# Milan System for Reporting Salivary Gland Cytopathology - A Two Years' Experience in a Referral Centre of Western Odisha

Bijayalaxmi Sahoo[1], Sunanda Nayak[2], Gitimadhuri Dutta[3], Shailaja Prabhala[4], Kulwant Lakra[5]

[1, 4] Department of Pathology, AIIMS, Bibinagar, Telangana, India. [2, 3] Department of Pathology, VSSIMSAR, Burla, Odisha, India. [5] Department of Community Medicine, VSSIMSAR, Burla, Odisha, India.

**ABSTRACT**

**BACKGROUND**

Neoplasms of salivary gland account for 2 - 6.5 % of all head and neck neoplasms. Fine needle aspiration cytology (FNAC) is sufficiently sensitive and relevant to the diagnosis and treatment of salivary gland pathologies for salivary gland lesions. The Milan system for reporting salivary gland cytopathology (MSRSGC) represents a stage for a structured, evidence-based international reporting system for salivary gland fine-needle aspiration (FNA). This system provides a guidance for diagnosis and management according to the risk of malignancy (ROM) in different categories. We wanted to study the various cytomorphological lesions of salivary gland and their cytological categorisation based on the MILAN system of reporting.

**METHODS**

A 2-year record-based study (January 2018 to December 2019) was conducted on FNAC of salivary gland lesions in the Department of Pathology, VSSIMSAR (Veer Surendra Sai Institute of Medical Sciences and Research), Burla, Odisha. Based on the classical system, all smears were studied and re-categorized into six groups according to the MILAN classification. Histological correlation was carried out in the available cases.

**RESULTS**

A total of 103 FNA cases were examined and 20 different categories were there in the original diagnosis. As per the categorisation based on MILAN System there were six categories, maximum cases were non-neoplastic 34 (33.0 %) followed by benign neoplasms 22 (21.35 %), malignant 14 (13.5 %), non-diagnostic 10 (9.7 %), atypia of undetermined significance 9 (8.7 %), suspicious for malignancy 8 (7.7 %) and neoplasms of uncertain malignant potential 6 (5.8 %). 43 cases (80.4 %) were found to be concordant out of 54 histopathology correlated cases.

**CONCLUSIONS**

The Milan system of reporting salivary gland cytopathology provided a uniform system of reporting salivary gland cytomorphology that may increase the effectiveness.

**KEYWORDS**

Milan System, Salivary Gland Lesions, FNAC, Risk of Malignancy (ROM)

*Corresponding Author:*
*Dr. Sunanda Nayak,*
*Patel Nursing Home Complex,*
*Kirba (Near VSSUT), Burla,*
*Sambalpur - 768018, Odisha, India.*
*E-mail: nayak_sunanda@yahoo.co.in*

*DOI: 10.18410/jebmh/2021/221*

*How to Cite This Article:*
*Sahoo B, Nayak S, Dutta G, et al. Milan system for reporting salivary gland cytopathology - a two years' experience in a referral centre of western Odisha. J Evid Based Med Healthc 2021;8(17):1146-1151. DOI: 10.18410/jebmh/2021/221*

*Submission 06-01-2021,*
*Peer Review 19-01-2021,*
*Acceptance 10-03-2021,*
*Published 26-04-2021.*

## BACKGROUND

Salivary glands are exocrine glands that are responsible for production and secretion of saliva and consist of the parotid, submandibular, sublingual and the minor glands situated in the submucosa of the whole upper aero digestive tract, from the lips and nasal cavity to the major bronchi. Microscopically, these glands are composed of tubulo-alveolar structures embedded in a mixed supporting stroma and possess acinar and duct system.[1] Salivary gland lesions (SGL) represent 3 % – 6 % of all tumours of the head and neck region.

