing, and assess the long-term outcomes of patients classified under this framework.

MATERIALS AND METHODS

Study Design and Duration

This was a cross-sectional study conducted over a period of one and a half years in the Department of Pathology, in collaboration with the Department of Surgical Oncology, Rajindra Hospital, Patiala. Based on departmental data from the previous three years (approximately 100 salivary gland FNAC cases), universal sampling was employed to include all cases received during the study period. Cytological-histological correlation was performed, and the risk of malignancy (ROM) was calculated for each diagnostic category.

Study Area and Population

The study included indoor and outdoor patients presenting with clinically palpable swellings of major and minor salivary glands or intraoral lesions who underwent FNAC at the Department of Pathology, Government Medical College, Patiala. Histopathological specimens of salivary gland lesions received in the department were also included for cytohistological correlation.

Inclusion Criteria

- Patients with clinically palpable salivary gland or intraoral swellings undergoing FNAC.

Exclusion Criteria

1. Patients unwilling to provide informed consent.
2. Patients with deranged coagulation profiles.
3. Samples deemed inadequate for cytological interpretation.

FNAC Procedure

FNAC was performed under aseptic precautions using a 22-gauge disposable needle, 20 cc plastic syringe, and Franzen handle. Aspirations were carried out by trained cytopathologists from multiple sites when necessary. Detailed clinical history and local examination findings were recorded for all cases. Informed written consent was obtained from all participants, and ethical clearance was secured from the institutional ethics committee.

Image 1: A 40-year-old male with a large right cheek swelling – diagnosed as **pleomorphic adenoma**.

Image 2: FNAC being performed on a 42-year-old female with left infra-auricular swelling.

Staining Techniques for Cytology

1. **May-Grünwald-Giemsa (MGG) Staining**
   MGG is a Romanowsky-type polychromatic stain combining May-Grünwald and Giemsa solutions.
   - May-Grünwald stain: methylene blue and eosin in methanol.
   - Giemsa stain: azure B, methylene blue, eosin in glycerine/alcohol.

Staining steps include methanol fixation, staining with May-Grünwald (5 min), rinsing, Giemsa staining (15 min), and mounting with DPX.

2. **Papanicolaou (PAP) Staining**
   A rapid PAP protocol was used:
   - Nuclear staining with R1 (60 sec)
   - Cytoplasmic staining using mixed R2A + R2B (60 sec)
   - Dehydration, clearing with xylene, and mounting with DPX.

3. **Hematoxylin and Eosin (H&E) Staining for Smears**
   - Fixation in ethanol
   - Staining with Harris Hematoxylin (15 min)
   - Differentiation with 1% acid alcohol

Counterstaining with 1% eosin, dehydration, clearing, and mounting

Histopathological Examination (HPE)

Resected specimens were fixed in 10% neutral buffered formalin, followed by detailed gross examination. Representative sections were processed, stained with H&E, and examined microscopically.

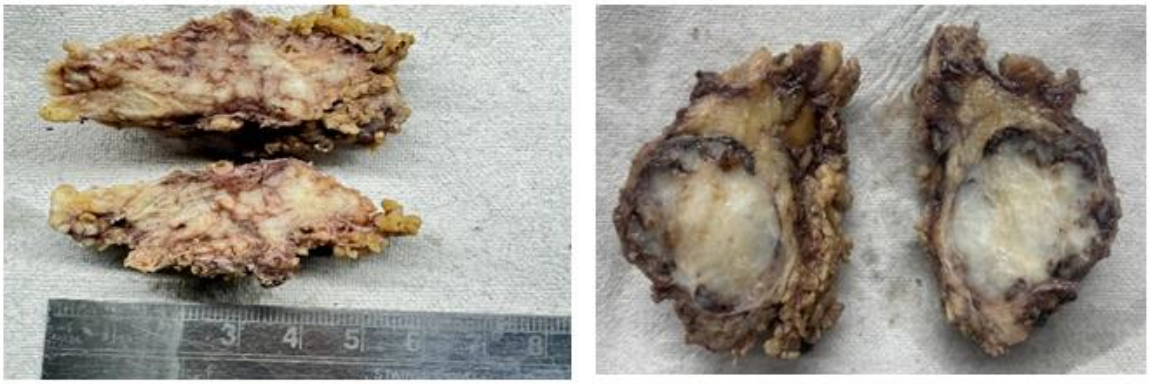


Image 3 & 4: Cut sections reveal **tan-white** areas and a **well-encapsulated tumor** consistent with pleomorphic adenoma.

H&E Staining for Histopathology

1. Slides incubated at 60°C (10 min)
2. Deparaffinization in xylene
3. Rehydration through descending alcohol grades
4. Hematoxylin staining (15 min)
5. Acid alcohol differentiation and tap water rinse
6. Eosin staining and dehydration
7. Clearing in xylene and mounting with DPX
8. Microscopy at low and high magnifications

Cytological Categorization and Correlation

All FNAC cases were classified using the **Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)** into seven categories:

- Non-diagnostic
- Non-neoplastic
- Atypia of undetermined significance (AUS)
- Benign neoplasm
- Neoplasm of uncertain malignant potential (SUMP)
- Suspicious for malignancy

- Malignant

Histopathological diagnoses were assigned based on **WHO classification**. **Cytohistological correlation** was performed, and for cases with available histology, **ROM** for each MSRSGC category was calculated.

