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Cytohistopathological evaluation of salivary gland lesions in tertiary care center of Eastern Nepal

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ABSTRACT

Background: Salivary gland tumors consist of a group of heterogeneous lesion with complex clinicopathological characteristics. Fine needle aspiration (FNA) cytology has been used as a quick, non-invasive diagnostic tool for the diagnosis of neoplastic and non-neoplastic lesion of salivary gland. **Aims and Objectives**: The aims and objectives of the study are to perform the cytopathological evaluation of minor and major salivary gland lesions (neoplastic and non-neoplastic) in terms of its various types, frequency, site, demographic distribution and to correlate with histopathology findings whenever available. **Materials and Methods**: This is a hospital-based 3-year study in which 155 cases of patient underwent FNA cytology for salivary gland swelling (non-neoplastic and neoplastic) of which seven cases were excluded due to scant and inadequate aspirate, and thus, only 148 cases were included in this study and histopathological correlation was available in 42 cases. Any metastatic lesion, repeat samples from same patient were excluded from the study. **Results:** Out of 148 cases, male patients were 72 (49%) and female patients were 76 (51%) with M: F ratio of 0.9:1. Benign lesion was commonly seen in 31–40 years, non-neoplastic lesion at 41–60 years (n = 18, 37.6%), and malignant lesions at 61–90 years (n = 9, 37.5%). Parotid was the most common salivary gland involved by neoplastic and non-neoplastic lesion accounting 65.5% (n = 97) followed by submandibular gland 29.7% (n = 34). Pleomorphic adenoma was most frequently diagnosed among all salivary gland lesions (60%). Mucoepidermoid carcinoma outnumbered the category (14%) of malignant salivary gland lesion. On histopathology correlation, 33 cases were correctly diagnosed in cytopathology whereas 9 cases showed discordant result. FNA cytology sensitivity was 66.6%, specificity was 93.3%, positive predictive value was 80.0%, and negative predictive value was 87.5%, respectively. Diagnostic accuracy was found to be 85.7%. **Conclusion:** Cytopathology examination of salivary gland can be used as safe and reliable method in primary diagnosis of lesions of salivary gland.

Key words: Fine needle aspiration cytology; Neoplastic; Non-neoplastic; Salivary gland

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INTRODUCTION

Salivary gland tumor represents an uncommon heterogeneous group of neoplasm with complex clinicopathological characteristics.[1] They constitute 3–10% of neoplasms of the head-and-neck regions.[2] Although a variety of neoplasm arise from salivary gland, the cytological features of common neoplastic and non-neoplastic lesions are well documented, and hence, accurate cytological diagnosis is possible in most of the cases which can direct management plans.[3] Salivary gland tumors predominantly affect the parotid gland in more than 70% of cases.[4] The age incidence also varies widely, extending from children to adults over 80 years of age.[5] The masses of salivary gland are easy target for fine needle aspiration (FNA) due to their superficial location and easy

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accessibility for procedure. FNA is indeed a useful method for early evaluation due to its low cost, rapid turnaround time, high specificity, and sensitivity.[6,7] The evaluation of salivary gland lesions can sometimes be problematic due to the heterogeneous nature of benign and malignant tumor with overlapping cytological features and inadequate sampling.[8,9] However, this limitation can be minimized by doing multiple aspirates from different sites of the tumor and by aspirating the residual fluid in cystic lesions after it gets collapse after initial aspiration.[8]

Aims and objectives

We aim to perform the Cytohistopathological evaluation of minor and major salivary gland lesions (neoplastic and non-neoplastic) in terms of its various types, frequency, site, demographic distribution and available histopathological correlation.