Proper management of these tumours requires an accurate diagnosis by the pathologist, radiologist and clinicians.[2] Fine-needle aspiration cytology (FNAC) of salivary gland is used world-wide for the diagnosis and management of salivary gland tumours. It provides a minimally invasive, safe, cost-effective, and accurate technique that is extremely useful in identifying a substantial subset of salivary gland nodules as benign and thus reduces extensive invasive surgical procedure in patients with benign diseases. It also guides the further management strategy.[3-6]

Milan system for reporting salivary gland cytopathology (MSRSGS) includes diagnostic criteria, explanatory notes, implied risk of malignancy (ROM), and a brief management plan for each diagnostic category. This is a six-category system: a category of "neoplasm" divided into "benign" and "salivary gland neoplasm of uncertain malignant potential (SUMP)". Each category has an associated cancer risk, ranging from 0 % to 67 % for the "non-diagnostic" category to high 57 % – 100 % for the "malignant" category.[7,8]

This study was carried out to classify salivary gland lesions under Milan counsel, to ascertain rate of malignancy and to determine the diagnostic accuracy in and around our institute by correlating the cyto-histopathological diagnoses wherever available.

## METHODS

A 2-year record-based study was conducted between (January 2018 to December 2019) on FNAC of salivary gland lesions in the Department of Pathology, VSSIMSAR (Veer Surendra Sai Institute of Medical Science and Research) Burla, Odisha. Patients of all ages and either gender were included. Clinical data of the cases were collected from the cytology records and FNA smears from salivary gland lesions were retrieved from the cytology section of Department of Pathology from January 2018 to December 2019. Then the FNA smears of salivary gland lesions were reclassified by using MSRSGC categories. The histological reports and clinical follow-up, wherever available were compared.

### The Six Categories as per Milan System

(1) Non-diagnostic (ND),
(2) Non-neoplastic (NN),
(3) Atypia of undetermined significance (AUS),
(4) Neoplastic (benign neoplasm (BN) and salivary gland neoplasm of uncertain malignant potential [SUMP]),
(5) Suspicious for malignancy (SFM)
(6) Malignancy (M).

For histopathology examination, 10 % neutral buffer formalin fixed, surgically resected specimen and biopsy tissues were received, processed, and stained with H and E (haematoxylin and eosin). The FNA outcomes previously diagnosed were re- categorized according to the Milan system. Histopathological data wherever available were retrieved and in these cases, ROM was calculated for each category. The histological diagnosis was considered as gold standard.

### Statistical Analysis

The age, sex, site of involvement, categories and risk of malignancy (ROM) were expressed in terms of percentage and frequencies.

## RESULTS

The distribution of 103 cases was done according to age, sex and site of involvement. Males (60.1 %) were found to be affected more than females (39.8 %). Most number of cases were seen in the age group of 31 - 50 years (49.2 %) followed by 51 - 70 years (22.2 %). Table 1 shows that majority of the cases involved parotid gland followed by submandibular gland. Table 3 shows the FNAC distribution of cases according to MSRSGC. The largest category was NN (Cat 2) 33 % followed by NB (Cat 4a) 21.35 %. M, ND, AUS, SM and SUMP constitute 13.5 %, 9.7 %, 8.7 %, 7.7 %, and 5.8 % respectively. We were able to follow only 3 cases in category 1 (ND) out of 10 and of these, 1 case turned out to be adenoid cystic carcinoma on histological follow up, Overall ROM for this category reported was 33.3 %.

Histological follow-up of 09 cases was performed in category 2 (NN), Out of total 34 cases, 1 case of benign tumour was reported, which was incorrectly diagnosed as category 2 (NN) chronic sialadenitis. Overall, ROM reported for this category was 4.8 %. Histological follow up of 2 out of 9 cases were available in category 3 (AUS). One case was reclassified as pleomorphic adenoma (PA), and the other as adenoid cystic carcinoma (ACC). Overall, the ROM was 50 % for this category. We had histological follow up for 20 cases out of 22 cases in category 4a (BN). Out of these, 16 cases were diagnosed by FNAC as Pleomorphic adenoma, 15 cases showed concordance on histological follow-up and 1 case was reclassified into malignant category that was found to be low grade mucoepidermoid carcinoma. Out of the remaining 4 cases available for follow up were diagnosed as basal cell adenoma (category benign) on FNAC, 3 cases were reclassified as pleomorphic adenoma on histological follow-up. Overall, ROM reported was 5 % in this category.

