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Milan System for Reporting of Salivary Gland Cytopathology: To Recognize Accuracy of Fine Needle Aspiration and Risk of Malignancy- A 4 Years Institutional Study

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ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) is a well established technique for categorization of salivary gland lesions preoperatively. It has apt sensitivity and specificity to diagnose various salivary gland pathologies. However, there is lack of uniformity in reporting of various pathologists. This results in lack of appropriate communication and management of the patients. To overcome this problem 'Milan system for reporting of salivary gland cytopathology' (MSRSGC) was introduced.

Aims and Objectives: This is a retrospective study to reclassify the previously diagnosed salivary gland lesions and to evaluate the risk of malignancy in different categories.

Material and methods: The clinical details, FNAC smears, histological reports were retrieved from the hospital records and the cases were reclassified according to Milan system. False positive, false negative, true positive and true negative cases were calculated by comparing with the final histopathological diagnosis and then the accuracy and risk of malignancy of each diagnostic category were calculated.

Results: A total of 288 cases were included in the study of which histological follow up was present in 118 cases. The sensitivity, specificity, negative predictive value and positive predictive value were 78.57 %, 98.83 %, 90.43 % and 97.06 % respectively. The overall diagnostic accuracy to differentiate the benign and malignant cases was 92.19%. Also, the risk of malignancy in each category was 20%, 14.3%, 100%, 4.2%, 100%, 83.3% and 100% respectively. The highest risk of malignancy in the present study was noted in category III and V.

Conclusion: Milan system for reporting of salivary gland cytopathology provides a better communication between pathologists and clinicians. This also results in effectiveness along with lesser false positive and false negative results. The ROM in the present study were according to MSRSGC except category III, atypia of undetermined significance which was 100%.

Keywords: Milan system, salivary gland, FNAC, Cytology, histopathology, risk of malignancy.

INTRODUCTION

Salivary gland lesions constitute around 3% to 6% of all head and neck pathologies. The adequate management of these lesions depends on accurate and timely diagnosis.[1] Fine needle aspiration cytology (FNAC) of salivary gland is a minimally invasive, safe, cost effective diagnostic tool with apt sensitivity and specificity which varies from 86% to 100% and 90% to 100% respectively according to various studies.[2-4] This is very helpful in accurate diagnosis of a subset of salivary gland lesions as well as to differentiate primary versus metastatic tumors.[5] However, due to the diverse and overlapping morphological spectrum of

various salivary gland lesions it is sometimes very challenging for the cytopathologists to provide an accurate diagnosis. The final diagnosis is also affected by site of aspiration of tumors (as in solid cystic tumors), the quality of smearing and staining, experience of the cytopathologist and absence of any category based reporting. To overcome this an uniform reporting system, Milan system, was proposed by American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC), in 2015 at Milan, Italy.

Milan system for reporting of salivary gland cytopathology (MSRSGC) is a six-tier system (Table 1.). It provides the diagnostic criteria, implied risk of malignancy and plan of management of various categories.[6] The objectives of the present study was to retrospectively reclassify the salivary gland lesions according to the Milan system, to assess the risk of malignancy of each category and to determine the diagnostic accuracy of these lesions in our institute.

Table 1. The Milan system for Reporting Salivary Gland Cytopathology: Implied risk of malignancy and recommended clinical management

Diagnostic category	Risk of malignancy (%) , (range)	Management
Non-diagnostic	25 (0-67)	Clinical and radiologic correlation/repeat FNAC
Non-neoplastic	10 (0-20)	Clinical follow up and radiological correlation
AUS	20 (10-35)	Repeat FNAC or surgery
Neoplasm Benign SUMP	<5 (0-13) 35 (0-100)	Surgery or clinical follow up
Suspicious of malignancy	60 (0-100)	Surgery
Malignant	90 (57-100)	Surgery

MATERIAL AND METHODS

This is a four year retrospective study conducted on all cases of salivary gland lesions coming to department of pathology for FNAC. Patients of both ages, all genders were included in the study. Histopathological correlation was done wherever available. There were total 288 cases. Smears of all the cases were retrieved from the records and were again classified according to MSRSGC into six categories including nondiagnostic, non-neoplastic, atypia of undetermined significance, neoplasm (benign or salivary gland neoplasm of uncertain malignant potential), suspicious for malignancy, and malignant. The discordant cases on histopathology were segregated. Number of false positive, false negative, true positive and true negative were identified. Sensitivity, specificity, positive predictive value and negative predictive value were calculated. Also, the risk of malignancy and diagnostic accuracy was assessed. SPSS software version 14 was used for all statistical analysis.