MATERIALS AND METHODS

This is a hospital-based 3-year study, 2-year retrospective (January 2017–December 2018), and 1-year prospective study (January 2019–December 2019) conducted in the Department of Pathology at BP Koirala Institute of Health Sciences, Dharan, Nepal, for a period of 1 year after receiving ethical approval from hospital Institutional Review Committee (Code number: IRC/1236/018). Data from retrospective cases were obtained from the record section of Department of Pathology after taking consent for the utilization of data from Department Head. In prospective cases, all the patients who presented with salivary gland swelling (minor and major salivary gland) during the study period and in whom FNA cytology (FNAC) was performed were included. In the present study, 155 cases of salivary gland swelling (non-neoplastic and neoplastic) were taken in which cytological studies were done and histopathological correlation was done whenever available. Seven cases were excluded due to scant and inadequate aspirate on FNAC, and thus, only 148 cases were included in this study and histopathological correlation was done in 42 cases. Any metastatic lesion, repeat samples from the same patient were excluded from the study. After proper examination of the lesion, detailed history, and consent, FNA was performed from different sites of the salivary gland swelling using a 10 mL disposable syringe and 21/23-gauge needle without local anesthesia. In case of deep-seated lesion, ultrasonography (USG)-guided FNA was performed in radiology department.

Smears were prepared and air-dried smears were stained with Giemsa stain and wet smears after fixing in 95% ethyl alcohol Papanicolaou staining was done in cytopathology laboratory and evaluated under microscope. For histopathological examination, paraffin-embedded tissue sections from salivary gland tissue were stained with hematoxylin and eosin (H and E). Data collection was done in predesigned proforma and data entry was done in Excel and analyzed in the Statistical Package for the Social Sciences version 11.5. The overall site, sex, age of occurrence, and morphological spectrum of all the non-neoplastic and neoplastic (benign and malignant) salivary gland swelling were studied. The data were analyzed in terms of percentage and frequency distribution. Sensitivity, specificity, negative predictive value, and positive predictive value were calculated.

RESULTS

During the study period, 148 cases were cytologically diagnosed as salivary gland neoplastic and non-neoplastic lesion. Out of 148 cases, number of male patients enrolled in the study were 72 (49%) and female patients were 76 (51%) with M: F ratio of 0.9:1.

Most of the patients enrolled in the study were between 31 and 40 years (20.3%) followed by 51–60 years (16.2%) of age. Benign lesion was commonly seen in age group of 31–40 years. The peak of non-neoplastic lesion was seen at 41–60 years (n=18, 37.6%) after which the frequency decreased with increasing age. Malignant lesions were common at 61–90 years of age (n=9, 37.5%) (Table 1).

Parotid was the most common salivary gland to be involved by neoplastic and non-neoplastic lesion accounting for 65.5% (n=97) followed by submandibular gland 29.7% (n=34). Minor salivary gland and sublingual gland involvement were seen in 4.1% (n=6) and 0.6% (n=1), respectively (Figure 1). Out of 148 cases, maximum number of cases were of benign category (n=76, 49%) followed by non-neoplastic lesions (n=48, 31%) and malignant lesion (n=24, 16%). Among the non-neoplastic lesion, chronic sialadenitis (33.3%) was most frequently diagnosed followed by sialadenosis (10%) (Table 2). In neoplastic lesion, benign neoplasm outnumbered the malignant neoplasm by 52%. Pleomorphic adenoma (PA) was the most frequently diagnosed among all salivary gland lesions (60%). Mucoepidermoid carcinoma outnumbered the category (14%) of malignant salivary gland lesion (Table 3).

