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Determination of Rates of Malignancy on Archival Salivary Gland Fine-Needle Aspiration Biopsy after Application of the Milan System for Reporting Salivary Gland Cytopathology in the Philippine General Hospital: A 1-Year Retrospective Study*

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ABSTRACT

Background. The Milan System for Reporting Salivary Gland Cytopathology (MSRGC) aims to increase the overall effectiveness of salivary gland FNAB by defining six general diagnostic categories with corresponding Rates of Malignancies (ROM). This study aims to use this system to categorize salivary gland FNAB in the Philippine General Hospital and stratify ROM per category.

Methodology. In this study a total of 326 cases have been collected and reviewed, of which 154 (47.2%) had either surgical or clinical follow-up. The cases were assigned a Milan category by 3 cytopathologists blinded from the original diagnoses and from each other's readings.

Results. The overall sensitivity, specificity, PPV, and NPV in detecting neoplasm is at 71.6%, 90.9%, 88.3%, and 76.9%, respectively. On the other hand, the sensitivity, specificity, PPV, and NPV in detecting malignancy is at 52%, 92.9%, 59.1%, and 90.7%, respectively. The computed ROM is as follows: Category I 7.89%, Category II 9.43%, Category III 20%, Category IVa 10.53%, Category IVb 60%, Category V 75%, and Category VI 100%.

Conclusion. The overall diagnostic utility of salivary gland FNAB, as well as the computed ROM per diagnostic category are comparable to internationally published literature. This study also validates the MSRSGC as a valuable tool in stratifying ROM in salivary gland lesions.

Key words: cytopathology, fine needle aspiration biopsy, FNAB, Milan System, salivary gland, rates of malignancy

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INTRODUCTION

Fine-needle aspiration biopsy (FNAB) is an accepted first-line investigation for palpable head and neck masses, and allows separation of inflammatory from neoplastic, and benign from malignant lesions.[1]

The diagnostic role of FNAB in the evaluation of salivary gland lesions has been well established by generating cost-effective care and appropriate management strategies.[2] The reported overall sensitivity and specificity of salivary gland FNAB range from 86-100% and 90-100%, respectively as reported in most series.[3] The ability of salivary gland FNAB to render a specific diagnosis is limited by sampling, lack of architectural details, and cytomorphologic overlap between different salivary gland lesions.[4] This challenge was further magnified by the lack of a uniform reporting system that resulted in reduced clarity of communication between cytopathologists and clinicians.[5]

This has led to the American Society of Cytopathology (ASC) and the International Academy of Cytology (IAC) to organize an international taskforce composed of cytopathologists, surgical pathologists, and head and neck surgeons with the proposal of a tiered classification system consisting of a limited number of diagnostic categories with clear definitions; each diagnostic category associated with an implied Rate of Malignancy (ROM). This unified effort

was then called "The Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)" in September 2015.[6]

To date, few studies have been published which tackled the role and impact of the MSRSGC in the diagnosis and management of salivary gland lesions; and with the assimilation of data from other institutions, the MSRSGC is expected to evolve and reflect the current knowledge of salivary gland FNAB.[7] With that said, the main objective of this study is to examine the effect of applying the MSRSGC to salivary gland aspirates and calculate the ROM associated with each category in Philippine General Hospital (PGH).

METHODOLOGY

This research utilized a retrospective cross-sectional study design. All of the salivary gland FNAB cases from both the PGH and the University of the Philippines-Pathology Research Laboratory (UP-PRL) for the year 2018 were reviewed.

Sampling

All service and pay salivary gland FNAB cases from the PGH and the UP-PRL done during the year 2018 were included. The FNAB done should be from indicated anatomic locations of major and minor salivary glands; which include the buccal mucosa, labial mucosa lingual mucosa, soft and hard palate, and floor of mouth.[8] FNAB cases of proven cases of salivary gland neoplasms who already underwent definitive surgery prior to the said cytologic biopsy (i.e., recurrences), and those with a history of malignancy (i.e., metastasis) were excluded in this study.