Malignancy risk (%)=	No. of cases turned out to be malignant in each category on HP examination
	No. of cases in each category in cytology.

Data Handling and Statistical Analysis

All data were recorded in a predesigned proforma and entered into an excel spreadsheet. Descriptive statistics and calculations of ROM were performed to analyze the diagnostic accuracy and performance of FNAC in salivary gland lesions.

OBSERVATIONS

This cross-sectional study was conducted in the Department of Pathology, Government Medical College and Rajindra Hospital, Patiala, to evaluate the risk stratification of salivary gland lesions using the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) and to correlate cytological findings with histopathology. All clinically palpable salivary gland swellings subjected to FNAC over 1.5 years were included after obtaining informed consent and ethics approval. Detailed cytological examination focused on nuclear and cytoplasmic features, and each case was categorized according to the six-tiered MSRSGC: Non-diagnostic, Non-neoplastic, Atypical, Benign Neoplasm, SUMP, Suspicious for Malignancy, and Malignant. A total of 100 patients underwent FNAC, with histopathological follow-up available for 52 cases. Cytohistological correlation was done, and the risk of malignancy (ROM) was calculated for each MSRSGC category by comparing cytological diagnoses with final histological outcomes.

TABLE-2 DISTRIBUTION OF PATIENTS ACCORDING TO AGE

Age Group (Years)	Patients	Percentage
<20	3	3
21-40	35	35
41-60	49	49
61-80	13	13
Total	100	100
Range	9- 74	
Mean±SD	44.89 ± 14.48	

This table shows that the mean age (± SD) of patients was 44.89±14.48 years. Majority of the cases were in the age-group of 41-60 years (49%) followed by 21-40 years (35%), 61-80 years (13%) and years (16%). Youngest patient was 9 years old and eldest patient was 74 years old. The median age was 45.9 years.

TABLE NO- 3 DISTRIBUTION OF PATIENTS ACCORDING TO GENDER

Gender	Patients	Percentage
Male	54	54
Female	46	46
Total	100	100

This table shows the distribution of patients as per the gender. Out of the total 100 patients evaluated for the current study, 54 (54%) were males and rest 46 (46%) were females. The male to female ratio being 1.17.

TABLE NO- 4 DISTRIBUTION OF CASES AS PER SITE INVOLVED

SITE	Patients	Percentage
Parotid	72	72
Submandibular	25	25
Minor salivary glands	3	3
Total	100	100

This table shows the distribution of cases as per the site of involvement. In the current study, the most commonly involved gland was parotid in 72 (72%) of the cases. This was followed by the submandibular in 25 (25%) of the cases and minor salivary glands in 3 (3%) of the cases.

TABLE NO- 5 DISTRIBUTION OF CASES AS PER THE CLINICAL FINDINGS

CHIEF COMPLAINT	Patients	Percentage
Lump	92	92
Lump+ Pain	8	8
Total	100	100

This tables depicts the distribution of cases as per the clinical findings of the patients. Majority of the patients in the current study – 92 (92%) presented with lump. The remaining 8(8%) of the patients came with pain associated with the lump.

TABLE NO- 6 RADIOLOGICAL INVESTIGATIONS

RADIOLOGICAL INVESTIGATIONS	Number of cases	Percentage
Pleomorphic adenoma	**35**	**35**
Bulky parotid	**12**	**12**
Hypoechoic lesion	**18**	**18**
Sialadenitis	**8**	**8**
Bulky submandibular	**5**	**5**
Warthin tumor	**3**	**3**
Sialadenitis with calculus	**3**	**3**
Hyperintense tract	**1**	**1**
NA	**15**	**15**
Total	**100**	**100**

This table shows the distribution of cases according to the radiological investigations. Out of the total 100 cases studied, radiological investigations were available for 85 (85%) of the cases. The most common finding on radiological investigation in the current study was pleomorphic adenoma in 35(35%) of the case. This was followed by hypoechoic lesion in 18(18%) of the cases, bulky parotid in 12 (12%).

TABLE NO- 7 CLASSIFICATION OF CASES AS PER THE CYTOLOGICAL DIAGNOSIS

Cytodiagnosis	Number of cases	Percentage
Non neoplastic	38	38
Benign neoplasm	50	50
Malignant neoplasm	12	12
Total	100	100

This table shows the distribution of the cases into categories of non neoplastic, benign neoplasm and malignant neoplasm as per their cytodiagnosis . Out of the total 100 cases studied, the highest number of cases came out to belong to the benign neoplasm category (50%) . Non neoplastic cases accounted for 38(38%) and malignant neoplastic ones came out to be 12(12%) of the total.