Category 4b (SUMP) included cases, where it was not possible to diagnose a specific neoplastic entity, and out of 02 cases available for follow up, 1 case was reclassified as chronic sialadenitis and the other as adenoid cystic

carcinoma. Overall, ROM reported in this category was 50 %.

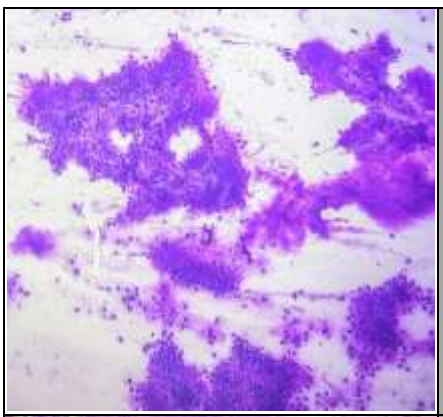

***Figure 1 (a). Category IVA - Benign Neoplasm Showing Cohesive Groups of Benign Looking Duct Epithelial Cells Along with Fibrillary Chondromyxoid Matrix (Diff Quik 100x)***

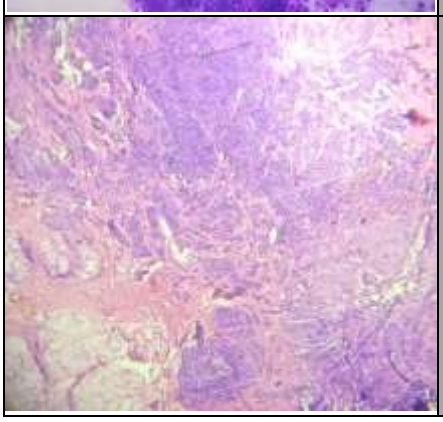

***Figure 1 (b). Histopathology Concordant - Pleomorphic Adenoma (H & E 100x)***

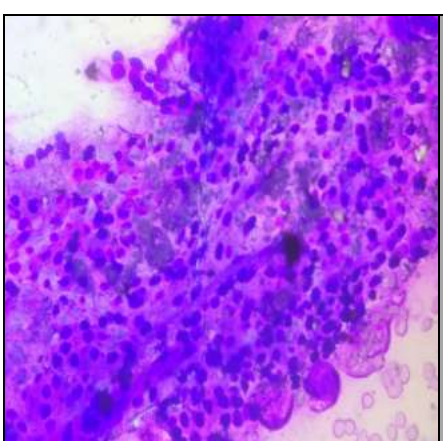

***Figure 2 (a). Category IVB - Salivary Gland Neoplasm of Uncertain Malignant Potential (SUMP) (Diff Quik 400x)***

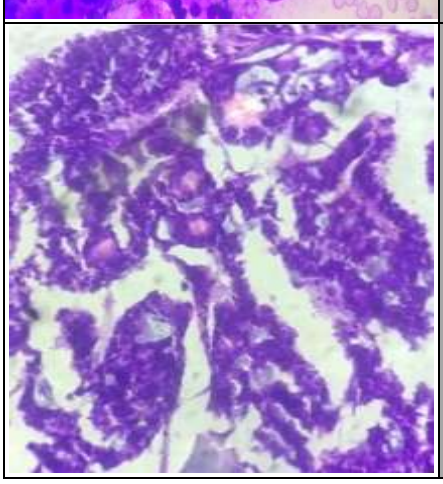

***Figure 2 (b). Histopathology Concordant - Adenoid Cystic Carcinoma (H & E 100x)***

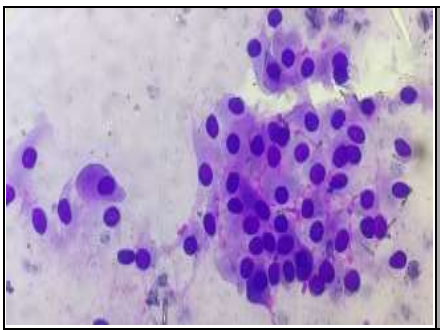

***Figure 3 (a). Category V - Suspicious for Malignancy (Diff Quik 400x)***

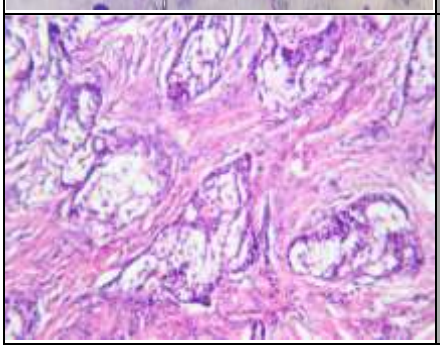

***Figure 3 (b). Histopathology Concordant - Mucoepidermoid Carcinoma Showing Nest of Squamous Cells, Mucinous Cells and Intermediate Cells (Diff Quik 400x)***

| | Parameters | No. of Cases N (%) |
|---|---|---|
| Sex | Male | 62 (60.1 %) |
| | Female | 41 (39.8 %) |
| Age (years) | < 30 | 21 (20.3 %) |
| | 31 - 50 | 49 (47.5 %) |
| | 50 - 70 | 24 (23.3 %) |
| | > 70 | 09 (8.7 %) |
| Glands involved | Parotid | 59 (57.2 %) |
| | Submandibular | 32 (31.06 %) |
| | Minor salivary gland | 12 (11.6 %) |

***Table 1. Case Distribution According to Age, Sex and Site of Involvement***

| Sl. No. | Diagnostic Category | Risk of Malignancy (%) | Management |
|---|---|---|---|
| I | Non-diagnostic | 25 | Clinical and radiological correlation / repeat FNAC |
| II | Non-neoplastic | 10 | Clinical follow up and radiological correlation |