RESULTS

The study included 288 cases of which males were more than females. (M:F = 1.4:1). The distribution of cases according to sex, age and site of aspiration are elaborated in table 2. The most commonly affected age group was from 21 to 40 years with 53.12% of cases. Parotid gland swelling was the most common presentation.

Table 2. Distribution of cases according to age, sex and site of lesion.

Parameters	Number of cases
Sex Male	168
Female	120
Age group (years)	
0-20	32 (11.11%)
21-40	153 (53.12%)
41-60	68 (23.61%)
61-80	29 (10.06%)
>80	06 (2.08%)
Salivary gland involved	
Parotid	186 (64.58%)
Submandibular	74 (25.69%)
Other minor glands	28 (9.72%)

Table 3. Cytohistological correlation with description of discordant cases.

Cytological diagnosis	No.of cases	No. of cases with histological correlation	Discordant diagnosis on histology
Non diagnostic	07	05	2(pleomorphic adenoma),2 (chronic sialadenitis),1 adenoid cystic carcinoma.
Chronic sialadenitis	36	02	Nil
Retention cyst	19	10	2(Low grade mucoepidermoid carcinoma)
Intraparotid lymph node	07	01	Nil
Sialadenosis	20	02	02(acinic cell carcinoma)
Pleomorphic adenoma	105	56	3 (basal cell adenoma), 2(myoepithelioma), 2 (adenoid cystic carcinoma),1(schwannoma),
Basal cell adenoma	18	08	2(pleomorphic adenoma) 1(adenoid cystic carcinoma)
Oncocytoma	04	03	1 (Myoepithelial carcinoma)
Warthins tumor	05	03	Nil
Lymphoepithelial cyst	02	02	1(Warthins)
Benign mesenchymal lesion	02	01	Nil
Neoplasm of uncertain malignant potential	02	02	Nil
Suspicious for malignancy	10	06	1(oncocytoma)
Low grade polymorphous epithelial tumor	4	02	Nil
Mucoepidermoid carcinoma	33	10	2 (squamous cell carcinoma)
Adenoid cystic carcinoma	05	02	Nil
Acinic cell carcinoma	02	01	Nil
Carcinoma ex pleomorphic adenoma	2	01	Nil
Adenocarcinoma	2	01	Nil
Lymphoproliferative disorder	1	01	Nil
Metastatic carcinoma	2	01	Nil
Total	288	118	

The cytological diagnosis along with description of discordant cases on histology is depicted in table 3. Histological correlation was available in 118 cases of which 25 cases were discordant. Five cases were paucicellular despite of repeated aspiration and were labelled as non diagnostic. Among these two cases were of chronic sialadenitis and pleomorphic adenoma each and one case was of adenoid cystic carcinoma. Non –neoplastic category out of 83 cases 14 cases had histopathological follow-up of which one were low grade mucoepidermoid as well as acinic cell carcinoma which were diagnosed as retention cyst and sialadenosis respectively on cytology. One case of retention cyst was reclassified as atypia of undetermined significance in Milan system which turned out to be low grade mucoepidermoid carcinoma on histopathology. The highest risk of malignancy of 100% was noted in category III, V and Salivary gland neoplasm of uncertain malignant potential (SUMP). One case of pleomorphic adenoma and oncocytoma each on cytology was diagnosed to be adenoid cystic carcinoma and myoepithelial carcinoma on histology. One of case diagnosed as suspicious for malignancy on cytology was diagnosed as a benign tumor oncocytoma. Rest all malignant cases were diagnosed as malignant on histology in category V and VI. (Figure 1 and 2)

Table 4. Recategorisation of cases according to Milan system for reporting of salivary gland cytopathology along with risk of malignancy.

