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ASSESSMENT OF RISK OF MALIGNANCY BY APPLICATION OF MILAN SYSTEM OF REPORTINGSALIVARY GLAND CYTOPATHOLOGY

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Abstract

Background: The diverse morphology and varying reporting terminology of salivary gland lesions present several challenges to pathologists and clinicians when making a cytological diagnosis. The Milan system for reporting salivary gland cytopathology was introduced as a solution to address these shortcomings. The objective of this study was to classify cases of salivary gland pathology that were diagnosed through histopathological examination using the Milan system, and to establish a correlation between the Milan system and the histopathological diagnosis. The objective of the study is to evaluate the effectiveness of the Milan system and the likelihood of malignancy in each category.

Materials and Methods: This study is a retrospective analysis that spanned a period of eighteen months. The study encompassed all instances of salivary gland pathology with fine-needle aspiration cytology findings recorded between March 2021 and September 2022. These cases were subsequently categorized based on the Milan system. Histopathology follow-up was conducted in 58 cases, and the risk of malignancy was assessed. The metrics of sensitivity, specificity, positive predictive value, and negative predictive value were computed by employing histopathological diagnosis as the reference standard.

Results: A total of 77 cytology slides were examined, and the Milan system was utilized for evaluation. Follow-up histopathology was obtained in 58 cases.The distribution of cases across different categories was as follows: nondiagnostic (9.27%), nonneoplastic (4.64%), atypia of undetermined significance (3.97%), benign neoplasm (23.84%), neoplasm of uncertain malignant potential (8.61%), suspicious for malignancy (11.92%), and malignant (37.75%). The Milan system demonstrated a sensitivity of 94.20%, specificity of 96.00%, positive predictive value of 98.48%, and negative predictive value of 85.71%.

Conclusion: The Milan system demonstrates superior sensitivity and specificity when compared to histopathology. This system is beneficial for both pathologists and clinicians as it ensures

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consistency in reporting terminology by categorizing salivary gland lesions into subcategories that have prognostic significance.

Keywords: Fine‑needle biopsy, predictive value of tests, salivary glands.

INTRODUCTION:

Salivary gland fine-needle aspiration cytology (FNAC) is a globally utilized method for diagnosing and treating salivary gland tumors. This technique offers a minimally invasive, safe, cost-effective, and precise method that is highly valuable for identifying a significant portion of salivary gland nodules as benign. As a result, it reduces the need for unnecessary invasive surgeries in patients with non-cancerous conditions. Furthermore, it provides guidance for the subsequent management strategy. [1, 2, 3, and 4.] Several studies have consistently demonstrated the high accuracy of FNAC in distinguishing between neoplastic and non-neoplastic lesions, as well as benign and malignant tumors. The sensitivity of FNAC varies between 86% and 100% across different studies, while the specificity ranges from 90% to 100%.[5, 6, 7, 8, 9, 10]. In addition, FNAC is a valuable tool for distinguishing between primary and metastatic lesions, particularly in cases of head and neck malignancies. This aids in determining the appropriate treatment plan.[11]".

Although salivary gland fine-needle aspiration cytology (FNAC) is a valuable and accurate tool for cytopathologists, it does face some challenges. These include the wide range and variability of salivary gland tumors, the similarity in appearance between different types of malignant tumors, and even the overlap in appearance between benign and malignant tumors. [12, 13, 14, 15].

The accuracy of subclassifying neoplasms using FNAC varies significantly across different studies, ranging from 48% to 94%. [1, 6, 13, 16]. The cytomorphological features such as the presence of basaloid cell component, oncocytoid changes, squamous metaplasia, and cystic component pose a diagnostic challenge in FNAC. Several studies suggest utilizing morphological pattern-based analysis to create a risk stratification method for categorizing salivary gland neoplasms and determining the risk of malignancy (ROM). This approach can also help guide the need for additional tests and the management plan.[3, 17, and 18]. Nevertheless, these studies exhibit significant disparity in the range of ROM across various categories, spanning from 6% to 100%, thereby indicating a lack of consensus in the approach. [17, 19, and 20.]

Another significant limitation is the inconsistency in the terminology used to report salivary fine-needle aspiration cytology (FNAC). Different reporting formats have been employed, ranging from a two-tiered system to one consisting of six or more tiers. The given input is the list [16, 21]. While some individuals have attempted to classify based on histological category, others have utilized terms such as atypical, suspicious, and malignant for diagnostic purposes. [17-22], inclusive.The wide range of classifications posed a challenge for the clinician in understanding the report and determining the appropriate course of action based on the range of motion (ROM). Therefore, a standardized terminology was developed to facilitate the reporting of salivary gland cytopathology. The American Society of Cytopathology and International Academy of Cytology have recently introduced a hierarchical international classification system known as the "Milan System for Reporting Salivary Gland Cytopathology" (MSRSGC). This system offers a framework for clinical management based on the risk of malignancy in various categories.[23,24] In this study, we have assessed the utility of the

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Milan system by correlating with histopathology and calculating the ROM in each category.