TABLE NO – 8 MILAN CYTOLOGICAL GRADING

MILAN Category	Diagnosis	Number of cases	Percentage
CATEGORY - I	Insufficient to report	6	6
CATEGORY-II	Sialadenitis Sialadenosis Benign cystic pathology Acute parotitis Granulomatous parotid	31	31
CATEGORY-III	Atypia of undetermined significance	1	1
CATEGORY-IVa	Pleomorphic adenoma Warthin's tumor Basal cell adenoma	47	47
CATEGORY-IVb	Atypical pleomorphic adenoma Salivary gland neoplasm of uncertain	2	2

	malignant potential (SUMP)		
CATEGORY-V	Suspicious of malignancy	1	1
CATEGORY-VI	Malignant aspirate Mucoepidermoid carcinoma Salivary duct carcinoma Mammary analogue of secretory carcinoma Adenoid cystic carcinoma Acinic cell carcinoma Squamous cell carcinoma Metastasis	12	12
Total		100	100

The above table shows the distribution of cases included in the current study into individual Milan categories based on the cytological diagnosis and the number of cases in each category. The first category that is non-diagnostic or insufficient to report included a total of 6 cases in the current study. The second category of non neoplastic lesions included 31 of the cases. One case belonging to category III of atypia of undetermined significance was noted. Category IV a of benign neoplasms included the highest number of cases i.e. 47 in the current study. Two cases belonging to category IV b were noted. One case was reported as suspicious for malignancy. A total of 12 malignancies belonging to category VI were observed.

TABLE NO- 9 CYTOLOGICAL CASES WITH HISTOLOGICAL FOLLOW UP

MILANCATEGORY	Cases	HISTO FOLLOW UP	Percentage
Category I	6	2	33.33
Category II	31	13	34.48
Category III	1	1	100
Category IVa	47	28	53.33
Category IVb	2	1	50
Category V	1	1	100
Category VI	12	6	81.25
Total	100	52	100

Out of the total 100 cases studied for cytology in the current study, histopathological follow-up was available for a total of 52 cases. The above table depicts the number and proportion of cases for which histological follow-up was available with respect to every Milan category. Out of the total 6 cases belonging to Category I as non-diagnostic, histological follow-up was available for 2 of the cases, for 13 cases out of 31 in category II, for the only case observed in category III. 28 cases were followed up histologically out of total 47 in category IVa. 50% of cases in category IVb and VI and the only case in category V had histological follow up available.

TABLE NO- 10 GROSS EXAMINATION

GROSS EXAMINATION	Patients	Percentage
Bosselated	21	40.38
Encapsulated	5	9.62
Globular	14	26.92
Nodular	12	23.08
Total	52	100

The above table depicts the distribution of cases as per the findings observed on gross examination of external surfaces of the 52 specimens received in the histopathological section of our department in the current study. Majority of the cases 21 (40.38 %) showed a bosselated appearance, followed by globular 14 (26.92 %) and nodular12(23.08%). 5(9.62%) of the cases showed encapsulated appearance.

TABLE NO- 11 CUT SECTION

Cut section	Patients	Percentage
Tan white nodular	20	38.46
Tan white	28	53.84
Tan brown with haemorrhage	4	7.69
Total	52	100

The above table depicts the distribution of cases according to the observations made on cut section of the 52 specimens received for the histopathological examination. In the current study, the most common observation on cut section was tan white appearance in 28 of the cases. This was followed by tan white nodular cut section in 20 cases. Only 4 of the cases showed a tan brown cut section with haemorrhages.

TABLE NO- 12 CYTOHISTOLOGICAL CORRELATION

MILAN CATEGORY	Cytological diagnosis	Histological follow up	Concordant	Discordant	Percentage correlation
I	Non-diagnostic	2	2	0	100
II	Non-neoplastic	13	13	0	100
III	Atypia of undetermined significance	1	1	0	100
IVa	Benign neoplasm.	28	26	2-Salivary duct carcinoma MEC	92.85
IVb	Salivary neoplasm of uncertain malignant potential (SUMP)	1	0	1 Carcinoma ex pleomorphic adenoma	0
V	Suspicious of malignancy	1	0	1 Mucoepidermoid carcinoma	0
VI	Malignant	6	5	1 Cellular pleomorphic adenoma	83.33
	Total	52	47	5	

The above table depicts the correlation of cytological diagnosis with their histological follow-ups along with calculating the concordant and discordant cases and the percentage correlation of each category. All the cases belonging to category 1, 2, and 3 came out to be concordant on histological follow-up and showed 100% correlation. Two of the cases out of the total 28 belonging in category IVa came out to be discordant, making the percentage correlation as 92.85%. One case each in category IVb and V came out malignant on histology making the correlation in current study as 0 in these two Categories. Out of the total 6 cases belonging to category VI, 1 case came out to be discordant and non malignant making the percentage correlation as 83.33%.

