Original Article

Evaluation and Application of Milan System in Cyto-Diagnosis of Salivary Gland Lesions at Tertiary Care Teaching Hospital

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Abstract

Background: Fine needle aspiration cytology (FNAC) of salivary gland lesions is an inexpensive, minimally invasive, easier to perform and outpatient diagnostic procedure, which is helpful to clinicians for earlier diagnosis and treatment because of rapid turnaround time.

Methods: The present study is conducted retrospectively over a period of one year to classify salivary gland lesions according to Milan system; all patients were subjected to FNAC by using 22-24 gauge needle attached to a 10 ml syringe, with at least two needle passes were made for each patient. Smears are stained an analyzed under light microscopy.

Results: Out of total (n=80) cases the number of cases in each category were: non-diagnostic 15% and 85% were diagnostic. Out of 85% diagnostic cases, neoplastic lesions were observed in 57.5% of patients, non-neoplastic lesions in 27.5% of patient.

Conclusion: Fine needle aspiration cytology is a reliable examination, providing important information to the surgeon in the preoperative diagnostic assessment when Milan system was applied.

Keywords: Milan system; salivary gland; fine needle aspiration cytology; malignancy.

Introduction

Salivary glands are the exocrine glands responsible for production and secretion of saliva and consist of the major salivary glands which include parotid, submandibular, sublingual, and the minor glands that are numerous and widely distributed throughout the mouth and oropharynx.[1] Salivary gland neoplasms are relatively uncommon and constitute about 2%-6.5% of all the head and neck lesions. [2, 3]

Fine Needle Aspiration Cytology (FNAC) is the primary investigation of choice for evaluating salivary gland lesions, helping to differentiate between non-neoplastic, benign, and malignant neoplasms. If fine needle aspiration cytology is not confirmatory due to complexity of the lesion, histopathological diagnosis is considered the gold standard.[4]

The accuracy of FNA to differentiate benign lesions from malignant lesions has been observed to be as high as 81% to 100%. However, the accuracy of FNA to provide a specific diagnosis has a wider range of 48% to 94%. [5]

Salivary gland cytopathology poses significant diagnostic challenges owing to the marked heterogeneity of benign and malignant lesions, as highlighted in the comprehensive World Health Organization (WHO) 2022 classification.[6] The

wide spectrum of cytological features within a particular tumour type, as well as the morphological overlap between various entities, pose challenges for the pathologist to accurately diagnose salivary gland lesions by Fine Needle Aspiration (FNA).[7, 8]

Introduced in 2018, the first edition of the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) provided a standardized approach to the interpretation and reporting of salivary gland FNAs. The MSRSGC laid down six categories intending to improve the communication between pathologists and clinicians, and to formulate therapeutic strategies for each category. Since the publication of the first edition of the MSRSGC in 2018, numerous studies have validated its utility and effectiveness as a standardized diagnostic framework for salivary gland cytopathology. However, available studies lacked uniformity in the inclusion of all categories.[9, 10] This abundant data was used in the preparation of the second edition of the MSRSGC.[11] The second edition, published in July 2023, features redefined risk of malignancy (ROM) estimates for each diagnostic category, a new chapter added on the role of imaging studies, detailed descriptions of various diagnostic scenarios with surgical follow-up, updates on recent ancillary techniques, and revised nomenclature aligned with the 2022 World Health Organization classification of head and neck tumors. [12]

Category wise description of MILAN system by cytomorphological features are as given below:

Category I (Non diagnostic) [11]: A Non-Diagnostic salivary gland aspirate is one that, for qualitative and/or quantitative reasons, provides insufficient diagnostic material to provide an informative interpretation.

Cytologic Criteria for this category are rare or absent cells or less than 60 lesional cells; poorly prepared slides with artifacts (e.g., air-drying, obscuring blood, and poor staining) that preclude the evaluation of the cellular components; along with non-neoplastic (normal) salivary gland elements in the context of a clinically or radiologically evident mass; etc.

Category II (Non neoplastic) [11]: They are relatively common, can clinically mimic a neoplasm due to the presence of a distinct mass. Acute and chronic sialadenitis that also include granulomatous disease are the most common non-neoplastic lesions; other lesions include Sialolithiasis, Reactive Lymph Node Hyperplasia, Benign Lymphoepithelial Lesion/Lymphoepithelial Sialadenitis, etc.

Category III (Atypia of Undetermined Significance) [11]: This category is applied to salivary gland FNAs that lack sufficient qualitative or quantitative cytomorphologic features to allow a confident diagnosis as either non-neoplastic or neoplastic.

In addition, the FNA exhibits an atypical cytomorphologic feature that excludes the possibility of classifying it as "Non-Diagnostic." Most samples will represent reactive atypia or poorly sampled neoplasms.