Category	No. of cases	Risk of malignancy
Nondiagnostic	07	1/5 (20%)
Non-neoplastic	83	2/14 (14.3%)
AUS	01	1/1 (100%)
Neoplasm Benign	134	3/71 (4.2%)
SUMP	02	2/2 (100%)
Suspicious of malignancy	10	5/6 (83.33%)
Malignant	51	19/19 (100%)
Total	288	

AUS- Atypia of undetermined significance, SUMP- Salivary gland neoplasm of uncertain malignant potential

The sensitivity, specificity, negative predictive value and positive predictive value of FNAC using Milan system were 78.57 %, 98.83 %, 90.43 % and 97.06 % respectively. The overall diagnostic accuracy to differentiate the benign and malignant cases was 92.19%.

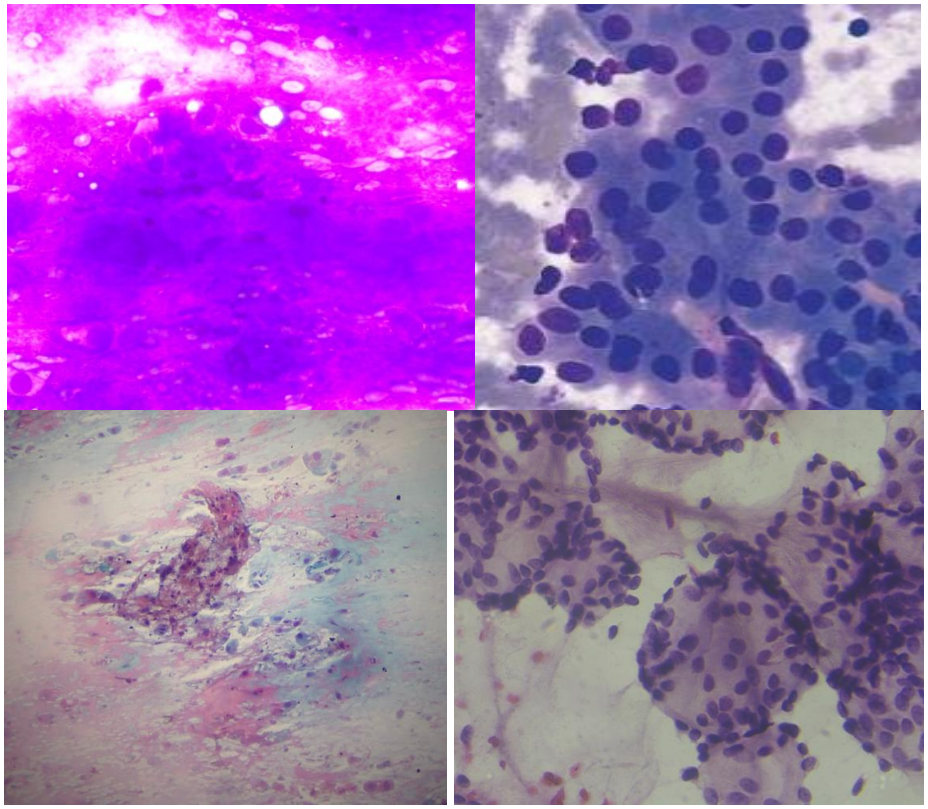

Figure 1. Fine needle aspiration cytology (A) Pleomorphic adenoma (B) oncocytoma (C) Mucoepidermoid carcinoma (D) Adenoid cystic carcinoma