MATERIALS AND METHODS

All instances of salivary gland abnormalities that were referred to the cytopathology section of Netaji Subhash Chandra Bose Medical College, Hospital Jabalpur (M.P) between March 2021 and September 2022 were considered for this study. In accordance with the standard procedure at our institution, all fine needle aspiration cytologies (FNACs) were performed only after obtaining informed consent from the patients. The fine needle aspiration cytology (FNAC) of salivary gland lesions was performed manually on palpable lesions using a 23-gauge needle. Ultrasound guidance was employed when the lesion was not detectable through manual palpation. Preparations of smears were made, some wet and some dry. The wet smears were preserved in 95% alcohol, while the dry smears were left to dry naturally. These were stained using the Papanicolaou stain and the May–Grunwald–Giemsa stain, respectively.

The cytology slides were retrieved from the department archives, and clinical data pertaining to these cases were collected. The cytology slides were reevaluated by three pathologists and classified using the Milan system into six categories. In case of discordance of opinion, the consensus opinion of at least two pathologists was used to allot a case into a specific category. The six categories are as follows:
Category I – Non diagnostic
(ND), Category II – Non
neoplastic (NN),
Category III – Atypia of undetermined significance
(AUS),Category IVa – Neoplasm: Benign (NB),
Category IVb – Neoplasm: Salivary gland neoplasm of uncertain malignant potential
(SUMP),Category V – Suspicious of malignancy (SM), and Category VI – Malignant
(M).
We had access to histopathology follow-up data for 58 cases that had undergone surgical procedures at our institute. The results of the cases were compared and matched with the histopathology findings. The histopathology diagnosis was regarded as the definitive and most reliable method.

Data analysis was conducted using Microsoft Excel. The patient's gender and the location of the lesion were the qualitative exposure variables, while the patient's age was the quantitative exposure variable under consideration. Frequency tables were generated based on the age, gender, and location of the patient's lesion. The median and interquartile range of age was computed. The qualitative outcome variables were benign and malignant lesions. The ROM (Rate of Malignancy) was determined for each category by analyzing the histopathological diagnosis and follow-up information. For statistical purposes, cytological diagnoses of malignancy were categorized as positive, while benign diagnoses were categorized as negative. Lesions that were initially diagnosed as benign based on cytology, but were later found to be malignant on histopathology, were classified as false negatives. Conversely, lesions that were initially diagnosed as malignant based on cytology, but were later found to be benign on histopathology, were classified as false positives. Calculations were performed to determine the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy.

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RESULTS

The study included a cohort of 77 patients with salivary gland lesions who satisfied the inclusion criteria. The patients' ages varied from 15 to 75 years, with a mean age of 42.93±14.68 years. The majority of patients (51.7%) were between the ages of 19 and 45. The parotid gland was the most frequently sampled site for fine needle aspiration cytology (FNAC), accounting for 65% of cases (n=50). The submandibular region/gland was the second most common site, comprising 23.3% of cases (n=18). The FNAC (Fine Needle Aspiration Cytology) was performed on 4 patients (5%) from the palatal regions, and on 5 patients (6.7%) from other sites. No statistically significant differences were observed in the age, gender ratio, and laterality of patients across different Milan system categories. Out of the 77 cases included in the study, they were categorized into six groups based on the MSRSGC classification. Out of the total cases, 3.33% were categorized as non- diagnostic and salivary gland neoplasm of uncertain malignancy (Category IV-b), and another 3.33% were classified as atypia of unknown significance (Category III). The majority of cases, 46.67%, were categorized as benign (Category IV-a).

Five cases, or 8.33%, were classified as suspicious for malignancy (Category V), while the remaining 21.67% were categorized as malignant (Category VI). Table 1 for further details

TABLE 1: Distribution according to FNAC (Milan system) diagnosis (N=77).

FNAC diagnosis	**No. of patients**	Percentage
Non-diagnostic (Category 1)	2	**3.33**
Inadequate	2	**3.33**
Non-neoplastic (Category 2)	12	**15.00**
Benign cystic lesion	1	**1.67**
Acute sialadenitis	0	**0**
Chronic sialadenitis	9	**11.67**
Sialadenosis	1	**1.67**
Atypia of undetermined significance (AUS) (Category 3)	1	**1.67**
Neoplastic: benign (Category 4a)	36	**46.67**
Basal cell adenoma	2	**3.33**
Oncocytic neoplasm	1	**1.66**
Pleomorphic adenoma	28	**36.6**
Warthin's tumor	4	**5.00**
Neoplastic: Salivary gland neoplasm of uncertain malignancy (Category 4b)	2	**3.33**
Suspicious of malignancy (Category 5)	6	**8.33**
Malignant (Category 6)	17	**21.67**
Acinic cell carcinoma	2	**3.33**
Adenoid cystic carcinoma	6	**8.33**
Mucoepidermoid carcinoma (incl. low grade and intermediate)	**8**	**10.00**

The FNAC diagnosis of patients in the Milan system was classified into six distinct categories. The study included a total of

77 cases. Out of these, 15 cases (20.0%) were classified as non-diagnostic, non-neoplastic, or atypia of

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unknown significance (Categories 1-3). 36 cases (46.67%) were determined to be benign (Category 4a), while the remaining 26 cases (33.33%) were found to be malignant (Categories 4a, 5, and 6). Within the cell block, 8.33% of cases were indeterminate, 13.33% were non-cancerous, 45.00% were determined to be benign, and the remaining 33.33% were diagnosed as malignant (Table 2).