The analysis of correctly diagnosing the salivary gland lesion by FNAC was done by comparing the diagnosis with available histopathological samples which showed that 33 cases were correctly diagnosed in cytopathology whereas 9 cases showed discordant result (Table 4). According to

Table 1: Age-wise distribution of neoplastic and non-neoplastic lesions

S. No.	Age range (years)	Number of cases (%)			
		Benign	Malignant	Non neoplastic	Total
1	0–10	0 (0.0)	0 (0.0)	6 (12.5)	6 (4.1)
2	11–20	6 (7.8)	2 (8.3)	4 (8.3)	12 (8.1)
3	21–30	13 (17.1)	2 (8.3)	6 (12.5)	21 (14.2)
4	31–40	18 (23.7)	4 (16.7)	6 (12.5)	28 (19.0)
5	41–50	10 (13.2)	4 (16.7)	9 (18.8)	23 (15.5)
6	51–60	12 (15.8)	3 (12.5)	9 (18.8)	24 (16.2)
7	61–70	11 (14.5)	3 (12.5)	5 (10.4)	19 (12.8)
8	71–80	5 (6.6)	4 (16.7)	1 (2.1)	10 (6.8)
9	81–90	1 (1.3)	2 (8.3)	2 (4.2)	5 (3.3)
	Total	76 (100)	24 (100)	48 (100)	148 (100)

Table 2: Frequency of non-neoplastic salivary gland lesions

S. No.	Non neoplastic lesion	Parotid (%)	Submandibular (%)	Sublinual	Minor salivary gland	Total (%)
1	Acute sialadenitis	1 (3.1)	1 (6.2)	-	-	2 (4.2)
2	Chronic sialadenitis	7 (21.9)	9 (56.3)	-	-	16 (33.3)
3	Sialadenosis	8 (25.0)	2 (12.5)	-	-	10 (20.8)
4	Intraparotid reactive lymphoid hyperplasia	8 (25.0)	1 (6.2)	-	-	9 (18.7
5	Granulomatous lymphadenitis	2 (6.2)	-	-	-	2 (4.2)
6	Suppurative lesion	3 (9.4)	-	-	-	3 (6.3)
7	Mucocele	3 (9.4)	3 (18.8)	-	-	6 (12.5)
	Total	32 (100)	16 (100)	-	-	48 (100)

Table 3: Frequency of neoplastic salivary gland lesions

S. No.	Neoplastic lesion	Parotid (%)	Submandibular (%)	Sublingual (%)	Minor salivary gland (%)	Total (%)
Benign neoplasm						
1	Schwannoma	1 (2.0)	-	-	-	1 (1.0)
2	Pleomorphic adenoma	36 (72.0)	18 (94.7)	-	6 (100)	60 (60.0)
3	Warthin tumor	12 (24.0)	-	-	-	12 (12.0)
4	Basal adenoma	1 (2.0)	1 (5.3)	1 (100)	-	3 (3.0)
	Total	50 (100)	19 (100)	1 (100)	6 (100)	76 (76.0)
Malignant neoplasm						
1	Mucoepidermoid carcinoma	9 (60.0)	5 (55.6)	-	-	14 (14.0)
2	Acinic cell carcinoma	2 (13.3)	-	-	-	2 (2.0)
3	Adenoid cystic carcinoma	4 (26.7)	3 (33.3)	-	-	7 (7.0)
4	Salivary duct carcinoma	-	1 (11.1)	-	-	1 (1.0)
	Total	15 (100)	9 (100)			24 (24)

Table 4: Comparison of cytological diagnosis with histopathology

S. No.	FNAC diagnosis	Number of cases	Histopathology diagnosis		
			Concordant	Discordant	Final histopathology diagnosis
1	Chronic sialadenitis	3	1	2	Pleomorphic adenoma- 1 Adenoid cystic carcinoma- 1
2	Pleomorphic adenoma	26	22	4	Mucoepidermoid carcinoma- 2 Adenoid cystic carcinoma- 1 Chronic sialadenitis- 1
3	Warthin tumor	3	1	2	Mucoepidermoid carcinoma- 1 Acinic cell carcinoma- 1
4	Mucoepidermoid carcinoma	5	4	1	Chronic sialadenitis- 1
5	Adenoid cystic carcinoma	4	2	2	Basal cell adenoma- 1 Lymphoepithelial carcinoma- 1
6	Salivary duct carcinoma	1	1	-	Salivary duct carcinoma- 1
	Total	42	33	9	