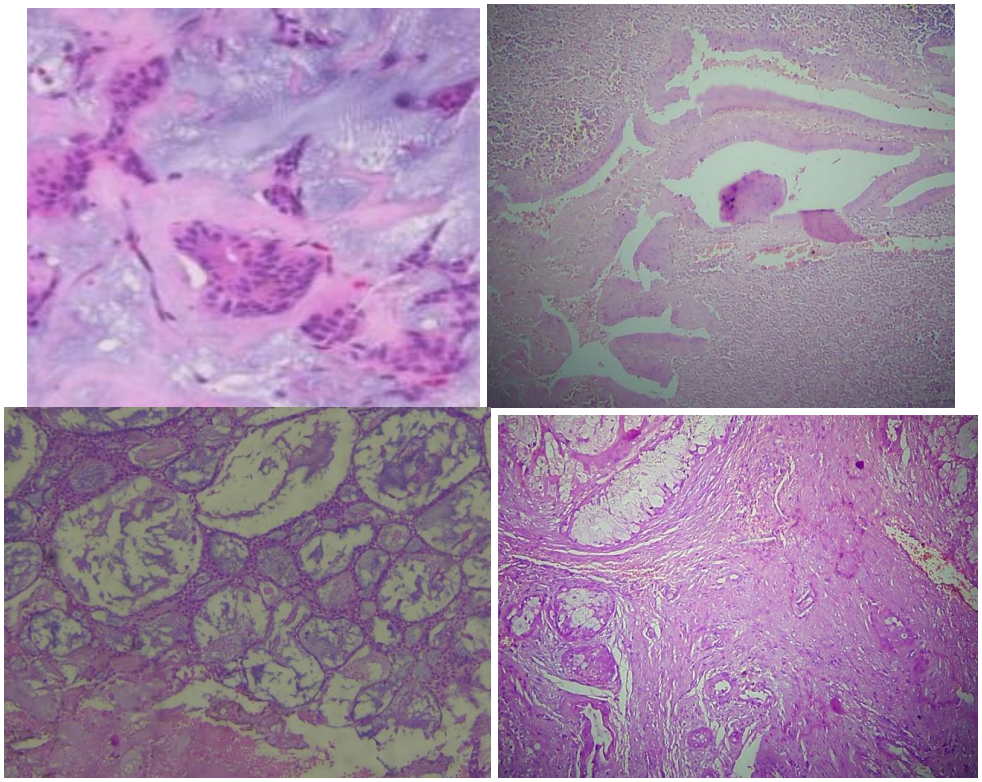

Figure 2. Histopathology (H&E) (A). Pleomorphic adenoma (B). Warthins tumor (C). Adenoid cystic carcinoma (D). Mucoepidermoid carcinoma.

DISCUSSION

FNAC has been widely accepted as a first line initial diagnostic tool among the clinicians due to ease of performance and rapid diagnosis. It provides line of management for salivary gland lesions by

providing not only preoperative categorization of benign versus malignant diagnosis but also an acculturate diagnosis in most of the cases. However, the specimen adequacy is still not well defined in the literature. Also, the overlapping morphological features and cytomorphological heterogenicity within the same lesions makes it difficult to identity and subcategorize a particular salivary gland lesion correctly. The clinical history and presentation also play an important role for correct diagnosis of these lesions. This highlights the importance of adequate communication between clinicians and pathologists. Thus to improve overall care and uniformity in diagnosis of salivary gland lesions a category based system, Milan system, was introduced.

Inadequate aspirate are a challenge on FNAC. This can be due to small size of lesion, deep location or dense fibrosis/sclerosis in the lesion. Rapid on site evaluation (ROSE) can reduce the number of inadequate samples but this requires an expert cytopathologist along with criteria of adequacy. Griffith et al. had proposed an adequacy criterion of presence of epithelial cells in more than four high power fields.[7] Milan system has recommended a minimum of 60 lesional cells in the diagnosis of salivary lesion as for now.[6]

Another reason for false negative cases is cystic lesions. A cyst lesion can be nonneoplastic, benign or malignant for example retention cyst, warthins tumor or mucoepidermoid carcinoma. The aspiration of only fluid in these cases can lead to a diagnostic pitfall. The fluid aspirated is paucicellular and the diagnosis in such cases is very difficult and challenging. Cystic lesion should be palpated after aspiration of the fluid to look for any solid areas and a second attempt should be done from these solid areas. Also, guided FNAC can be useful in such cases to aspirates the representative area. In the present study two of the cystic lesion which were found to be low grade mucoepidermoid carcinoma on histopathology were diagnosed as retention cyst incorrectly on cytology. One of these cases was recategorized into AUS category according to Milan system due to presence of few atypical cells with very low cellularity.