TABLE 2: Distribution of cases according to cell block diagnosis (N=77).

Cell block diagnosis	**No. of patients**	Percentage
Non-diagnostic	6	**8.33**
Inadequate	6	**8.33**
Non-neoplastic	10	**13.33**
Sialadenosis	1	**1.67**
Chronic sialadenitis	9	**11.67**
Benign	35	**45.00**
Basal cell adenoma	1	**1.67**
Pleomorphic adenoma	27	**35.00**
Warthin's tumor	4	**5.00**
Oncocytic neoplasm	1	**1.67**
Sialolipoma	1	**1.67**
Salivary gland neoplasm of uncertain malignant potential	0	**0.00**
Suspicious of malignancy	1	**1.67**
Malignant	24	**31.67**
Acinic cell carcinoma	2	**3.33**
Adenoid cystic carcinoma	8	**10.00**
Epithelial myoepithelial carcinoma	1	**1.67**
Mucoepidermoid carcinoma	12	**15.00**
Salivary duct carcinoma	**1**	**1.67**

Histopathology was conducted in a total of 60 cases. Out of these, 31 cases (51.06%) were determined to be benign, while the remaining 29 cases (48.93%) were classified as malignant (Table 3). Only 58 cases were included to assess the agreement between FNAC, cell block, and histopathology. The results showed a significant increase in concordance of diagnosis (Table 4). Insufficient or inconclusive non-cancerous findings were excluded from the diagnosis of fine-needle aspiration cytology (FNAC), as well as cell block analysis.

TABLE 3	
FNAC diagnosis (Milan Categories)	**No. of cases on FNAC**
Non-diagnostic (Category 1)	**2**
Non-neoplastic (Category 2)	**9**
Benign cystic lesion	**0**
Acute sialadenitis	**0**
Chronic sialadenitis	**7**
Sialadenosis	**1**
Atypia of undetermined significance (AUS) (Category 3)	**1**
Neoplastic: benign (Category 4a)	**28**

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Basal cell adenoma	**2**
Oncocytic neoplasm	**1**
Pleomorphic adenoma	**22**
Warthin's tumor	**3**
Neoplastic: Salivary gland neoplasm of uncertain malignancy (Category 4b)	**2**
Suspicious of malignancy (Category 5)	**5**
Malignant (Category 6)	**13**
Acinic cell carcinoma	**2**
Adenoid cystic carcinoma	**5**
Mucoepidermoid carcinoma	**6**

FNAC: fine-needle aspiration cytology, HPE: histopathological examination.

TABLE 4: Agreement of FNAC and cell block diagnosis, cell block and histopathology (HPE), and FNAC and histopathology (N=58).

Diagnosis	**Sensitivity**	**Specificity**	**PPV**	**NPV**	Diagnostic accuracy
FNAC and cell block	80.0	84.0	80.0	84.0	**82.2**
FNAC and HPE	72.7	82.6	80.0	76.0	**77.8**
Cell block and HPE	**82.6**	**95.5**	**95.0**	**84.0**	**88.9**

FNAC: fine-needle aspiration cytology, PPV: positive predictive value, NPV: negative predictive value, HPE: histopathological examination.

An agreement between the FNAC Milan system and cell block diagnosis was found in 82.2% (48 out of 58) of cases, in detecting both benign and malignant salivary gland lesions. The FNAC Milan system demonstrated a diagnostic efficacy of 80.0% for sensitivity, 84.0% for specificity, 80.0% for positive predictive value (PPV), and 84.0% for negative predictive value (NPV) when compared to the cell block diagnosis. The FNAC Milan system demonstrated a diagnostic precision of 82.2%, which was significantly higher than the cell block method ($k=0.640$; $p<0.001$).

The concordance between cell block and histopathological diagnosis was observed in 52 out of 58 cases, resulting in an agreement rate of 88.9%. The cell block diagnosis demonstrated a diagnostic efficacy, when compared to histopathology, with a sensitivity of 82.6%, specificity of 95.5%, positive predictive value (PPV) of 95.0%, and negative predictive value (NPV) of 84.0%. The cell block method demonstrated a diagnostic precision of 88.9% when compared to histopathology ($k=0.778$; $p<0.001$).

The concordance between the FNAC Milan system and histopathology was observed in 45 out of 58 cases, resulting in a percentage agreement of 77.8%. The FNAC Milan system demonstrated a diagnostic efficacy, when compared to histopathology, with a sensitivity of 72.7%, specificity of 82.6%, positive predictive value (PPV) of 80.0%, and negative predictive value (NPV) of 76.0%. The FNAC Milan system demonstrated a diagnostic precision of 77.8% when compared to histopathology ($k=0.554$; $p<0.001$).