Materials and methods

FNABs that are done at the UP-PRL utilized a 25-gauge needle attached to 10 cc syringe, assisted by an aspirator gun/syringe holder. At least 1 air-dried slide smear and 1 alcohol-fixed slide smears are rendered from the aspirate. The air-dried slide is prepared with Diff-Quik staining while the alcohol-fixed slide is prepared with Papanicolaou staining. In some cases, cell block is prepared from cystic aspirates. Rapid on-site evaluation is performed to evaluate for adequacy of material.

FNABs done at the PGH Outpatient Department (OPD) are sent to either the UP-PRL or the OPD laboratory for processing. FNABs done at the wards are sent to the PGH central laboratory for processing. The gauge of the needle used, utilization of a syringe holder, and actual technique in aspiration are uncertain for cases not performed at the UP-PRL.

Data collection

The FNAB results from the UP-PRL and PGH were reviewed by an independent data extractor (IDE), and salivary gland FNAB cases for the year 2018 were retrieved. Salivary gland FNAB include those cytologic studies done for lesions indicated as having been obtained from the pre-auricular, post-auricular, submandibular, submental, maxillary, and floor of mouth areas. For cases with more than one FNAB performed on the same lesion but on separate occasions, the latest FNAB was selected and the earlier one was not used.

These FNAB cases were examined for presence of definitive surgical follow-up by the IDE through searching the OpenMRS using available patient identifiers. For cases with diagnoses that fell under the non-diagnostic, non-neoplastic/ inflammatory category with no available histopathologic follow-up, a clinical follow-up via chart review was done by the ORL co-investigator to check for medical management and outcome of the biopsied lesion. All the gathered data were recorded in standardized Case Data Forms. The definitive follow-up of the cases, whether surgical or clinical, were then classified as either "Non-Neoplastic," "Benign," or "Malignant," based on the retrieved histopathology report. Cases with no definitive follow-up available were classified under "Non-Diagnostic."

Classification using the MSRSGC

The slides of all the included cases, each accompanied by a standardized Cytopathologist Milan Classification Form, were sent separately to the three cytopathologists for slide review and independent blinded classification using the MSRSGC. The final Milan category for a particular case was based on the agreement of at least two of the three cytopathologists. FNAB cases in which the three cytopathologists have differing classifications were grouped together and were not assigned a final Milan category.

Data analysis

All necessary information were entered into an electronic spreadsheet via MS Excel 2018. Descriptive statistics were done, and the number of cases per Milan category were tallied together with their corresponding definitive outcomes. The sensitivity, specificity, PPV, NPV of salivary gland FNAB in (i) differentiating neoplastic from non-neoplastic lesions, and (ii) detecting malignancy were computed with 95% CI. Only FNAB cases with definitive outcomes were included in these computations.

In the calculation for presence or absence of neoplasm and malignancy, SG-FNAB cases classified as Category III (AUS) and IVb (SUMP) were grouped under positive for neoplasm and malignancy, respectively. This is based on the finding by Wang et al., in 2017 of a high percentage of Category III and IVb cases with malignant histopathologic follow-up.[9] Lastly, the ROM and OROM per Milan category were computed with 95% CI.

RESULTS

A total of 326 cases were identified for the year 2018. Majority of these cases were from the UP-PRL composed of 271 cases (83%), while the remainder come from PGH OPD and PGH Central Laboratory, with 29 (9%) and 26 (8%) cases, respectively. The age of the patients ranged from 1 to 87 (Mean = 40); 139 (42.6%) of which were male and 187 (57.4%) were female. Of the 326 lesions, 167 (51.2%) were from the location of the parotid gland, 93 (28.5%) were from the submandibular area, 33 (10.1%) were from the submental/sublingual area, and 33 (10.2%) were from areas where minor salivary glands are present (e.g., lip, oral cavity, maxilla, zygomatic area). Among those with slides (n = 272), the mean number of slides per case was 2 (68%) with a range of 1-8 slides per case. 93 cases (34.2%) had both Diff Quik and Papanicolaou-stained slides, none had Diff Quik slides only, 179 cases (65.8%) had Papanicolaou-