| III | Atypia of undetermined significance | 20 | Repeat FNAC or Surgery |
| IV | Neoplasm<br>A: Benign<br>B: Salivary gland neoplasm of uncertain malignant potential | < 5<br>35 | Surgical or clinical follow up Surgery |
| V | Suspicious for malignancy | 60 | Surgery |
| VI | Malignant | 90 | Surgery |

***Table 2. The Milan System for Reporting Salivary Gland Cytopathology : Risk of Malignancy and Recommended Clinical Management***

| Milan Categories | Cat 1 | Cat 2 | Cat 3 | Cat 4a | Cat 4b | Cat 5 | Cat 6 | Total |
|---|---|---|---|---|---|---|---|---|
| No. of cases | 10 (9.7 %) | 34 (33.0 %) | 09 (8.7 %) | 22 (21.35 %) | 06 (5.8 %) | 08 (7.7 %) | 14 (13.5 %) | **103** |
| Cases with histological follow up | 03 (5.5 %) | 09 (16.6 %) | 02 (3.7 %) | 20 (37.03 %) | 082 (3.7 %) | 04 (7.4 %) | 14 (25.9 %) | **54** |
| Benign A. non-neoplastic | 01 | 08 | - | 01 | 01 | - | - | |
| B. Neoplastic | 01 | 01 | 01 | 18 | - | 01 | - | |
| Malignant | 01 | - | 01 | 01 | 01 | 03 | 14 | |
| Risk of malignancy | 33.3 % | 4.8 % | 50 % | 5 % | 50 % | 75 % | 100 % | |

***Table 3. Histological Follow Up of MILAN System Categories***

We had cases in category 5 (SFM) those were suspicious for malignancy on FNAC and histological follow-up of 4 cases were available and all the cases were found to

be concordant with diagnosis of malignancy except 1 case with features of pleomorphic adenoma. For this category overall ROM reported was 75 %. Histological monitoring of all 14 cases was available in category 6 (M) and all the cases were found to be concordant with diagnosis of malignant category. 7 cases of mucoepidermoid carcinoma, 3 cases of adenoid cystic carcinoma, 1 case of epithelial myoepithelial carcinoma, 1 case of acinic cell carcinoma, 1 case of lymphoepithelial carcinoma and 1 case of lymphoma were reported, and overall, ROM was 100 % in this category.