Out of the total 77 FNAC cases, histopathology results were obtained for only 60 cases. Among these, 31 cases (51.07%) were determined to be benign, while the remaining 29 cases (48.93%) were

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diagnosed as malignant neoplasm's. There was a lack of histopathology for Category I. Among the nine cases in Category II, only one case had histopathology data, which revealed a benign condition. Within Category III, a single case was determined to be malignant based on histopathology. Within Category IVa, there were a total of 36 cases diagnosed through fine needle aspiration cytology (FNAC). However, only 32 cases had corresponding histopathology results. Among these, 25 cases were determined to be benign, while 8 cases were identified as malignant. Category IVb had a total of two cases, with one case being benign and the other case being malignant. Out of the 6 instances classified as Category V, one was determined to be non-cancerous while the remaining 5 were found to be cancerous. Among the 17 cases in Category VI, 3 were found to be benign, while the remaining 14 cases were determined to be malignant (Table 3). The current study found that the risk of malignancy for FNAC Milan Categories I, II, III, IVa, IVb, V, and VI is 0%, 0%, 100%, 24%, 50%, 80%, and 84.6% respectively (Tables 5, 6).

TABLE 5: Histological follow-up of FNAC according to Milan system diagnostic categories.

	Cat. I	**Cat. II**	**Cat. III**	**Cat. IVa**	**Cat. IVb**	**Cat V**	**Cat VI**	Total
No. of cases	3 (3.3%)	12(15.0%)	1 (1.7%)	36(46.7%)	2(3.3%)	6 (8.3%)	17 (21.7%)	**77**
No. of histological follow-up	0	1	1	32	3	6	17	**60**
Benign	0	1	0	25	1	1	3	**31**
Malignant	0	0	1	8	1	5	14	**29**
Risk of malignancy	**0.0**	**0.0**	**100.0**	**24.0**	**50.0**	**80.0**	**84.6**	**48.9**

FNAC: fine-needle aspiration cytology, Cat.: Category.

TABLE 6	
Milan Categories of all study participants	
Milan Category	**No.**
I (Inadequate)	**0**
II (Non-neoplastic)	**0**
III (Atypia of undetermined significance)	**100**
IVa (Neoplastic benign)	**24**
IVb (Neoplastic uncertain malignant potential)	**50**
V (Suspicious)	**80**
VI (Malignant)	**84.6**

Immunocy to chemical markers were utilized to accurately classify the tumor subtype on the cell block section. For non- threatening cases such as pleomorphic adenoma, we employed ICC markers such as P63, CK7, and SOX-10 to assess the presence of nuclear and cytoplasmic markers, and reported their positivity. Nevertheless, the presence of leukocyte common antigen (LCA) and CK7 was assessed in Warthin's tumor. However, in aggressive cases such as carcinoma ex pleomorphic adenoma, markers Plag-1, CK7, and P63 were employed. Furthermore, S-100, SOX-10, and P63 were used to test for mucoepidermoid carcinoma, while SOX-10 and CK7 were used to test for acinic cell carcinoma. Additionally, CD117, SOX-10, and Calponin were used as markers to test for adenoid cystic carcinoma.

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DISCUSSION

Salivary gland tumors exhibit a diverse range of characteristics, including different clinical presentations, histopathology, and rates of malignancy. Diagnosing salivary gland lesions is a complex and demanding task [23]. Tumors in the head and neck region, which are primarily of epidermal origin, make up approximately 2% to 6.5% of all tumors [24-26]. Recently, fine-needle aspiration cytology has become a valuable, efficient, dependable, and widely accepted technique for assessing salivary gland abnormalities [27-30]. Although FNAC is widely used for diagnosing salivary gland tumors, there is a lack of standardization in reporting cytological results. A recent international agreement has been reached on how to report FNAC results in order to classify salivary gland lesions based on their potential for malignancy [31]. Later on, researchers have assessed its usefulness in categorizing the likelihood of cancer in salivary gland tumors across various regions globally. In this study, we aimed to evaluate the suitability of the Milan system for reporting salivary gland cytology, as well as the effectiveness of a panel of immunocy to chemistry (ICC) markers in diagnosing salivary gland neoplasm's at our facility. This study involved the enrolment of 60 patients with salivary gland lesions who underwent fine-needle aspiration cytology (FNAC), cell block analysis, and immunocy to chemistry (ICC). The results of these tests were then compared to the findings from histopathology.