The present study had male to female ratio of 1.4:1 which is comparable to other studies.[8] Parotid gland was most commonly involved followed by submandibular gland and minor salivary glands. Similar findings were noted by Kala and Sonal et al.[8,9] The sensitivity and specificity of the present study is 78.57 % and 98.83 % along with diagnostic accuracy of 92.19% to differentiate benign lesions from malignant lesions. This is comparable to other studies done by Zubair et al., Santosh et al. and Katta et al.[10,11,12]

Amongst the non neoplastic, benign and malignant lesions chronic sialadenitis (43.37%; 36/83), pleomorphic adenoma (49.65%; 71/134) and mucoepidermoid carcinoma (64.71%; 33/51) are the most common lesions in the present study. The percentage of chronic sialadenitis were in concordance to previous studies. But the percentage of pleomorphic adenoma were lesser whereas mucoepidermoid carcinomas were higher than other studies.[12,13]

The present study had maximum cases in category IV (47.22%) followed by category II (28.82%) and category VI (17.71%) which is similar to studies conducted by Sheetal et al. and Yogambal et al.[14-16]

Pleomorphic adenoma have a characterstic chondromyxoid background which provides hint towards the diagnosis however, hyaline globules or basement membrane like material can also be confused with this background which can result in incorrect diagnosis as seen in the present study. The presence various types of myoepithelial cells further adds difficulty in its diagnosis. Two cases of each basal cell adenoma, myoepithelioma, adenoid cystic carcinoma and one case of schwannoma were misdiagnosed as pleomorphic adenoma on cytology in the present study.

The category AUS is for lesions that contained limited atypia and a neoplastic process cannot be excluded. The cases diagnosed as AUS is expected <10% of all salivary gland FNAs. Higher rates likely represent overuse of this category. In the present study this group had only one case (1.1%). On histopathology this category had ROM of 100% which is higher due to presence of only one case in this category that too was malignant on histopathology. This could have affected the ROM in the present study as it is reported to be 0% to 73% in other studies.[17]

An update of Milan Classification System for Salivary Gland Tumors was presented by Esther et al. to provide an emphasis on diagnostic pitfalls, differential diagnosis to provides a uniform and practical reporting system with the risks of malignancy.[18]

The present study depicted that the risk of malignancy, diagnostic accuracy, sensitivity and specificity of FNAC to differentiate benign versus malignant lesions of salivary glands at our institute were comparable to other studies as shown in table 5 and 6.

Table 5. Statistical comparison of the present with other studies.

	Present study (%)	Karuna et al(%)[19]	Rohilla et al.(%)[20]
Diagnostic accuracy	92.19	94.59	91.40
Sensitivity	78.57	85.00	79.40
Specificity	98.84	98.14	98.30
PPV	97.06	94.44	--
NPV	90.43	94.64	--

PPV- Positive predictive value, NPV- Negative predictive value

Table 6. Comparision of risk of malignancy of various categories of Milan system of the present study with other studies.

Category	Present study	Karuna et al.[19]	Rohilla et al.[20]	Liu et al.[21]
Nondiagnostic (%)	20	0.0	--	--
Non-neoplastic (%)	14.3	0.0	17.4	--
AUS	100	50	100	--
Neoplasm Benign (%) SUMP (%)	 4.2 100	 02.44 33.33	 07.3 50	 -- 24.1
Suspicious of malignancy (%)	83.33	100	--	--
Malignant (%)	100	93.33	96	--

CONCLUSION

The Milan system of reporting salivary gland cytopathology is a six tier system which provides risk stratification with ROM which is helpful in deciding the further course of management and patient counselling. This will further reduce the descriptive reports, false positive and false negative cases on FNAC. However, further studies involving large number of cases are required to prove its efficacy.

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