TABLE NO- 13 RISK OF MALIGNANCY

Cytological category	Cases with histological follow up	Cases that came out to be malignant	Estimated risk of malignancy (%)	Risk of malignancy as per MSRSGC (%)
CATEGORY- I	2	0	0	25
CATEGORY-II	13	0	0	10
CATEGORY- III	1	0	0	20
CATEGORY- IVa	28	2	7.14	<5
CATEGORY- IVb	1	1	100	35
CATEGORY- V	1	1	100	60
CATEGORY- VI	6	5	83.33	90

The above table depicts the estimated risk of malignancy for each category and comparison of that risk with the proposed risk of malignancy as per MSRSGC. None of the cases of category I, II and III came out to be malignant making the risk of malignancy as 0% for each of these categories. Out of the total 28 cases included in Category IVa, 2 came out to be malignant with the diagnosis of salivary duct carcinoma and mucoepidermoid carcinoma hence making the risk of malignancy as 7.14 %. The only case observed under category IV b came out to be malignant on histopathology with the diagnosis of carcinoma ex pleomorphic adenoma, hence making the risk of malignancy for the current study as 100%. 5 of the cases out of the total 6 observed in Category VI came out to be malignant on histopathology, hence making the risk

of malignancy as 83.33%. The risk of malignancy calculated for every individual category in the current study is compared with the risk of malignancy given as per Milan system of reporting salivary gland cytology (MSRSGC).

True positive cases- 5. True negative cases- 42
False negative cases- 4 False positive cases- 1
Senstivity of the test came out to be 55.56%. **Specificity** - 97.67%.
PPV- 83.33% NPV- 91.30% Diagnostic accuracy of the test- 90.38%

A statistical analysis was performed for the 52 cases for which histopathological follow-up was available and a sensitivity of 55.56% was observed and the specificity that was observed was as 97.67%. The diagnostic accuracy for differentiating benign from malignant disease was 90.38% and the positive and negative predictive values were 83.33% and 91.30% respectively.

CYTOHISTOLOGICAL IMAGES

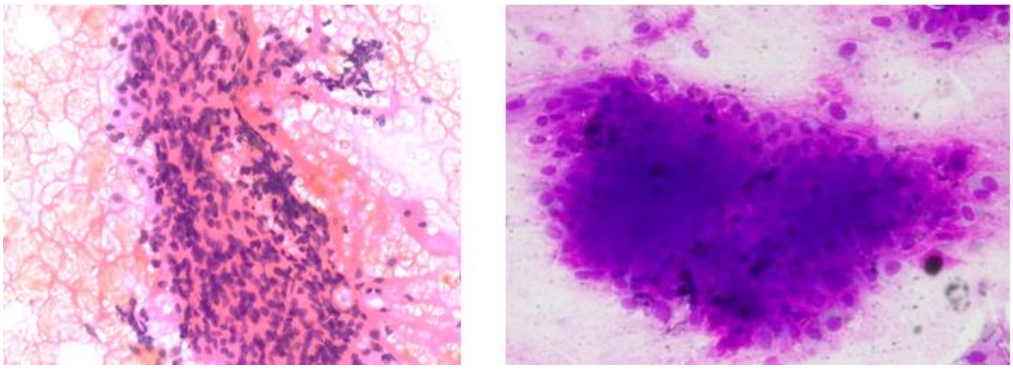


IMAGE 5 & 6- CYTOLOGICAL SMEARS OF PLEOMORPHIC ADENOMA (H&E)100x and (MGG)400X- WITH DUCTAL EPITHELIAL CELLS AND MYOEPITHELIAL CELLS AGAINST FIBRILLARY CHONDROMYXOID GROUND SUBSTANCE.

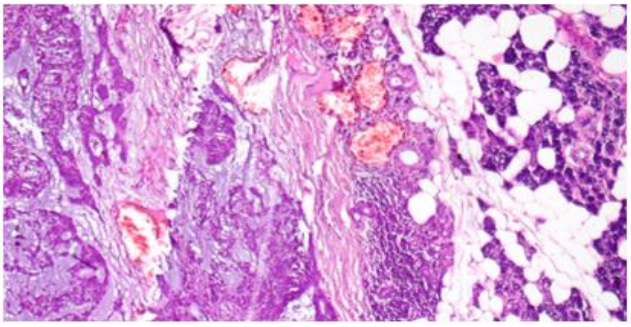


IMAGE 7- HISTOLOGICAL IMAGES OF PLEOMORPHIC ADENOMA (H&E) 100X - MIXED TUMOR COMPRISING OF EPITHELIAL AND MYOEPITHELIAL COMPONENTS ALONG WITH ABUNDANT CHONDROMYXOID STROMA.