The patients' ages spanned from 15 to 75 years. 51.7% of the individuals fell within the age range of 19 to 45 years, with females comprising 35% and males constituting the remaining 65%. A recent study conducted in Karnataka by Amita *et al*.
[32] revealed a diverse age distribution among patients, ranging from nine to 83 years (with a mean age of 48.3 years), and a predominance of male participants (67.7%). In a separate study conducted in Chandigarh, Rohilla *et al*. [33] found that the age of the patients ranged from one to 95 years, with an average age of 43.7 years. Additionally, 63.0% of the patients were male. In a separate study conducted in Meerut, northern India, Karuna *et al*. [34] discovered a total of 105 patients ranging in age from under 10 years to over 61 years. The proportion of patients aged 31 to 60 years was 54.3%, while the overall percentage of male patients was 69.5%. In a study conducted in Rajasthan, Bharti *et al*. [35] found that the age of participants ranged from three to 86 years, with a mean age of 39 years. Additionally, 61.3% of the participants were men. Hence, the age and sex distribution of the patients in this study is similar to that of other recent reports from different regions of India. The majority of cases (96.7%) in the current study exhibited unilateral involvement. There were only two cases (3.3% of the total) where both sides were affected. The right side exhibited a higher frequency of involvement (32/62; 51.6%) in comparison to the left side (30/62; 48.4%). The parotid gland was the most commonly affected site, accounting for 65% of cases, followed by the submandibular region at 23.3%. In contrast to the current study, Rohilla *et al*. [33] found that the parotid gland was the most prevalent (61.3%) and the submandibular gland was the second most prevalent (35.7%). In the research conducted by Karuna *et al*. [34], it was found that 62.4% of individuals had involvement of the parotid gland, while 31.2% had involvement of the submandibular gland.

Among the benign non-neoplastic lesions (n=28) examined in this study, pleomorphic adenoma (n=22) was the most frequently diagnosed, followed by Warthin's tumor (n=3). In their study, Amita *et al*. [32] identified a total of 68 non- neoplastic lesions. Among these, they observed 22 cases of pleomorphic adenoma and 6 cases of Warthin's tumor, both of which were classified as benign subtypes. Karuna *et al*. [34] also made similar observations, identifying 41 out of 54 benign neoplastic lesions as

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pleomorphic adenoma and 6 out of 54 as Warthin's tumor. In their study, Bharti *et al*. [35] identified 66 out of 85 benign non-neoplastic lesions, including pleomorphic adenoma and Warthin's tumor, which accounted for 10 out of 85 cases. The current study's findings indicate that there is no discernible distinction in the cytological diagnosis of non- neoplastic benign lesions compared to other recent studies conducted in India.

Among the 13 malignant lesions in this study, the highest number (n=6) were diagnosed as mucoepidermoid carcinoma, followed by adenoid cystic carcinoma (n=5) and acinic cell carcinoma (n=2), respectively. In Amita *et al*.'s study [32], out of the 23 malignant lesions examined, 12 were identified as mucoepidermoid carcinoma, four as acinic cell carcinoma, and three as squamous cell carcinoma. The remaining four cases (one each) were classified as other types of malignant conditions. Nevertheless, Rohilla *et al*. [33] found that out of the 61 malignant cases they identified, the highest number of cases (n=20) were classified as carcinoma not otherwise specified (NOS), followed by mucoepidermoid carcinoma (n=15) and adenoid cystic carcinoma (n=8) as the primary diagnoses. In their study, Karuna *et al*. identified mucoepidermoid carcinoma as the most prevalent malignant type (n=9) among 17 cases of malignant FNAC. Adenoid cystic carcinoma was the second most common malignant type, with three cases. The study conducted by Bharti *et al*. [35] identified a total of 35 cases of malignancy, with eight different types of malignancies diagnosed. Among these, mucoepidermoid carcinoma was the most prevalent, with 14 cases diagnosed. The present study's findings correlate with other studies, indicating that mucoepidermoid carcinoma is the most prevalent form of malignancy (Table 3). A study was conducted to assess the efficacy of fine-needle aspiration (FNA) as a preoperative diagnostic procedure in 43 patients with salivary gland tumors. Out of the total number of tumors, nine were classified as malignant and 34 were classified as benign. The FNA had a diagnostic sensitivity of 88.9% (8 out of 9), a specificity of 94.1% (32 out of 34), and an accuracy of 93.0% (40 out of 43). The results suggest that FNA is a screening procedure with high sensitivity and specificity [36].

According to the Milan system, the non-neoplastic category (Category 2) was the second largest diagnostic category in the current study, with a total of 9 cases. Within this category, the highest number of cases were diagnosed as chronic sialadenitis (n=7). One case was confirmed as a benign cystic lesion, and another case was confirmed as sialadenosis. In contrast, Amita *et al*. [32] also identified chronic sialadenitis as the primary type of non-neoplastic lesion, accounting for 37 out of 68 cases. However, their study also revealed a significant number of non-neoplastic cases (26 out of 68) that were classified as acute sialadenitis. In their study, Rohilla *et al*. [33] classified 352 cases as non-neoplastic. However, they discovered benign neoplastic lesions in 188 patients and malignant lesions in 61 patients. The researchers classified sialadenitis into two categories, chronic and acute, and found that it was the second most prevalent non-neoplastic type, with a total of 141 cases. In the research conducted by Karuna *et al*. [34], out of the 17 cases that were not related to tumors, seven were identified as chronic sialadenitis and three as acute sialadenitis. Additionally, a total of six cases were diagnosedas sialadenosis. In contrast, Bharti *et al*. [35] identified sialadenitis as the most prevalent non-neoplastic category lesion in their study, with a total of 16 cases. The second most common type was a benign cyst, with a total of 12 cases. Indeed, while there may be variations in the range of non-neoplastic abnormalities, the results of this study align with other recent studies conducted in India, which also indicate that sialadenitis is the most prevalent non-neoplastic type (Table 6).