stained slides only, and 26 cases (9.6%) had cell block preparations. Based on the MSRSGC categorization, 102 cases (31.3%) were grouped as Category I, 107 cases (32.8%) as Category II, 8 cases (2.5%) as Category III, 75 cases (23%%) as Category IVa, 16 cases (4.9%) as Category IVb, 8 cases (2.5%) as Category V, and 4 cases (1.2%) as Category VI. 6 cases (1.8%) were not assigned to any of the above categories and grouped under "Unclassified" because there was no consensus between the three cytopathologists for these cases. Definitive follow-up, whether surgical or clinical, was available for 154 cases (47.2%): 95 cases (24.48%) turned out to be non-neoplastic while 91 cases (23.45%) were neoplastic. Benign histopathologic follow-up comprises 57 cases (14.69%) while 34 cases (8.76%) were malignant. There were 202 cases (52.06%) with no available definitive surgical or clinical follow-up.

As shown in Table 1, out of the 102 cases under Category I, 64 (62.7%) had no surgical and/or clinical follow-up thus classified under cases with no definitive diagnosis; while 25 (25%) turned out to be non-neoplastic, 10 (9.8%) turned out to be benign, and 3 (2.94%) turned out to be malignant. There were 107 FNAB cases under Category II; 54 (50.5%) had no definitive diagnosis, 45 (42.1%) turned out to be non-neoplastic, 3 (2.8%) were benign, and 5 (4.67%) were malignant. Out of the 8 cases under Category III, 3 (37.5%) had no definitive diagnosis, 4 (50%) were non-neoplastic, none was benign, and 1 (12.5%) turned out to be malignant. Of the 75 cases under category IVa, 37 cases (49.3%) had no definitive diagnosis, 1 case (1.3%) turned out to be non-neoplastic, 33 cases (44%) were benign, and 4 cases (5.3%) were malignant. There were 16 cases under Category IVb; 6 (37.5%) of which had no definitive diagnosis, 1 (6.25%) was non-neoplastic, 3 (18.75%) were benign, and 6 (37.5%) turned out to be malignant. Out of the 8 cases in Category V, 4 (50%) had no definitive diagnosis, 1 (12.5%) was non-neoplastic, none were benign, and 3 (37.5%) were malignant. Lastly, of the 4 cases under Category VI, only 1 (25%) had no definitive diagnosis while the remaining 3 cases (75%) were malignant.

The diagnostic utility of FNAB in detecting both salivary gland neoplasm and malignancy are shown in Table 2. The sensitivity, specificity, PPV, and NPV of FNAB in detecting salivary gland neoplasm are as follows: 71.62%, 90.91%, 88.33%, 76.92%, respectively. On the other hand, the sensitivity, specificity, PPV, and NPV of FNAB in detecting salivary gland malignancy are as follows: 52%, 92.86%, 59.09%, and 90.7%,respectively. The OROM and ROM per Milan category is summarized in Table 3. The calculated OROM for each Milan category are as follows: Category I (2.94%), Category II (4.67%), Category III (12.5%), Category IVa (5.33%), Category IVb (37.5%), Category V (37.5%), and Category VI (75%). The cumulative OROM across all categories is at 8.59%. On the other hand, the calculated ROM for each Milan category are as follows: Category I (7.89%), Category II (9.43%), Category III (20%), Category IVa (10.53%), Category IVb (60%), Category V (75%), and Category VI (100%). The cumulative ROM across all categories is at 18.18%.

Unclassified cases (n = 6) were not included in the computation of OROM, ROM, as well as in computing for sensitivity, specificity, PPV, and NPV. Out of the 6 cases, 3 cases (50%) were lost to follow-up, while the remaining 3 cases (50%) turned out to be malignant on definitive biopsy or surgery. Among those with available follow-up data, one is a case of a 42-year-old female with right submandibular mass initially diagnosed on FNAB as "atypical cells present favor non-small cell carcinoma," which turned out to be Diffuse Large B-Cell Lymphoma (DLBCL) after tissue biopsy and further investigation with immunohistochemistry studies. Another case is that of a 56-year-old female with a mass on the floor of mouth initially diagnosed on FNAB as "rare epithelial cells suggestive of a neoplastic process," but turned out to be Adenoid Cystic Carcinoma on definitive surgery. The last case is that of a 63-year-old female with a left buccal mass initially signed out on FNAB as "atypical cells present," but on definitive surgery turned out to be Sebaceous Carcinoma. Each case is composed of 2 Papanicolaou-stained slides only.