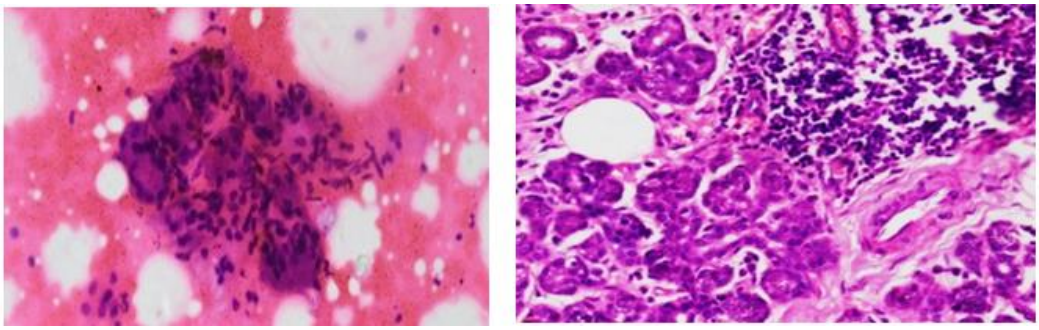


IMAGE 8 & 9- CYTOLOGICAL ANDHISTOLOGICAL IMAGE OF CHRONIC SIALADENITIS (H&E) 40X AND 400X –BENIGN SALIVARY GLAND ACINI WITH INFILTRATION BY CHRONIC INFLAMMATORY CELLS.

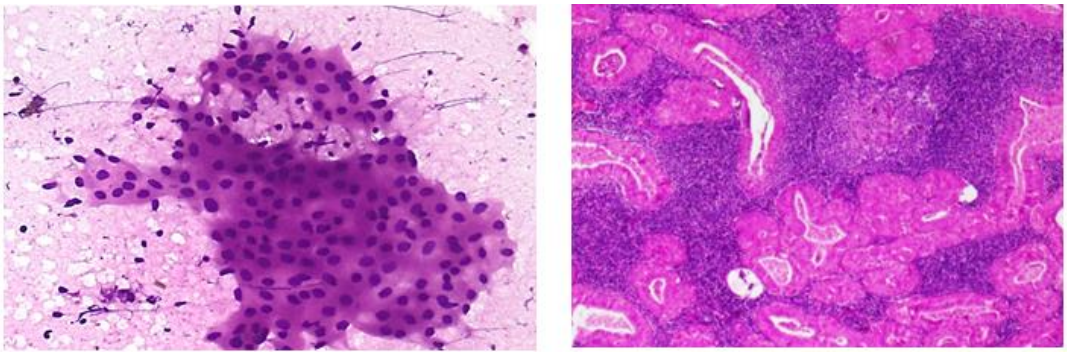


IMAGE NO-10- CYTOLOGICAL AND HISTOLOGICAL IMAGES OF WARTHIN'S TUMOR (H&E) 400X and 100x– CLUSTERS OF ONCOCYTIC CELLS WITH LYMPHOCYTES IN THE BACKGROUND.

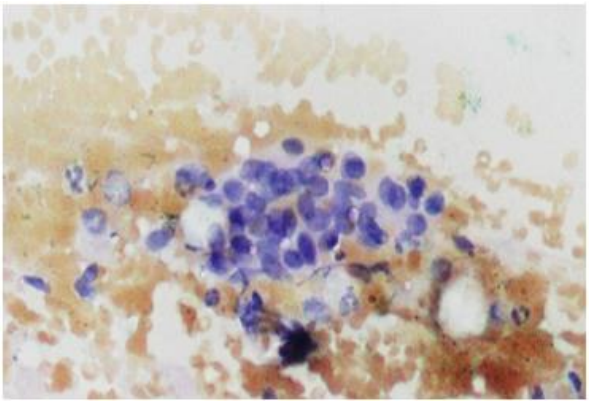


IMAGE NO 11- CYTOLOGICAL IMAGE OF SALIVARY GLAND NEOPLASM OF UNCERTAIN MALIGNANT POTENTIAL(SUMP)- (PAP) 400X- CLUSTERS OF SALIVARY EPITHELIAL CELLS WITH ROUND, OVAL NUCLEI AND MILD DEGREE OF ANISONUCLEOSIS

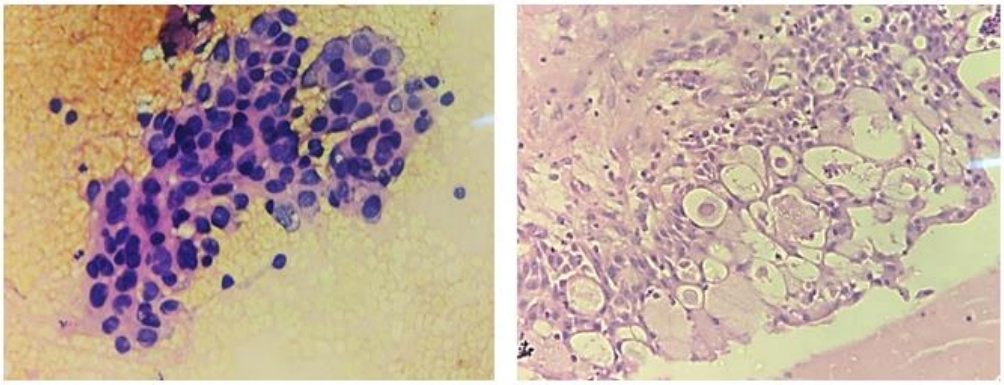
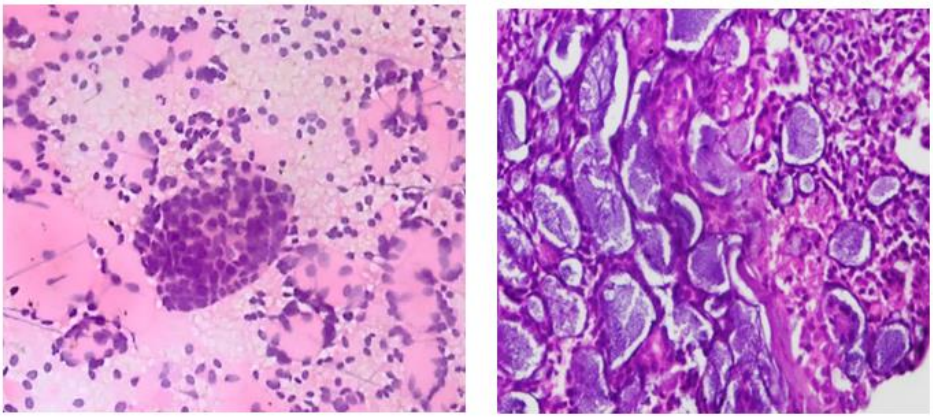