Category IVA (Neoplasm Benign) [11]: This category will include classic cases of FNA specimens showing cytomorphologic features of a benign epithelial or mesenchymal neoplasm: 1) Epithelial origin: a. Pleomorphic Adenoma, b. Warthin Tumor, c. Oncocytoma; 2) Mesenchymal origin: a. Lipoma, b. Schwannoma, c. Lymphangioma, d. Hemangioma.

Category IVB (SUMP) [11]: FNA specimens showing cytomorphologic features diagnostic of a neoplastic process, but a malignant neoplasm cannot be excluded.

Entities commonly classified under this category include: (1) Cellular basaloid neoplasms, (2) Cellular oncocytic or oncocytoid neoplasms, and (3) Cellular neoplasms exhibiting clear cell features.

Category V (Suspicious for malignancy-SM) [11]: A salivary gland FNA is classified as SM when some, but not all the criteria for a specific diagnosis of malignancy are present, and yet the overall cytologic features are suggestive of malignancy.

Markedly atypical cells with poor smear preparation, poor cell preservation, fixation artifact, or obscuring inflammation and blood; and Presence of limited cytologic features of a specific malignant lesion in an otherwise sparsely cellular aspirate are observed in this category.

Category VI (Malignancy) [11]: Salivary gland aspirates classified as "Malignant" contain a combination of cytomorphologic features that, either alone or in combination with ancillary studies, is diagnostic of malignancy.

It include: 1) Low-grade like- Acinic Cell Carcinoma, Secretory Carcinoma, Epithelial-Myoepithelial Carcinoma, etc. 2) Indeterminate or multiple Grade Carcinomas like- Mucoepidermoid Carcinoma, Adenoid Cystic Carcinoma, Carcinoma ex Pleomorphic Adenoma, Secondary Malignant Tumors, etc. 3) High-Grade Carcinomas like- Salivary Duct Carcinoma, Lymphoepithelial Carcinoma, etc.

Materials and Methods

The present study is a retrospective study done in cytopathology section of department of pathology at B J medical college, Ahmedabad, over a period of 1 year from March 2024 to March 2025.

Detailed clinical data of age, sex, clinical history were retrieved from the laboratory Information system (LIS). Fine-needle

aspiration cytology was carried out using a 22–24-gauge needle and a 10 mL plastic syringe, without local anaesthesia. Air dried and 95% ethanol fixed smears were stained using Giemsa stain and Papanicolaou stain / Hematoxylin & Eosin (H & E), respectively. The slides along with details of the patient were studied and findings were recorded. We classified our FNAC results into six categories according the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC).

Selection Criteria

Inclusion Criteria:

- All the patients who give consent for fine needle aspiration procedure.
- All cases with clinically palpable salivary gland lesions presented at the cytology section of department of pathology within the study period.

Exclusion Criteria:

- Salivary gland–like tumors arising in organs other than the salivary glands were excluded from the study.

Results

A total 80 FNAC cases of salivary gland lesions were included in the study in a period of one year. Various parameters of study are as described below:

The age of these studied cases range from 5 to 79 yrs. The highest number of cases occurred in the 41–50 years age group, followed by the 51–60 years age group. Males were more commonly affected in the study population, with a male-to-female ratio of 1.2:1. The distribution of cases by age and gender is summarized in Table 2.

Out of 80 cases, 26 (32.5%) cases were inferred as benign neoplasm, 12 (15%) cases were non-diagnostic, 22 (27.5%) cases were non-neoplastic, 4 (5%) cases were diagnosed as category of atypia of undetermined significance with cells showing atypical cytomorphologic feature, 6 (7.5%) cases were diagnosed as salivary gland neoplasm of uncertain malignant potential, 10 (12.5%) cases were found to be malignant. There were no cases diagnosed as 'Suspicious for Malignancy' in the present study. According to cytomorphological distribution Chronic sialadenitis was the most common diagnosis among non-neoplastic lesions (45.5%, N=22). Pleomorphic adenoma was the most common benign neoplastic lesion (92.3%, N=26) observed in present study. Mucoepidermoid carcinoma most common malignant lesion (90%, N=10) of salivary glands were observed in present study as shown in Table 3.

In the present study most common lesion observed belonged to the category belonged to category IVA (26 cases-32.5%), followed by category II (22 cases-27.5%). Predominance of these lesions was corroborated with the previously reported number of studies of Deepti Arora et al. [13], Kala C et al. [9], Gaikwad VP et al. [14], et al Singh et al. [15]. Comparison between various peer group studies is shown in Table 4.