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Additionally, in the current investigation, we conducted cell block and immunocytochemical assessment. Upon examination of the cell block, it was found that 8.33% of the sections were not able to provide a diagnosis, 13.3% were non-cancerous, 45% were benign, 1.7% had a potential for malignancy, 1.7% were suspected to be malignant, and 31.7% were confirmed to be malignant based on the Milan system's reporting category.

While FNAC is widely recognized as a commonly used method for initial cytological evaluation of salivary gland tumors, its effectiveness is often restricted when it comes to diagnosing specific conditions like pleomorphic adenoma and Warthin's tumor. This occurs due to potential issues related to inadequate cellularity or suboptimal aspirate quality. To address these challenges, we employ supplementary techniques, such as the creation of cell blocks and the application of immunocy to chemistry. The use of cell block allows for the assessment of the histological pattern of the disease, which is not feasible with FNAC smears.

The utilization of cell block in conjunction with immunocy to chemistry (ICC) and fine needle aspiration cytology (FNAC) was implemented with the aim of enhancing the ultimate diagnosis. The utilization of cell block aided in the detection of 18 instances of malignancy, surpassing the 13 cases identified through FNAC. FNAC identified a total of 18 cases that were suspected or confirmed to be malignant. A total of 20 cases were diagnosed as suspected of malignancy and malignancy when the cell block was utilized. Cell block analysis not only enhanced the overall detection of malignancies, but also facilitated definitive malignant diagnosis in a significant number of cases.

Naz *et al*. [37] also discovered in a previous study that the use of cell block with immunocy to chemistry enhances the accuracy of diagnosing salivary gland lesions. Comparing the histopathological assessment to the final assessment, we discovered that the use of cell block significantly enhanced both sensitivity and specificity, with rates of 82.6% and 95.5% respectively, in contrast to FNAC which had rates of 80% and 84%. In line with the results of the current study, Oberoi *et al*. [38] also observed an increase in sensitivity, from 77.8% for fine needle aspiration cytology (FNAC) to 88.8% for cell block. In a study conducted by Wadhwa *et al*. [39], an assessment of head and neck lesions revealed that the use of cell block with immunocytochemistry (ICC) resulted in improved sensitivity and specificity compared to fine-needle aspiration cytology (FNAC). Specifically, the sensitivity increased from 88.8% to 96%, and the specificity increased from 95.7% to 100%. The current study's findings are also consistent with this.

In this study, the risk of malignancy for the Milan Categories I, II, III, IVa, IVb, V, and VI was 0%, 0%, 100%, 24%, 50%, 80%, and 84.6% respectively. Comparing the results of the current study with other recent studies reveals that Categories I, II, IVa, and IVb have a very low likelihood of developing cancer, whereas Categories III, V, and VI have the highest risk. The findings demonstrate the utility of the Milan system in risk stratification. Several studies suggest a lower incidence of cases in Categories V to VI, all of which carry a high risk of malignancy [33,35]. Nevertheless, we recommend utilizing a cell block in this particular scenario as it significantly enhances the accuracy of diagnosing Category V lesions. A constraint of the current study was the limited number of participants, resulting in excessively high proportional values for certain risk stratification categories. Additional research is advised, utilizing a more extensive sample size. It is advisable to utilize cell block as a supplementary tool to FNAC (Fine Needle Aspiration Cytology) in conjunction with risk stratification using the Milan

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system of reporting, due to its improvisation value and the capability to present its findings. Moreover, by expanding the range of ICC markers for salivary gland tumors, the potential for salivary gland FNAC to become a more crucial component in assessing salivary gland lesions will be heightened.

CONCLUSIONS

Cell block and ancillary techniques, such as immunocytochemistry, are crucial factors for enhancing the diagnostic accuracyof FNAC (fine needle aspiration cytology) in salivary gland lesions. We suggest conducting a comprehensive study involving multiple centers and utilizing a large sample size to provide detailed descriptions. Our primary focus was to categorize all salivary gland lesions based on MSRSGC in order to assess its diagnostic precision and determine the likelihood of malignancy for each category. This information can be valuable for guiding the clinical treatment of the patient.