IMAGE NO 12- CYTOLOGICAL and HISTOLOGICAL IMAGES OF LOW GRADE MUCOEPIDERMOID CARCINOMA (H&E)- 400X - CLUSTERS OF MALIGNANT EPITHELIAL CELLS WITH NUCLEAR PLEOMORPHISM. AT PLACES, THE CELLS SHOW PINKISH EOSINOPHILIC HYALINE MATRIX. BACKGROUND SHOWS MUCINOUS MATERIAL.



MAGE NO 13 and IMAGE 14- CYTOLOGICAL AND HISTOLOGICAL IMAGE (H&E) 400X OF ADENOID CYSTIC CARCINOMA. BASALOID TUMOR CELLS ARRANGED IN CYSTS AND MICROCYSTS, HAVING HYPERCHROMATIC NUCLEI AND SCANT CYTOPLASM.

DISCUSSION

Salivary gland tumors constitute about 6% of all head and neck neoplasms and 0.5% of allhuman malignancies. Clinically, patients often present with a palpable lump, sometimes accompanied by pain, prompting the need for prompt evaluation. Diagnosing salivary gland lesions poses challenges due to their diverse morphology and overlapping features. Among various diagnostic modalities, fine-needle aspiration cytology (FNAC) stands out as a safe, cost-effective, minimally invasive, and reliable initial diagnostic tool. FNAC not only facilitates early diagnosis but also assists in clinical triage, helping avoid unnecessary surgeries in non-neoplastic cases.

FNAC offers advantages over frozen section analysis by enabling preoperative assessment.The introduction of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) has brought structure and clarity to salivary gland cytology, offering defined diagnostic categories with corresponding risks of malignancy. This system enhances communication between cytopathologists and clinicians, improving treatment planning and patient outcomes.

In the present study, 100 FNAC cases were evaluated using the MSRSGC system, with histopathological correlation available in 52 cases. This approach allowed accurate classification, aiding in risk stratification and better clinical management. The study affirms the value of MSRSGC as a standardized and effective tool in the diagnostic workup of salivary gland lesions.

TABLE NO-14 AGE DISTRIBUTION COMPARISON

Study	Age Range	Most Affected Age Group	Peak Incidence (%)
Present Study	9–74	41–60 yrs	49%
Naz et al. (2018)[14]	10–75	31–50 yrs	45%
Reddy et al. (2021)[15]	12–72	41–60 yrs	52%
Mallick et al. (2016)[16]	15–80	40–60 yrs	47%

The table compares age distribution across four studies, showing that salivary gland lesions affect a wide age range (9–80 years). Despite this broad spectrum, the peak incidence consistently falls in the 41–60 years age group. In the present study, 49% of cases occurred in this age group, closely matching findings by Reddy et al. (2021) at 52%, Naz et al. (2018) at 45%, and Mallick et al. (2016) at 47%. This consistency suggests a middle-age predilection, likely due to cumulative risk factor exposure and age-related glandular changes contributing to lesion development.

TABLE NO -15 GENDER DISTRIBUTION COMPARISON

Study	Male (%)	Female (%)	Male:Female Ratio
Present Study	54	46	1.17:1
Yadav et al. (2020)[17]	52	48	1.08:1
Das et al. (2015)[18]	56	44	1.27:1
Kalbi et al. (2017)[19]	49	51	0.96:1

The comparative table shows a slight male predominance in salivary gland lesions, with a male-to-female ratio of 1.17:1 in the present study, aligning with findings by Yadav and Das. Kalbi et al. reported a slight female predominance. Overall, most studies suggest marginalmale preponderance due to differential risk exposure.