Table 1: Second edition of Milan system for reporting salivary gland cytopathology (MSRSGC) with risk of malignancy and recommended clinical management [11]

Diagnostic category	Risk of malignancy (ROM) %	Management
I, Non-Diagnostic	15	Clinical & Radiological correlation/Repeat FNA
II, Non-Neoplastic	11	Clinical follow up & Radiological correlation
III, Atypia of undetermined significance	30	Repeat FNA/Surgery
IV A, Neoplasm Benign	< 3	Surgery/Clinical Follow up
IV B, SUMP (Salivary gland neoplasm of uncertain malignant potential)	35	Surgery
V, Suspicious for malignancy	83	Surgery
VI, Malignant	> 98	Surgery

Discussion

In the present study, 80 cases of salivary gland lesions evaluated by FNAC were categorised according to MSRSGC category. Various cytomorphological parameters were evaluated in FNAC samples of salivary gland lesions in the present study. These

Table 2: Distribution of cases according to Age and Gender in present study (n=80)

Variables		No. of cases (%)
Age (Years)	0-10	2 (2.5%)
	11-20	6 (7.5%)
	21-30	9 (11.25%)
	31-40	14 (17.5%)
	41-50	17 (21.25%)
	51-60	15 (18.75%)
	61-70	14 (17.5%)
	>70	3 (3.75%)
Gender	Male	44 (55%)
	Female	36 (45%)

Table 3: Cytomorphological spectrum of salivary gland lesions in present study (n=80)

Diagnostic category	Cytopathological Diagnosis	No. of cases	Percentage (%)
I. Non-diagnostic	Inadequate for interpretation	12	15
II. Non-neoplastic	Acute Sialadenitis	1	1.25
	Acute on chronic Sialadenitis	2	2.5
	Chronic non-specific Sialadenitis	10	12.5
	Granulomatous Sialadenitis	2	2.5
	Sialadenosis	2	2.5
	Benign lesion of minor salivary gland	2	2.5
	Benign lympho-epithelial lesion	2	2.5
	Benign cystic lesion	1	1.25
III. Atypia of undetermined significance	Cells with atypia	4	5
IV A. Neoplasm Benign	Pleomorphic Adenoma	24	30
	Warthin's tumor	2	2.5
IV B. SUMP	Cellular basaloid neoplasm	3	3.75
	Cellular oncocytic neoplasm	1	1.25
	Salivary gland neoplasm	2	2.5
V. Suspicious for malignancy	-	0	0
VI. Malignant	Mucoepidermoid Carcinoma	9	11.25
	Salivary Duct Carcinoma	1	1.25
Total	-	**80**	**100**

Table 4: Incidence of salivary gland lesions according to MSRSGC observed by various other studies

MSRSGC Categories	Deepti Arora et al [13] (n=106) (Year-2019)	Kala C et al [9] (n=293) (Year-2019)	Gaikwad VP et al [14] (n=79) (Year-2020)	Singh et al [15] (n=133) (Year-2020)	Present study (n=80) (Year-2025)
CATEGORY I	5 (5%)	18 (6%)	1 (1%)	5 (4%)	12 (15%)
CATEGORY II	37 (34%)	112 (38%)	24 (31%)	29 (22%)	22 (27.5%)
CATEGORY III	3 (3%)	8 (3%)	4 (5%)	4 (3%)	4 (5%)
CATEGORY IVA	49 (46%)	98 (33%)	37 (47%)	77 (58%)	26 (32.5%)
CATEGORY IVB	2 (2%)	6 (2%)	1 (1%)	3 (2%)	6 (7.5%)
CATEGORY V	4 (4%)	7 (3%)	1 (1%)	1 (1%)	0 (0%)
CATEGORY VI	6 (6%)	44 (15%)	11 (14%)	14 (10%)	10 (12.5%)

information are useful in showing patterns of salivary gland lesions in our region. We have correlated results of our study with several other studies.

Common age group affected in benign salivary gland tumour was 41 to 50 years which was in concordance with studies conducted by Deepti Arora et al. [13]. The overall male to female ratio was 1.2:1 which was in concordance with Kala C et al. [9], Desai P et al. [16], and Junnudevi et al. [17]. However, the study of Roma et al. [18] showed slight female preponderance.

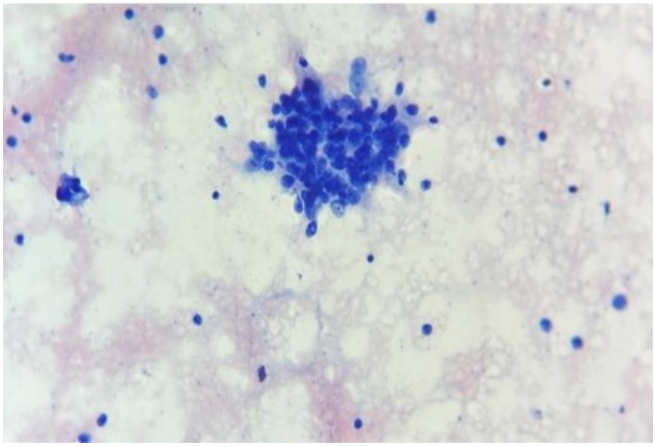

Figure 1: Category II, Non-Neoplastic: Chronic sialadenitis. Small atrophic ductal group with background chronic inflammation (Papanicolaou stain; high power view)