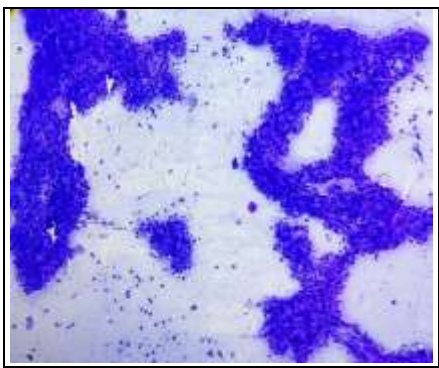

***Figure 4 (a). Category VI - Malignant (Diff Quik 100x)***

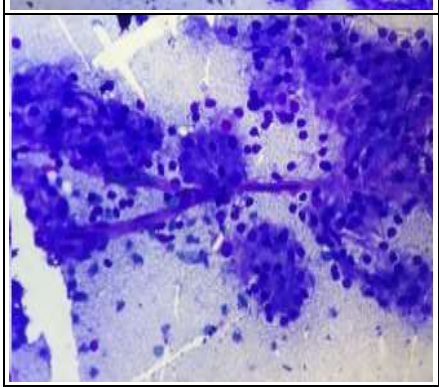

***Figure 4 (b). Category VI - Malignant (Diff Quik 400x)***

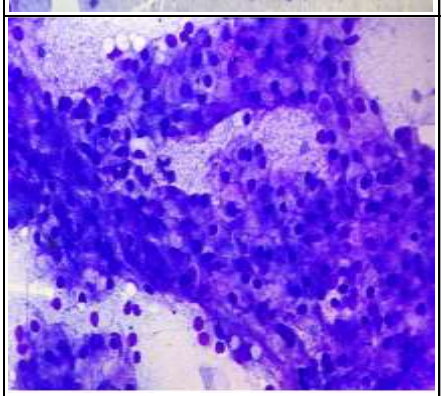

***Figure 4 (c). Category VI – Malignant (Diff Quik 400x)***

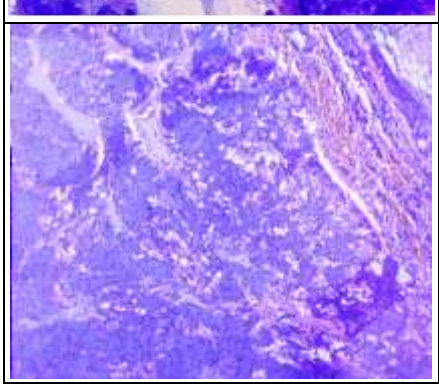

***Figure 4 (d). Histopathology Concordant - Acinic Cell Carcinoma***

## DISCUSSION

Fine-needle aspiration cytology (FNAC) has become widely accepted as a first line diagnostic test in the diagnosis and management of salivary gland lesions. FNAC is used in conjunction with both clinical and radiologic findings in the initial evaluation of any mass in the major and minor salivary glands.[9-13] MSRSGC is a newer salivary gland lesion reporting system with the aim of providing a better communication between clinicians and cyto-pathologists. This system is divided into six categories that reflect the risk of malignancy and each category has a clinical management strategy.