Table 1. Distribution of definitive follow-up per Milan category

Milan category	Total cases	Non-diagnostic	Non-neoplastic	Neoplastic	
I	102	64 (62.7%)	25 (25%)	13 (12.75%)	
				Benign 10 (9.8%)	Malignant 3 (2.94%)
II	107	54 (50.5%)	45 (42.1%)	8 (7.48%)	
				Benign 3 (2.8%)	Malignant 5 (4.67%)
III	8	3 (37.5%)	4 (50%)	1 (12.5%)	
				Benign 0	Malignant 1 (12.5%)
IVa	75	37 (49.3%)	1 (1.3%)	37 (49.3%)	
				Benign 33 (44%)	Malignant 4 (5.3%)
IVb	16	6 (37.5%)	1 (6.25%)	9 (56.25%)	
				Benign 3 (18.75%)	Malignant 6 (37.5%)
V	8	4 (50%)	1 (12.5%)	3 (37.5%)	
				Benign 0	Malignant 3 (37.5%)
VI	4	1 (25%)	0	3 (75%)	
				Benign 0	Malignant 3 (75%)

Table 2. Diagnostic utility of FNAB in detecting salivary gland neoplasm and malignancy

	Detecting neoplasm (%)	95% CI	Detecting malignancy (%)	95% CI
Sensitivity	71.6	59.9 – 81.5	52.00	31.3 – 72.2
Specificity	90.9	82.2 – 96.3	92.86	86.9 – 96.7
PPV	88.3	78.6 – 94.0	59.09	41.0 – 75.1
NPV	76.9	69.7 – 82.8	90.70	86.6 – 93.6

Table 3. Computed OROM and ROM per Milan category

Milan category	Malignant on follow-up (n)	Total FNAB (n)	FNAB with follow-up (n)	OROM (%)	ROM (%)	95% CI
I	3	102	38	2.94	7.89	(1.6 - 21.4)
II	5	107	53	4.67	9.43	(3.1 – 20.6)
III	1	8	5	12.50	20.00	(0.5 – 71.6)
IVa	4	75	38	5.33	10.53	(2.95 – 24.8)
IVb	6	16	10	37.50	60.00	(26.2 – 87.8)
V	3	8	4	37.50	75.00	(19.4 – 99.4)
VI	3	4	3	75.00	100.00	(29.2 – 100)
Total	28	326	154	8.59	18.18	

Table 4. False negative cases in detection of malignancy

	Case control #	Location	Initial FNAB	Milan category	Definitive diagnosis
1	179	Infraauricular mass	Scant atypical squamous epithelium	I	Trichilemmal carcinoma
2	309	Preauricular mass	Hemorrhagic cyst fluid only	I	Adenoid cystic carcinoma
3	400	Submandibular mass	Hemorrhagic aspirate	I	Langerhans cell histiocytosis
4	84	Infraauricular mass	Atypical cells present suspicious for malignancy	II	Non-Hodgkin diffuse large B-cell lymphoma
5	174	Preauricular mass	Scattered salivary acinar cells in an acute on chronic inflammatory background	II	Non-Hodgkin lymphoma
6	244	Preauricular mass	Acute inflammatory pattern	II	Squamous cell carcinoma.
7	326	Submandibular mass	Polymorphous lymphocytic population suggestive of a reactive process. Recommend solid tissue biopsy	II	Atypical round cell proliferation, consider Non-Hodgkin lymphoma
8	340	Submandibular mass	Benign cyst contents	II	Mucoepidermoid carcinoma
9	49	Infraauricular mass	Cell findings consistent with benign mixed tumor	IVa	Non-invasive adenocarcinoma arising from a BMT
10	183	Parotid mass	Consistent with malignant epithelial neoplasm, cannot rule out a possible salivary gland or thyroid origin	IVa	Adenocarcinoma
11	246	Parotid mass	Basaloid neoplasm with fibromyxoid stroma, cannot rule out an adenoid cystic carcinoma	IVa	Adenoid cystic carcinoma
12	399	Parotid mass	Benign mixed tumor	IVa	Salivary duct carcinoma ex-pleomorphic adenoma

Note: The Milan Category was assigned after these cases were independently and blindly reviewed by 3 cytopathologists without knowledge of the actual initial FNAB diagnosis.