TABLE NO -16 SITE DISTRIBUTION COMPARISON

Study	Parotid (%)	Submandibular (%)	Minor Glands (%)
Present Study	72	25	3
Sengupta et al. (2018)[20]	68	28	4
Bansal et al. (2019)[21]	75	20	5
Lobo et al. (2016)[22]	70	25	5

The comparative table shows the parotid gland as the most commonly involved site in salivary gland lesions across all studies, including the present one (72%). Similar findings were reported by Lobo et al. (70%) and Sengupta et al. (68%), with Bansal et al. noting the highest (75%). Submandibular gland involvement was consistently second (20–28%), while minor salivary gland lesions were least common (3–5%), likely due to their smaller size, deeper location, and relative anatomical scarcity.

TABLE NO – 17 RADIOLOGICAL FINDINGS COMPARISON

Study	Most Common Finding	Other Common Findings
Present Study	Pleomorphic adenoma (35%)	Hypoechoic lesion, bulky parotid
Pai et al. (2021)[23]	Pleomorphic adenoma (38%)	Sialadenitis, Warthin tumor
Sharma et al. (2017)[24]	Hypoechoic lesions (40%)	Sialadenitis, cysts
Rajwade et al. (2016)[25]	Pleomorphic adenoma (30%)	Parotid swelling, neoplastic changes

The comparative table shows pleomorphic adenoma as the most common salivary gland lesion, reported in 35% of cases in the present study, closely matching findings by Pai et al. (38%) and Rajwade et al. (30%). This reaffirms its status as the most prevalent benign salivary gland tumor, especially in the parotid. Common clinical features included hypoechoic lesions and bulky parotid glands. Sharma et al. (2017) emphasized hypoechoic lesions (40%) along with sialadenitis and cysts, reflecting a broader spectrum of inflammatory and non-neoplastic lesions. Despite this diversity, pleomorphic adenoma consistently dominates salivary gland pathology.

TABLE NO- 18 MILAN CATEGORY DISTRIBUTION

Study	I (%)	II (%)	III (%)	IVa (%)	IVb (%)	V (%)	VI (%)
Present Study	6	31	1	47	2	1	12
Rossi et al. (2017)[26]	5	33	3	43	3	2	11
Pusztaszeri et al. (2015)[27]	8	29	4	42	5	4	8
Baloch et al. (2020)[28]	7	30	2	45	3	3	10

This comparative table analyzes salivary gland lesion distribution using the Milan System across four studies. In the present study, category IVa (benign neoplasm) was most common (47%), aligning closely with Rossi (43%), Pusztaszeri (42%), and Baloch (45%), confirming the predominance of benign tumors in salivary gland cytology. Category II (non-neoplastic) was the second most frequent, comprising 31% of cases, consistent with a 29–33% range in other studies. Non-diagnostic (category I) and malignant cases (category VI) showed relatively low but similar frequencies, reported as 6% and 12%, respectively, in the present study. Categories III (AUS) and IVb (SUMP) were less frequent across all studies, reflecting their lower diagnostic yield. The consistent distribution across multiple studies underscores the reliability and reproducibility of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC), promoting diagnostic uniformity, risk stratification, and effective clinical decision-making through standardized cytological reporting.

TABLE NO- 19 CYTOHISTOLOGICAL CORRELATION

Study	Concordance Rate (%)	Discordant Cases	Most Misdiagnosed Category
Present Study	90.38	5	IVa (false negative)
Nayar et al. (2018)[29]	89.1	6	IVa
Dwivedi et al. (2021)[30]	91.2	4	VI
Gupta et al. (2019)[31]	88.7	7	IVb

The table compares histopathological-cytological concordance across four studies using the Milan System. The present study showed a high concordance rate of 90.38%, similar to Nayar (89.1%), Dwivedi (91.2%), and Gupta (88.7%), supporting FNAC's diagnostic reliability. Most discordances involved category IVa in the present and Nayar's studies, while Dwivedi and Gupta observed errors in categories VI and IVb, respectively, underscoring the need for careful evaluation in these diagnostically challenging categories.

TABLE NO-20 RISK OF MALIGNANCY (ROM) COMPARISON BY CATEGORY

Milan Category	ROM (Present Study)	ROM in MSRSGC (%)	ROM Range in Other Studies
I	0	25	10–30[32-38]
II	0	10	0–10[32-38]
III	0	20	10–25[32-38]
IVa	<5	<5	0–10[32-38]
IVb	100	35	30–50[32-38]
V	100	60	60–80[32-38]
VI	83.3	90	80–100[32-38]

The table compares Risk of Malignancy (ROM) across Milan System categories. Categories I–III in the present study showed 0% ROM, aligning with MSRSGC expectations. Category IVa had ROM <5%, consistent with benchmarks. However, category IVb showed 100% ROM, exceeding the expected 30–50%, suggesting underestimated malignancy risk. Categories V and VI showed high ROMs of 100% and 83.3%, respectively. These findings support the Milan System's diagnostic accuracy while emphasizing caution in interpreting indeterminate categories like IVb (SUMP).