The categories include: non-diagnostic, non-neoplastic, atypia of undetermined significance, neoplastic (benign and neoplasm of uncertain malignant potential), suspicious for malignancy and malignancy. A non-diagnostic salivary gland aspirate is one which provides insufficient diagnostic material to provide an informative interpretation for qualitative and / or quantitative reasons. "Non-neoplastic" category is used for specimens exhibiting benign nonneoplastic changes, including those associated with acute or chronic reactive responses to inflammation, structural alterations and infection. The intention of using "non-neoplastic" category should be in conjunction with available clinical and radiologic information.

Atypia of undetermined significance category refers to cases that lack either qualitative or quantitative cytomorphological characteristics to be confidently diagnosed as non-neoplastic or neoplastic, along with those cases that have an atypical cytomorphologic feature that excludes the possibility of classifying it as "non-diagnostic".

Neoplasm: Benign category is for the cases when an FNA specimen shows characteristic cytomorphologic features of a specific benign epithelial or mesenchymal neoplasm of the salivary gland. Salivary gland neoplasm of uncertain malignant potential category should be used for cases where a malignant neoplasm cannot be excluded.

Suspicious for malignancy category is for samples showing features that are highly suggestive of, but not unequivocal for malignancy. Malignant category is for specimens that have features diagnostic of malignancy.

In the current study, we also categorized salivary gland FNA based on MSRSGC and reported the ROM as 33.3 %, 4.8 %, 50 %, 5 %, 50 %, 75 %, 100 % respectively for each category. In category 1, out of 3 cases, 1 case was reclassified as chronic sialadenitis, the misdiagnosis might be due to presence of few inflammatory cells only and the other was reclassified as Warthin tumour which was falsely diagnosed, and the reason might be the presence of necrotic debris and no viable cells. One case was found to be adenoid cystic carcinoma on histological follow-up which showed cystic change along with ductal and myoepithelial cells. The misinterpretation might be due to acellular aspirate from non-representative area.

Category 2 had 9 cases, out of which one was found to be pleomorphic adenoma (Figure 1) which was wrongly interpreted as chronic sialadenitis, the misdiagnosis was due to lack of the usual fibrillary character of the stroma and mimics thick mucin.

In category 3 we found 2 cases for histological correlation. One was adenoid cystic carcinoma which was categorized under AUS due to the presence of basaloid cell with atypia and the other being pleomorphic adenoma (Figure 2) which was placed in this category due to the high cellularity, mild atypia and scanty matrix.

Category 4a had one case misinterpreted as benign which was found to be low grade mucoepidermoid carcinoma (Figure 3) on histological follow up. The misinterpretation was probably because of the presence of the mucoid background and absence of malignant epithelial component.

In category 4b there was one case showing basaloid cells with mixed stroma which was reclassified as adenoid cystic carcinoma (Figure 4) on histopathology.

Category 5 had 3 malignant cases concordant with histopathology and one case showing atypical cytologic features in a group of cells with other features of pleomorphic adenoma. Category 6 had a total of 14 cases for histopathological correlation and all the cases were found to be concordant.

| Authors | Non-Diagnostic (%) | Non-Neoplastic (%) | Atypia (%) | Benign (%) | SUMP (%) | Suspicious of Malignancy (%) | Malignancy (%) |
|---|---|---|---|---|---|---|---|
| Layfield et al.[14] | 12 | 05 | 19 | 05 | 40 | 60 | 93 |
| Thiryayi et al.[15] | 8.5 | 1.6 | 0 | 1.9 | 26.7 | 100 | 100 |
| Farahani et al.[16] | 17 | 08 | 34 | 4 | 42 | 58 | 91 |
| Amita et al.[17] | - | 6.25 | 100 | 0 | 25 | 100 | 100 |
| Present study | 33.3 | 4.8 | 50 | 5 | 50 | 75 | 100 |

***Table 4. Comparison of Risk of Malignancy with Other Studies***

## CONCLUSIONS

Hence, we conclude that the Milan system of reporting salivary gland cytopathology provided a uniform system of reporting salivary gland cytomorphology that may increase the rate of diagnostic accuracy and determine the risk of malignancy in and around our institute by correlating the cyto-histopathological diagnoses wherever available.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

## REFERENCES

[1] McHugh JB. Major and minor salivary glands. In: Goldblum JR, Lumps LW, Mc Kenney JK, et al, eds. Rosai and Ackerman's Surgical Pathology. 11th edn. Philadelphia: Elsevier 2018: p. 235-268.