FNAC: Fine needle aspiration cytology

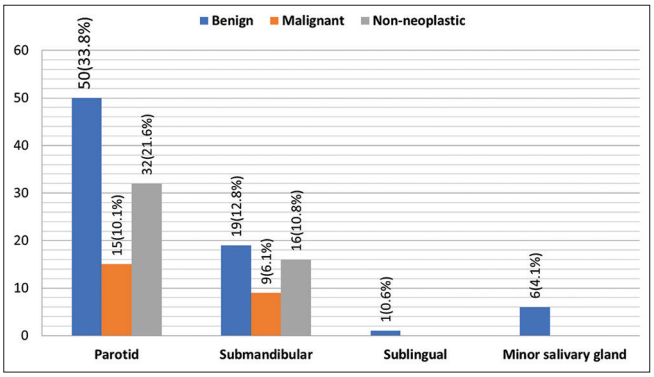

Figure 1: Bar diagram showing site distribution of salivary gland lesions

this, FNAC sensitivity was 66.6%, specificity was 93.3%, positive predictive value was 80.0%, and negative predictive value was 87.5%, respectively. Diagnostic accuracy was found to be 85.7%.

DISCUSSION

Salivary gland lesions constitute a wide range of lesion from inflammatory, granulomatous, obstructive to benign, and malignant. This lesion shows a range of age, sex, and site-wise distribution. In a study done by Kakoty et al., maximum cases of salivary gland lesions were seen in the third decade (30%) which is comparable with the present study.[10] Study conducted by Khandekar et al., showed that benign tumor and malignant tumor were common in age groups 31–45 years and 16–30 years, respectively.[8] Another similar study done in India showed that non-neoplastic lesion was predominant in age group 20–29 years whereas benign and malignant lesions showed peak in 30–39 years and 60–69 years, respectively.[7] The finding is similar to the present study except for non-neoplastic lesion which showed peak at 4th–5th decade of life.

Parotid (52%) was the most common salivary gland to be affected followed by submandibular gland (17%) and minor salivary gland (11%). The benign tumors were more frequent in parotid (49%), whereas malignant tumors predominated in minor salivary glands (11%) in a study done by Sandhu et al.[9] Another study done by Nepal et al showed parotid tumor (69%) outnumbered all other sites followed by submandibular (18%) and minor glands (13%).[11] The finding aligned with the present study (Figure 2).

Study conducted by Arul et al.,[12] revealed benign neoplasm (64.3%) outnumbered the malignant neoplasm (16.5%) and non-neoplastic lesions (15.9%). Chronic sialadenitis was the most common non-neoplastic lesion (15.9%) whereas PA and mucoepidermoid carcinoma were the most common benign (50%) and malignant (5%) neoplasm, respectively.