REFERENCES

1. Colella G, Cannavale R, Flamminio F, Foschini MP. Fine-needle aspiration cytology of salivary gland lesions: A systematic review. *J Oral MaxillofacSurg.* 2010;68:2146–53. [PubMed: 20580145]
2. Jain R, Gupta R, Kudesia M, Singh S. Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison. *Cytojournal.* 2013;10:5. [PMCID: PMC3623452] [PubMed: 23599724]
3. Schindler S, Nayar R, Dutra J, Bedrossian CW. Diagnostic challenges in aspiration cytology of the salivary glands.4. *SeminDiagnPathol.* 2001; 18:124–46. [PubMed: 11403256]
5. Chakrabarti S, Bera M, Bhattacharya PK, Chakrabarty D, Manna AK, Pathak S, *et al*. Study of salivary gland lesions with fine needle aspiration cytology and histopathology along with immunohistochemistry. *J Indian Med Assoc.* 2010; 108:833–6. [PubMed: 21661459]
6. Schmidt RL, Hall BJ, Wilson AR, Lay field LJ. A systematic review and meta-analysis of the diagnostic accuracy of fine-needle aspiration cytology for parotid gland lesions. *Am J ClinPathol.* 2011;136:45–59. [PubMed: 21685031]
7. Liu CC, Jethwa AR, Khariwala SS, Johnson J, Shin JJ. Sensitivity, specificity, and posttest probability of parotid fine- needle aspiration: A systematic review and meta-analysis. *Otolaryngol Head Neck Surg.* 2016;154:9–23. [PMCID: PMC4896151] [PubMed: 26428476]
8. Schmidt RL, Narra KK, Witt BL, Factor RE. Diagnostic accuracy studies of fine-needle aspiration show wide variation in reporting of study population characteristics: Implications for external validity. *Arch Pathos Lab Med.* 2014; 138:88–97. [PubMed: 24377815]
9. Song IH, Song JS, Sung CO, Rohm JL, Choi SH, Nam SY, *et al*. Accuracy of core needle biopsy versus fine needle aspiration cytology for diagnosing salivary gland tumors. *J PatholTransl Med.* 2015; 49:136–43. [PMCID: PMC4367109] [PubMed: 26148740]
10. Tyagi R, Dey P. Diagnostic problems of salivary gland tumors. *DiagnCytopathol.* 2015; 43:495–509. [PubMed:25614439]
11. Wei S, Layfield LJ, LiVolsi VA, Montone KT, Baloch ZW. Reporting of fine needle aspiration (FNA) specimens of salivary gland lesions: A comprehensive review. *DiagnCytopathol.* 2017;45:820–7. [PubMed: 28371507]
12. Pusztaszeri MP, Faquin WC. Update in salivary gland cytopathology: Recent molecular advances and diagnostic

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

applications. *SeminDiagnPathol.* 2015; 32:264–74. [PubMed: 25613003]

13. 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. *ActaCytol.* 2013; 57:567–74. [PubMed: 24107383]
14. Hughes JH, Volk EE, Wilbur DC Cytopathology Resource Committee. College of American Pathologists. Pitfalls in salivary gland fine-needle aspiration cytology: Lessons from the College of American Pathologists Interlaboratory Comparison Program in Nongynecologic Cytology. *Arch Pathos Lab Med.* 2005;129:26–31. [PubMed: 15628905]
15. Layfield LJ, Tan P, Glasgow BJ. Fine-needle aspiration of salivary gland lesions. Comparison with frozen sections and histologic findings. *Arch Pathos Lab Med.* 1987; 111:346–53. [PubMed: 3030228]
16. Novoa E, Gurtler N, Arnoux A, Kraft M. Diagnostic value of core needle biopsy and fine needle aspiration in salivary gland lesions. *Head Neck.* 2016; 38:E346–52. [PubMed: 25581781]
17. Griffith CC, Pai RK, Schneider F, Duvvuri U, Ferris RL, Johnson JT, *et al*. Salivary gland tumor fine needle aspiration cytology: A proposal for a risk stratification classification. *Am J ClinPathol.* 2015;143:839–53. [PMCID: PMC5257286] [PubMed: 25972326]
18. Rossi ED, Wong LQ, Bizzarro T, Petrone G, Mule A, Fadda G, *et al*. The impact of FNAC in the management of salivary gland lesions: Institutional experiences leading to a risk-based classification scheme. Cancer Cytopathol. 2016;124:388–96. [PubMed: 26959289]
19. Griffith CC, Schmitt AC, Little JL, Magliocca KR. New developments in salivary gland pathology: Clinically useful ancillary testing and new potentially targetable molecular alterations. *Arch Pathos Lab Med.* 2017;141:381–95. [PubMed: 28234570]
20. Arab SE, Maleki Z, Zhao HQ, Rossi ED, Bo P, Chandra A, *et al*. Inter-institutional variability for malignancy in "suspicious" salivary gland fine needle aspiration: A multi-institutional study [abstract] *Mod Pathos.* 2017;30:87A. Abstract 336.
21. Malik A, Maleki Z, Zhao HQ, Rossi ED, Bo P, Chandra A, *et al*. Inter-institutional variability of "atypical" salivary gland fine needle aspiration: A multi-institutional study [abstract] *Lab Invest.* 2017;97:107A. Abstract 411.
22. Wang H, Fundakowski C, Khurana JS, Jhala N. Fine-needle aspiration biopsy of salivary gland lesions. *Arch Pathos Lab Med.* 2015; 139:1491–7. [PubMed: 26619021]
23. Griffith CC, Schmidt AC, Pantonowitz L, Monaco SE. A pattern-based risk-stratification scheme for salivary gland cytology: A multi-institutional, interobserver variability study to determine applicability. *Cancer Cytopathol.* 2017; 125:776–85. [PMCID: PMC5647230] [PubMed: 28834233]
24. Pfeiffer J, Ridder GJ: Diagnostic value of ultrasound-guided core needle biopsy in patients with salivary gland masses. Int J Oral Maxillofac Surg. 2012, 41:437-43. 10.1016/j.ijom.2011.12.005
25. Eveson JW, Auclair P, Gnepp DR, El-Naggar AK: Tumours of the salivary glands . World Health Organisation Classification of Tumours Pathology and Genetics of Head and Neck Tumours. Barnes L, Eveson JW, Reichart P, Sidransky D (ed): IARC Press, Lyon; 2005. 164.
26. Loyola AM, de Araújo VC, de Sousa SO, de Araújo NS: Minor salivary gland tumours: a retrospective study of 164 cases in a Brazilian population. Oral Oncol Eur F Câncer. 1995, 31:197-201. 10.1016/0964- 1955(95)00001-x
27. Rivera-Bastidas H, Ocanto RA, Acevedo AM: Intraoral minor salivary gland tumours: a