TABLE NO- 21 DIAGNOSTIC ACCURACY COMPARISON

Study	Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Present Study	55.56	97.67	90.38	83.33	91.30
Viguer et al. (2018)[39]	65	95	89	85	90
Shintaku et al. (2020)[40]	60	94	88	80	88
Fernando et al. (2021)[41]	70	93	90	82	90

The table compares FNAC diagnostic performance metrics for salivary gland lesions across studies. In the present study, specificity (97.67%) and negative predictive value (91.30%) were high, reflecting FNAC's strong ability to exclude malignancy. Accuracy stood at 90.38%, aligning with Fernando et al. (90%) and Viguer et al. (89%), affirming FNAC's overall diagnostic reliability. However, sensitivity was comparatively low at 55.56%, indicating a higher risk of false negatives, especially in low-grade or misinterpreted malignancies. The positive predictive value was 83.33%, consistent with other studies, showing reliable identification when FNAC suggests malignancy. These findings confirm FNAC's usefulness as a first-line diagnostic modality with excellent specificity and accuracy but also underscore the need for improved sensitivity—potentially through adjunctive techniques or repeat sampling—to better detect malignancies with subtle cytological features.

TABLE NO-22 COMMON CYTOLOGICAL DIAGNOSES COMPARISON

Study	Most Common Diagnosis	%	Other Common Diagnoses
Present Study	Pleomorphic adenoma	43%	Sialadenitis, MEC, Warthin
Nagarkar et al. (2016)[42]	Pleomorphic adenoma	48%	Warthin, benign cyst
Roy et al. (2020)[43]	Pleomorphic adenoma	44%	MEC, sialadenitis
Sangoi et al. (2015)[44]	Pleomorphic adenoma	41%	Warthin, carcinoma

The table highlights the diagnostic distribution of salivary gland lesions, with pleomorphic adenoma consistently identified as the most common tumor. In the present study, it constituted 43% of cases, closely paralleling findings by Roy et al. (44%), Nagarkar et al. (48%), and Sangoi et al. (41%). This consistency confirms pleomorphic adenoma as the predominant benign salivary gland neoplasm, especially in the parotid gland. Other commonly observed lesions include Warthintumor, sialadenitis, and mucoepidermoid carcinoma, reflecting a spectrum of both benign and malignant conditions. The frequent occurrence of inflammatory and cystic lesions further highlights the cytological diversity in salivary gland FNAC. Accurate identification, particularly of pleomorphic adenoma, is essential due to its frequency and recognizable cytomorphological features.

TABLE NO- 23 HISTOLOGICAL DIAGNOSES COMPARISON

Study	Most Common Histology	%	Rare Diagnoses
Present Study	Pleomorphic adenoma	17/52	Oncocytoma, carcinoma ex PA
Chaudhary et al.	Pleomorphic adenoma	19/50	Lymphoepithelial cyst

(2018)[45]			
Biswas et al. (2019)[46]	Pleomorphic adenoma	18/45	SDC, MASC
Goyal et al. (2017)[47]	Pleomorphic adenoma	21/55	Granulomatous lesion

The table compares histopathological diagnoses across four studies, consistently identifying pleomorphic adenoma as the most common finding. In the present study, it constituted 17 of 52 cases, similar to Chaudhary et al. (19/50), Biswas et al. (18/45), and Goyal et al. (21/55), reaffirming its predominance among salivary gland neoplasms. While pleomorphic adenoma dominates, each study also reported a range of less common diagnoses, emphasizing the histological heterogeneity of salivary gland lesions. The present study documented rare entities like oncocytoma and carcinoma ex pleomorphic adenoma, whereas other studies identified unusual lesions such as lymphoepithelial cysts, salivary duct carcinoma (SDC), mammary analogue secretory carcinoma (MASC), and granulomatous inflammation. These findings underscore the diagnostic challenges posed by salivary gland tumors and highlight the need for detailed histopathological analysis to ensure accurate identification of both common and rare entities, which is crucial for appropriate treatment planning and prognosis.

SUMMARY AND CONCLUSION

The present study evaluated the diagnostic efficacy of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) in 100 cases of salivary gland lesions, with histopathological correlation in 52 cases. The most affected age group was 41–60 years, with a slight male predominance. The parotid gland was the most commonly involved site (72%), and most patients presented with a painless lump. Pleomorphic adenoma was the most frequent cytological and histological diagnosis.

The majority of cases fell under Category IVa (47%), followed by Category II (31%). Cytohistological concordance was 90.38%, with most discordances in Category IVa due to misclassified malignancies. Diagnostic sensitivity was moderate (55.56%), but specificity (97.67%) and accuracy (90.38%) were high, affirming FNAC's reliability. Risk of malignancy (ROM) matched MSRSGC benchmarks, except for Category IVb, which showed unexpectedly high ROM (100%).

The findings were consistent with prior studies, reinforcing MSRSGC's diagnostic utility. The system standardizes reporting, aids communication, and informs clinical decisions. It is especially effective in identifying benign neoplasms but requires caution in indeterminate or overlapping cases. Integration of ancillary techniques and larger studies are recommended to enhance diagnostic sensitivity and further validate the system's applicability.

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