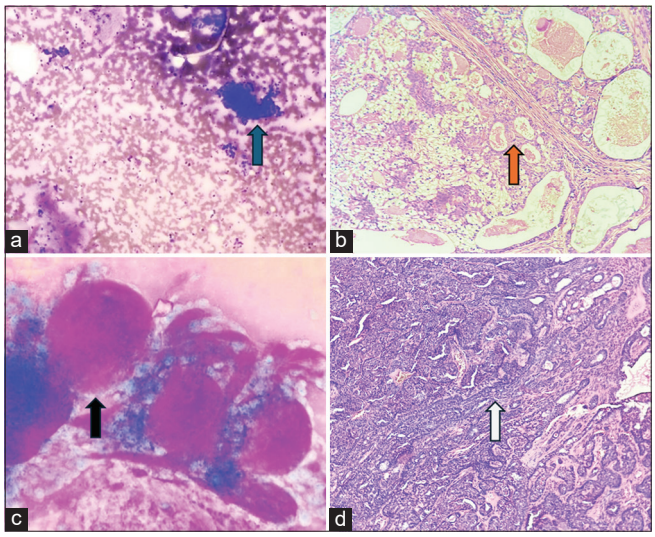

Figure 2: (a) The uniform epithelial cells (green arrow) and scattered cells along with extracellular mucin which was misinterpreted as epithelial and myoepithelial cells and chondromyxoid stroma of pleomorphic adenoma, histopathology came out to be low-grade mucoepidermoid carcinoma (yellow arrow) (b). (c) presence of uniform small cells with hyaline globules (black arrow) led to this erroneous diagnosis of adenoid cystic carcinoma, the histopathology of which came as basal cell adenoma (white arrow) (d)

In another similar study by Joshi et al.,[2] also found a similar results where benign neoplasm (86.9%) outnumbered the neoplastic lesion (40.6%) and malignant neoplasm (13.2%). Sialadenitis, PA, and mucoepidermoid carcinoma were the most common diagnosed non-neoplastic (21.9%), benign (48.4%), and malignant (4.69%) neoplasm, respectively. The present study correlated with these studies.

Histopathology was available in 42 cases for correlation with cytological diagnosis. Discordant results between cytological diagnosis compared with histopathological diagnosis were observed in 9 cases (false negative: 21%). The rate of false-negative diagnosis on cytology ranges from 0% to 37% in literature.[13] Out of 9 discordant cases, maximum number of discripancy was seen in PA (n=4) where two cases of mucoepidermoid carcinoma (MEC), one case of adenoid cytic carcinoma, and one case of chronic sialadenitis were misdiagnosed as PA in FNAC.

Two of the case which was diagnosed as PA in FNAC came out to be low grade MEC in histopathology (Figure 2a and b). One of the cases showed uniform epithelial cells, metaplastic cells along with extracellular mucin which was misinterpreted as epithelial and myoepithelial cells and chondromyxoid stroma of PA. Similarly, the other case showed sheets and fragments of basaloid cells and scant matrix in FNAC. There was a predominance of intermediate cells with few squamoid cells and occasional mucus cells in histopathology which were absent in cytology smears. The

FNA smear was non-representative of the lesion which might be the reason for false-negative diagnosis.

One case of adenoid cystic carcinoma (AdCC) was misdiagnosed as PA in FNAC. The uniform epithelial cells in sheets, clusters, and scattered singly with acellular stromal component lead to misdiagnosis of PA as such feature is also seen in case of AdCC. Similar findings were seen in study done by Singh et al.,[14] Arul et al.,[12] and Khandekar et al.[8]

Similarly, in the present study, the cases of MEC and acinic cell carcinoma were misdiagnosed as Warthin tumor in FNAC. Such an example of false-negative result could be due to sampling error, especially when the tumor is cystic.[3,15] In such circumstances where the lesion is cystic and low yield, USG-guided FNAC can help in proper representation of lesion.

Another diagnostic dilemma occurs in tumor having basaloid morphology. In the present study, one case of basal cell adenoma was misdiagnosed as AdCC in FNAC (Figure 2c and d). The presence of uniform small cells with hyaline globules leads to this erroneous diagnosis. Similar finding was observed by Arul et al. and highlighted the point that such hyaline globules are not specific to AdCC and can also be seen in basal cell adenoma and other salivary gland tumors.[12]

Limitations of the study

There were limited number of cases available for histopathological correlation.

CONCLUSION

FNAC is a safe, quick, and minimally invasive procedure that can be performed on out-patient basis for the initial evaluation of salivary gland lesion. While interpreting any lesion of major and minor salivary gland, care must be taken for possible regenerative changes, metaplastic changes, false sampling of the lesion which can cause an erroneous diagnosis and wrong treatment. The radiological correlation along with behaviors of the lesion and age of the patient should also be taken into consideration during interpretation of aspiration slides. Whenever possible, confirmation of the lesion can be done on histopathological examination.