[2] Artur CV, Felipe N, Luise M, et al. Clinicopathological analysis of salivary gland tumors over a 15-year period. Bio Reprod 2016;30:1-2.

[3] Colella G, Cannavale R, Flamminio F, et al. Fine-needle aspiration cytology of salivary gland lesions: a systematic review. J Oral Maxillofac Surg 2010;68(9):2146-2153.

[4] Jain R, Gupta R, Kudesia M, et al. Fine needle aspiration cytology in diagnosis of salivary gland lesions: a study with histologic comparison. CytoJournal 2013;10:5.

[5] Schindler S, Nayar R, Dutra J, et al. Diagnostic challenges in aspiration cytology of the salivary glands. Semin Diagn Pathol 2001;18(2):124-146.

[6] Chakrabarti S, Bera M, Bhattacharya PK, et al. Study of salivary gland lesions with fine needle aspiration cytology and histopathology along with immunohistochemistry. J Indian Med Assoc 2010;108(12):833-836.

[7] Zubair B, Andrew SF, Nora K, et al. The Milan System for reporting salivary gland cytopathology. In: William CF, Esther DR, eds. The Milan System for reporting salivary gland cytopathology. 1st edn. American Society of Cytopathology. Springer International Publishing AG 2018: p. 2-4.

[8] Pukhramban GD, Laishram RS, Marina A, et al. Study of the cytomorphology of salivary gland lesions using the Milan System of reporting in a tertiary care hospital. J Evid Based Med Healthc 2019;6(46):2926-2930.

[9] Ahn S, Kim Y, Oh YL. Fine needle aspiration cytology of benign salivary gland tumors with myoepithelial cell participation: an institutional experience of 575 cases. Acta Cytol 2013;57(6):567-574.

[10] Colella G, Cannavale R, Flamminio F, et al. Fine-needle aspiration cytology of salivary gland lesions: a systematic review. J Oral Maxillofac Surg 2010;68(9):2146-2153.

[11] Griffith CC, Pai RK, Schneider F, et al. Salivary gland tumor fine-needle aspiration cytology: a proposal for a risk stratification classification. Am J Clin Pathol 2015;143(6):839-853.

[12] Hughes JH, Volk EE, Wilbur DC. Pitfalls in salivary gland fine-needle aspiration cytology: lessons from the College of American Pathologists Interlaboratory Comparison Program in Nongynecologic Cytology. Arch Pathol Lab Med 2005;129(1):26-31.

[13] Liu CC, Jethwa AR, Khariwala SS, et al. Sensitivity, specificity and posttest probability of parotid fine needle aspiration: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 2016;154(1):9-23.

[14] Layfield LJ, Baloch ZW, Hirschowitz SL, et al. Impact on clinical follow-up of the Milan System for salivary gland cytology: a comparison with a traditional diagnostic classification. Cytopathology 2018;29(4):335-342.

[15] Thiryayi SA, Low YX, Shelton D, et al. A retrospective 3-year study of salivary gland FNAC with categorisation using the Milan reporting system. Cytopathology 2018;29(4):343-348.

[16] Farahani SJ, Baloch Z. Retrospective assessment of the effectiveness of the Milan system for reporting salivary gland cytology: a systematic review and meta-analysis of published literature. Diagn Cytopathol 2019;47(2):67-87.

[17] Amita K, Rakshitha HB, Singh A, et al. Evaluation of accuracy of milan system for reporting salivary gland cytology: review of morphology and diagnostic challenges in each category. Journal of Cytology 2020;37(1):18-25.