DISCUSSION

The overall follow-up rate of salivary gland FNAB in this study is at 47.2% (154 out of 326 cases). These include cases that were found out to be non-neoplastic, benign, or malignant based on definitive histopathology or clinical follow-up. This value is comparable[10,11] and even higher[5,12,13] compared to other studies. Majority of those with no follow-up came from the Category I group at 62.7% followed by the Category II group at 50.5%. A possible reason for this is that inflammatory conditions are the most common pathology affecting the salivary glands.[14] In addition, when the non-diagnostic cohort is excluded in both the initial FNAB and the definitive outcome, the most common lesion affecting salivary glands belong to the non-neoplastic category. Some may have resolved spontaneously thus causing the patient to no longer seek follow-up. Interestingly, a significantly high percentage of cases under Category IVa (49.3%) and Category V (50%) also have poor follow-up for reasons that are yet unclear. A plausible explanation is that some of these patients might have been referred or voluntarily transferred to a nearer and more accessible health facility for definitive management.

In this study, more than half (51.23%) of the lesions sampled were said to have been taken from the parotid gland. This is followed by lesions taken from the sub-mandibular gland at 28.5%. These findings are consistent with published data; majority of salivary gland lesions arise from the parotid gland.[15-17] All cases had alcohol-fixed Papanicolaou-stained smears while only 93 cases (34.2%) had the complimentary air-dried Diff Quik-stained smears. This means that only 34.2% of the cases followed the recommendation of the MSRSGC wherein a combination of air-dried and alcohol-fixed smears should be the mainstay in evaluating salivary gland FNAB. The inherent qualities of the matrix material, cytoplasmic features, and the nature of a proteinaceous or mucinous background is better appreciated using air-dried Diff Quik preparations. On the other hand. Alcohol-fixed Papanicolaou slides can be useful for the assessment of nuclear qualities and degree of cytologic atypia.[3]

The sensitivity of FNAB in detecting salivary gland neoplasm is higher (71.62%) as compared to that in detecting salivary gland malignancy (52%). This means that 21 out of the 74 FNAB cases reported to be neoplastic on definitive follow-up had been initially classified as non-neoplastic. The false negative rate for detecting neoplasm is computed at 28.4%. Out of these 21 cases, 13 (62%) were initially grouped under Milan Category I (Non-Diagnostic) on FNAB. These non-diagnostic smears were reported as either hemorrhagic, acellular smears, or as smears consisting of cyst fluid only. The even lower sensitivity of FNAB in detecting salivary gland malignancies (52%) seen in this study indicate a higher false negative rate of 48% for detecting malignancies. In our study, 12 cases had been initially classified as non-malignant on FNAB but turned out otherwise on definitive follow-up. These are tabulated in Table 4.

Published data have shown that sensitivity in detecting neoplasm and malignancy range from 50%[10] to 95%.[18] In a local study by Santiago et al., a similarly low sensitivity for diagnosis of malignancy at 46% was noted.[19] False negative results are often caused by inadequate sampling with insufficient cellularity of the aspirate[10] and heterogeneity in the performance and level of experience among clinicians and pathologists.[20] This scenario is true in the PGH as not all FNABs are done by pathologists; some are performed by clinicians and medical interns at the OPD (8.9%) or at the bedside in the wards (8%). Moreover, some FNABs from the PRL were also performed by clinicians and were just sent for staining and interpretation. However, data on the number of these PRL cases that were sent from clinicians are beyond the scope of this study. Low sensitivity and high-performance heterogeneity show the greatest room for improvement in salivary gland FNAB.[4]

On the contrary, the results for specificity in this study means that there is high true negative rate, and that FNAB can be used as a tool to confirm a high clinical suspicion that is indicative of a neoplasm or malignancy. The specificity of FNAB in detecting salivary gland neoplasm and malignancy is at 90.9% and 92.9%, respectively. These are comparable to published values in international studies.[10-12,15-17, 21, 22-26]