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REFERENCES

1. Araya J, Martinez R, Niklander S, Marshall M and Esguep A. Incidence and prevalence of salivary gland tumours in Valparaiso, Chile. Med Oral Patol Oral Cir Bucal. 2015;20(5):e532-e539. https://doi.org/10.4317/medoral.20337
2. Joshi AR, Jadhav D, Baste B and Ranka S. A study of fine needle aspiration cytology in salivary gland lesions in a rural population. Int J Adv Med. 2017;4(2):307-310. https://doi.org/10.18203/2349-3933.ijam20170613
3. Inancl HM, Kanmaz MA, Ural A and Dilek GB. Fine needle aspiration biopsy: In the diagnosis of salivary gland neoplasms compared with histopathology. Indian J Otolaryngol Head Neck Surg. 2013;65(Suppl 1):121-125. https://doi.org/10.1007/s12070-012-0608-4
4. Roychoudhury AK and Dhar R. A clinicopathological study of non-neoplastic and neoplastic lesions of salivary glands. Int J Curr Res. 2016;8(12):43097-43100.
5. Tessy PJ, Jayalekshmy PS, Cicy PJ and Poothiode U. Fine needle aspiration cytology of salivary gland lesions with histopathological correlation - A two year study. Int J Healthc Biomed Res. 2015;3(4):91-99.
6. Jain R, Gupta R, Kudesia M and Singh S. Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison. Cytojournal. 2013;10:5. https://doi.org/10.4103/1742-6413.109547
7. Omhare A, Kumar SK, Nigam JS and Sharma A. Cytohistopathological study of salivary gland lesions in Bundelkhand region, Uttar Pradesh, India. Pathology Res Int. 2014;2014:804265. https://doi.org/10.1155/2014/804265
8. Khandekar MM, Kavatkar AN, Patankar SA, Bagwan IB, Puranik SC and Deshmukh SD. FNAC of salivary gland lesions with histopathological correlation. Indian J Otolaryngol Head Neck Surg. 2006;58(3):246-248. https://doi.org/10.1007/BF03050831
9. Sandhu VK, Sharma U, Singh N and Puri A. Cytological spectrum of salivary gland lesions and their correlation with epidemiological parameters. J Oral Maxillofac Pathol. 2017;21(2):203-210. https://doi.org/10.4103/jomfp.JOMFP_61_17
10. Kakoty S, Baruah TD and Babu CP. FNAC and histopathological correlation of salivary gland lesions: An observational study. Int Surg J. 2017;4(7):2148-2152. https://doi.org/10.18203/2349-2902.isj20172624
11. Nepal A, Chettri ST, Joshi RR, Bhattarai M, Ghimire A and Karki S. Primary salivary gland tumors in eastern Nepal tertiary care hospital. J Nepal Health Res Counc. 2010;8(1):31-34.
12. Arul P, Akshatha C, Masilamani S and Jonathan S. Diagnosis of salivary gland lesions by fine needle aspiration cytology and its histopathological correlation in a tertiary care center of Southern India. J Clin Diagn Res. 2015;9(6):EC07-EC10. https://doi.org/10.7860/JCDR/2015/14229.6076
13. Ashraf A, Shaikh AS, Kamal F, Sarfraz R and Bukhari MH. Diagnostic reliability of FNAC for salivary gland swellings: A comparative study. Diagn Cytopathol. 2010;38(7):499-504. https://doi.org/10.1002/dc.21211
14. Singh A, Haritwal A and Murali BM. Correlation between cytology and histopathology of the salivary gland. Australas Med J. 2011;4(2):66-71. https://doi.org/10.4066/AMJ.2011.518
15. Fernandes H, D'souza CR, Khosla C, George L and Katte NH. Role of FNAC in the preoperative diagnosis of salivary gland lesions. J Clin Diagn Res. 2014;8(9):FC01-FC03. https://doi.org/10.7860/JCDR/2014/6735.4809

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