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

retrospective study of 62 cases in Venezuelan population. J Oral Pathol Med. 1996, 25:1-4. 10.1111/j.1600- 0714.1996.tb01214.x

28. Ashraf A, Shaikh AS, Kamal F, Sarfraz R, Bukhari MH: Diagnostic reliability of FNAC for salivary gland swellings: a comparative study. Diagn Cytopathol. 2010, 38:499-504. 10.1002/dc.21211
29. Altin F, Alimoglu Y, Acikalin RM, Yasar H: Is fine needle aspiration biopsy reliable in the diagnosis of parotid tumors? Comparison of preoperative and postoperative results and the factors affecting a ccuracy. Braz J Otorhinolaryngol. 2019, 85:275-81. 10.1016/j.bjorl.2018.04.015
30. Gudmundsson JK, Ajan A, Abtahi J: The accuracy of fine-needle aspiration cytology for diagnosis of parotid gland masses: a clinicopathological study of 114 patients. J Appl Oral Sci. 2016, 24:561-7. 10.1590/1678- 775720160214
31. Shalley S, Chand N, Aggarwal A, Garg LN, Yadav V, Yadav A: Diagnostic accuracy of fine needle aspiration cytology in lesions of oral cavity and salivary glands: a clinico-pathological study. Open Dent J. 2018, 12:782-90. 10.2174/1745017901814010782
32. Rossi ED, Baloch Z, Pusztaszeri M, Faquin WC: The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC): an ASC-IAC-sponsored system for reporting salivary gland fine- needle aspiration. J Am Soc Cytopathol. 2018, 7:111-8. 10.1016/j.jasc.2018.02.002
33. Amita K, Rakshitha HB, Singh A, Shankar SV: Evaluation of accuracy of Milan System for Reporting Salivary Gland Cytology: review of morphology and diagnostic challenges in each category. J Cytol. 2020, 37:18-25. 10.4103/JOC.JOC_191_18
34. Rohilla M, Singh P, Rajwanshi A, Gupta N, Srinivasan R, Dey P, Vashishta RK: Three-year cytohistological correlation of salivary gland FNA cytology at a tertiary center with the application of the Milan system for risk stratification. Cancer Cytopathol. 2017, 125:767-75. 10.1002/cncy.21900
35. Karuna V, Gupta P, Rathi M, Grover K, Nigam JS, Verma N: Effectuation to Cognize malignancy risk and accuracy of fine needle aspiration cytology in salivary gland using "Milan System for Reporting Salivary Gland Cytopathology": a 2 years retrospective study in academic institution. Indian J Pathol Microbiol. 2019, 62:11-6. 10.4103/IJPM.IJPM_380_18
36. Bharti JN, Elhence P, Rao M, Nalwa A, Khera S: Risk stratification by application of Milan system for reporting salivary gland cytopathology: a tertiary care experience. Cytojournal. 2021, 18:19. 10.25259/Cytojournal_26_2020
37. Shintani S, Matsuura H, Hasegawa Y: Fine needle aspiration of salivary gland tumors . Int J Oral Maxillofac Surg. 1997, 26:284-6. 10.1016/s0901-5027(97)80870-3
38. Naz S, Hashmi AA, Khurshid A, Faridi N, Edhi MM, Kamal A, Khan M: Diagnostic role of fine needle aspiration cytology (FNAC) in the evaluation of salivary gland swelling: an institutional experience. BMC Res Notes. 2015, 8:101. 10.1186/s13104-015-1048-5
39. Oberoi J, Umap P, Patil S, Agrawal S: Comparative study of fine needle aspiration and cell block technique in salivary gland lesions. Int J Adv Res. 2020, 8:285-90. 10.21474/IJAR01/11290
40. Wadhwa K, Bagga PK, Singh B, Paul S: Comparative analysis of cell block preparation versus smear examination in the fine needle aspirates of head and neck lesions with application of IHC markers on cell block preparation. Int J Contemp Med Res. 2019, 6:45-9.

ISSN:0975 -3583,0976-2833 VOL 15, ISSUE 01, 2024

10.21276/ijcmr.2019.6.6.42