The MSRSGC emphasized risk stratification rather than specific diagnoses, providing an ROM for each category, with corresponding recommended management that would guide clinicians for better patient care.[7] The total

Table 5. Comparison of computed ROM with select internationally published data

Authors	Country	Sample size*	I	II	III	IVa	IVb	V	VI
Faquin and Rossi (MSRSGC)	Italy	—	25 (0-67%)	10 (0-20%)	20 (10-35%)	<5 (0-13%)	35 (0-100%)	60 (0-100%)	90 (57-100%)
Cablao et al.	Philippines	154	7.9	9.4	20.0	10.5	60.0	75.0	100.0
Wei et al.	USA	4514**	25.0	10.2	12.5	3.4	37.5	58.6	91.9
Liang et al.	USA	110	50.0	60.0	12.5	3.2	72.7	100.0	100.0
Viswanathan et al.	India	373	6.7	7.1	38.9	5.0	34.2	92.9	92.3
Kala et al.	India	172	25.0	5.0	20.0	4.4	33.3	85.7	97.5
Thiryayi et al.	UK	138	8.5	1.6	0.0	1.9	26.7	100.0	100.0
Choy et al.	Singapore	376	14.5	26.7	29.3	2.7	19.1	87.5	100.0

*Only those with histopathologic and clinical follow-up
**From 29 reviewed studies worldwide

OROM, which is the number of malignant cases divided by the total number of FNABs across all diagnostic categories estimates the rate at which a certain salivary gland lesion is malignant prior to doing a biopsy. In our study the calculated total OROM is at 8.59%, meaning there is an 8.59% chance that any particular salivary gland lesion from a patient who presents to the clinic could be malignant. This aspect was not explored in previous studies.

What is more important, however, in the diagnostic point of view, as is suggested in the MSRSGC, is the ROM per diagnostic category. Table 5 summarizes the computed ROMs per Milan diagnostic category of some selected and available published studies. The estimated ROMs reported by Faquin and Rossi, the proponents of the MSRSGC, lifted from available literature is also presented.

The computed ROM for Category I (7.9%) is lower compared to the estimates of Faquin and Rossi published in the MSRSGC (25%). However, they also reported that ROM values for this category may range from 0% to 67%.[3] The result from this study is comparable to the findings of Viswanathan et al., (6.7%)[24] and Thiryayi et al., (8.5%).[27] There may be an overestimation in the other studies wherein certain non-diagnostic cases were still taken into the equation even though there were succeeding FNABs with diagnostic findings on follow-up. In the present study, non-diagnostic cases that had another diagnostic FNAB on follow-up were not counted in the computation for ROM. In the present study, majority of the definitive diagnoses in Category I was classified under non-neoplastic (65.8%), followed by benign neoplasm (26.3%).

There is agreement between results of this study for the ROM of Categories II and III with that published in the MSRSGC. The ROM for Category II (9.4%) is comparable to that published in the MSRSGC (10%)[3], as well as in studies by Wei et al., (10.2%)[18] and Viswanathan et al., (7.1%).[24] On the other hand, comparable ROMs have also been observed in this study (20%) with that published in the MSRSGC (20%)[3] and with the study by Kala et al., (20%).[28] Also, the percentage of cases under Category III at 2.5% is well within the recommended desirable number of <10% of all salivary gland FNAB samples in an institution.[3] However, one caveat in this diagnostic category, according to the MSRSGC is that the ROM is not yet well defined due to the lack of literature pertaining to salivary gland aspirates classified as AUS.

As for Category IVa (Benign), the present study's ROM (10.5%) is higher compared to those published in literature. 4 out of 38 cases initially classified under Category IVa up turned out to be malignant on definitive follow-up. In the MSRSGC, they reported a mean ROM of <5% for this category. However, they also cited that the ROM for benign neoplasms on FNAB may range from 0% to 13%.