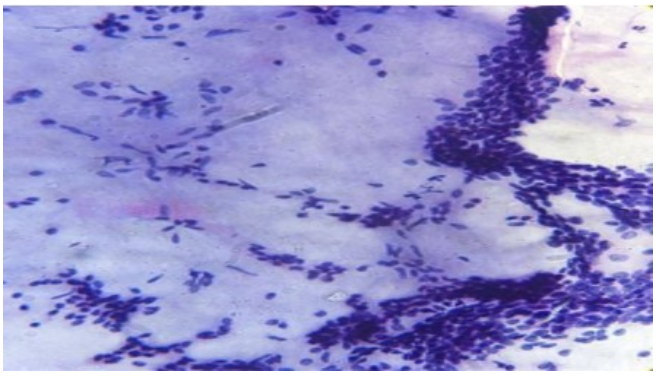

Figure 2: Category IV A, Neoplasm benign: Pleomorphic Adenoma, Moderately cellular smear with epithelial cells in sheets with myoepithelial cells being embedded within chondromyxoid matrix. (H & E stain; high power view)

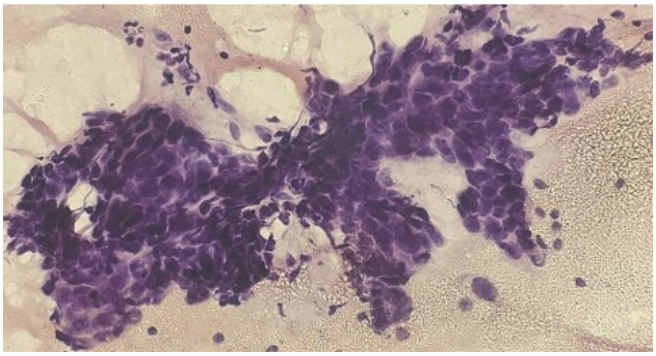

Figure 3: Category IV B, SUMP: Basaloid tumor cells arranged in a cellular cohesive group with nuclear crowding and minimal to no stroma (Papanicolaou stain; high power view)

In the study group, majority cases (32.5%) were in benign neoplastic group (Cat IVA), followed by 27.5% in non-neoplastic group (Cat II), and 12.5% in malignant group (Cat VI). These results were in concordance with the findings of studies conducted by Karuna V et al. [10], Subrata P et al. [19], and Sheetal GG et al. [20]

The most common benign neoplasm found was pleomorphic adenoma (30%) in present study, which was consistent with the studies done by Roma et al. [18], Desai P et al. [16], Vaishali et al. [21], and Junnudevi et al. [17].

Conclusion

To conclude, present study includes FNAC analysis of total 80 cases of salivary gland lesions performed over a period of one year in our institute. In present study, we found that Pleomorphic adenoma (30%) was the commonest benign neoplastic salivary gland lesion, while Mucoepidermoid Carcinoma (11.25%) was the commonest malignant neoplastic salivary gland lesion. We had compared the results of our study with other peer group studies and we found that data were comparable for

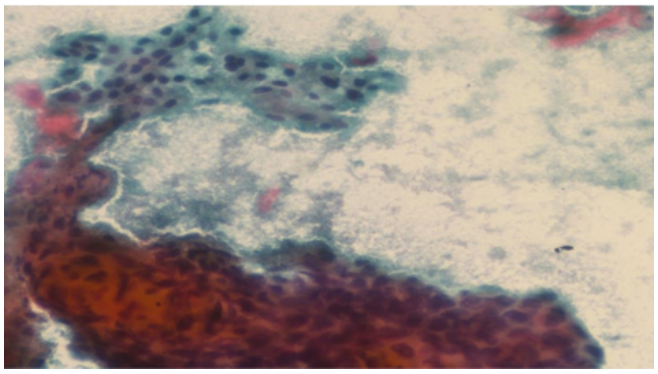

Figure 4: Category VI, Malignancy: High grade Mucoepidermoid Carcinoma. Highly cellular smear shows cohesive flat sheets of squamoid cells with pleomorphic nuclei, intermediate cells and mucous cells on a necrotic background. (Papanicolaou stain; high power view)

various parameters in the study. Due to paucity of precise architectural details, low grade malignancies can be reported as benign or vice versa. So, the categorization makes it very effective and universal mode of reporting by which clinicians and patients get non subjective information regarding the disease, further investigations, and treatment required. Thus, MSGSRC enhances diagnostic accuracy of salivary gland lesions with valuable impact on clinical management of patient.

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