This study's computed ROM for Category IVb (60%) is also higher compared to that reported in the MSRSGC (35%).[3] However, it should be noted that in the same literature, they also cited an ROM at a range of 0 to 100% for this category. Liang et al., reported a higher ROM for this category (72.7%).[29] In a study by Hang et al., in 2018, wherein Category IVb cases were further explored and subtyped based on predominant cytomorphology, they found varying values for ROM within the same diagnostic category. For those with a predominant oncocytic or squamoid component, the ROM reached as high as 61% which is comparable with that in our study. Other subgroups were those with basaloid cytomorphology (ROM = 40%) and myoepithelial cytomorphology (ROM = 18.8%).[9]

Results for Category V (Suspicious for Malignancy) and Category V (Malignant) are slightly higher at 75% and 100%, respectively, when compared to values estimated by the MSRSGC. Faquin and Rossi estimated the ROM of Category V to range from 0% to 100%, while that of Category VI to range from 57% to 100%.[3] Also, in general values derived in this study are comparable with other international studies, which range from 58.6% to 100% for Category V and 91.9% to 100% for Category VI.

Lastly, it is worth looking into the possible reasons behind the 6 unclassified cases in this study. In all cases, at least one cytopathologist assigned a category of AUS (Category III). These cases are often associated with pre-analytical factors such as technique in aspiration and smearing, air drying artifacts, obscuring background, or the inherent characteristics of the lesion resulting in scant numbers of well-preserved cells.[3] It can be noted that in 3 of these cases, a note on the limited number and quality of cells had been made. Currently, adequacy criteria for salivary gland FNAB are not well established.[13] None of these cases had repeat FNABs done. Another thing that is common among all unclassified cases is that each case has only 2 Papanicolaou-stained slide smears. A combination of air-dried Diff Quik-stained smears and alcohol-fixed Papanicolaou-stained smears is the mainstay of salivary gland FNAB.[3] The lack of air-dried Diff Quik slides limits evaluation of matrix material, cytoplasmic features, and nature of proteinaceous or mucinous background in these cases. The lack of radiologic and clinical data (e.g., size of mass, duration of symptoms, rate of growth, associated pain/paresthesia, accompanying infection or fever) provided to

the cytopathologists during the study also played a major role in the difficulties that arose in classifying cases. As emphasized in the literature, FNAB forms an integral part together with clinical examination and radiologic investigation in the assessment of salivary gland lesions.[11]

Also, worth looking into is the ROM in this subgroup. 3 out of 6 (50%) had definitive follow-up and all of them turned out to be malignant. In this light, difficult cases should always be examined more closely with the proper clinical and radiologic data. Moreover, the really challenging cases should have the concurrence of at least one cytopathologist, and a repeat FNAB should be suggested whenever possible.

LIMITATIONS

The study is limited by the lack or inadequacy of clinical and radiologic information for some FNAB cases. There is likewise a lack of uniformity in the use of both air-dried and alcohol-fixed slide smears in the evaluation of salivary gland FNAB. Another limitation is the heterogeneity in the performance of FNAB. Procedures done at the UP-PRL use the prescribed 25-gauge needle attached to a 10 cc syringe with an aspirator. Rapid on-site evaluation is performed for specimen adequacy at the UP-PRL. In the clinics, however, the gauge of the needle, size of the syringe, and utilization of an aspirator, are unknown. Moreover, there is no rapid on-site adequacy evaluation. These factors restrict the diagnostic potential of FNAB in detecting neoplasm and malignancy of the salivary glands.

CONCLUSION

The low sensitivity in detecting neoplasm (71.6%) and malignancy (52%) indicate that the FNAB should not be indiscriminately used as a screening tool in evaluation salivary gland lesions. However, FNAB proves to be an excellent tool in confirming a clinical suspicion of neoplasm or malignancy, as evidenced by its high specificity in detecting neoplasm (90.9%) and malignancy (92.86%). As a whole, the sensitivity, specificity, PPV, and NPV of FNAB; and the ROM per diagnostic category computed in the study are comparable to that in published literature. To our best knowledge, this is the first Philippine study which looked into the ROM of salivary gland FNAB using the diagnostic categories recommended by the Milan system. More so, this study validates the MSRSGC as a valuable tool in stratifying ROM in salivary gland lesions to better guide clinical management.

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