

Accuracy of Fine needle aspiration cytology in diagnosis of salivary gland lesions: A study with histologic comparison

Prepared By: Taye Jemberu,MD, Pathology resident
Adviser: Bereket Birhane,MD, Assistance professor of pathology

Table content

1. Acknowledgment.....	2
2. Abbreviations.....	3
3. Abstract.....	4
4. Introduction.....	5-6
5. Literature review.....	7-8
6. Methodology.....	9
7. Results.....	10-17
8. Discussion.....	18-21
9. Reference.....	22-23

Acknowledgement

I would like to use this opportunity to express my gratitude to everyone who supported me through the span of residency program. I am thankful for their aspiring guidance, constructive criticism and friendly advice during study period. I would like to express my special appreciation and thanks to my advisor Dr Bereket Brehane. I like to thank you for encouraging my research and allow me to grow both as pathologist and researcher. I would also like to thank our department member Almaz and isreal for participating in this research. Finally, I have special thanks to my mother (Alem Abera) and my wife (Lidya Habtewolde), I cannot express how grateful I am to have you as family, Thank you very much.

Abbreviations

ACC: Adenoid cystic carcinoma;
AciCC: Acinic cell carcinoma
CL: Cystic lesion
CSA, Chronic Sialadenitis
INC: Inconclusive for diagnosis
CPA: Carcinoma ex pleomorphic adenoma
EMC: Epithelial-myoepithelial carcinoma
LEC: Lymphoepithelial cyst
MEC: Mucoepidermoid carcinoma
MU: Mucela
SA: Sialadenosis
SGT: Salivary gland tumor
PA: Pleomorphic adenoma
UH: Unremarkable histology
UM: Undifferentiated malignancy

Abstract

Background: Fine needle aspiration cytology (FNAC) is a sensitive and specific and yet an economically effective technique for diagnosis of salivary gland lesions. FNAC of salivary glands has achieved a pivotal role in the diagnosis and management of salivary gland lesions since its induction by Stewart et al in 1933. However, it has always been under scrutiny when compared to histopathology. Histopathology of salivary gland lesions is still the final method to establish diagnosis and predicting prognosis in these lesions.

Methods: A retrospective observational study of 156 patients with excisional/incisional biopsy of salivary gland lesions was done from september 2015 to May 2019. For 60 patients presurgical FNAC was done in our hospital. Cases with histopathological correlation were included in calculating diagnostic accuracy. The cytological findings were correlated with that of the histopathological diagnosis to obtain the accuracy of the cytological diagnosis. The parameters of diagnostic validity of the cytological technique in terms of sensitivity, specificity and accuracy.

Results: Study population included patients of age group ranging from 5-78 years. In the present study out of 156 lesions, 77 (49.4%) were more common in the parotid gland. These were followed by submandibular gland 69 (44.2%) and 5 cases (3.2%) occurred in the minor salivary glands. Salivary gland lesions were classified into 3 diagnostic classes: Non-neoplastic lesions 34(21.8%), benign lesions 78(50%), and malignant lesions 44(28.2%). PA and MEC were the commonest benign and malignant entity respectively. Histopathological correlations were available in 60 cases with 22 cases being the malignant lesions. In the present study, the specificity and the sensitivity were found to be 73% and 90 % respectively.

Conclusions: Fine Needle Aspiration Cytology is thus a safe, reliable, quick, convenient and accurate method of diagnosis and should be considered as one of the first line of investigations in the evaluation of salivary gland lesions. However, the accuracy of FNAC can be improved by using standard reporting and adding subspecialty to our department.

Keywords: Diagnostic accuracy, FNAC, Mucoepidermoid carcinoma, Pleomorphic adenoma, Salivary gland lesions, sensitivity, specificity.

Introduction

Salivary glands are exocrine organ responsible for production and secretion of saliva. They comprise the three paired major glands: the parotid, submandibular and sublingual, and the minor salivary glands. Salivary gland lesions encompass a heterogeneous group of disorders and are broadly classified as neoplastic and non-neoplastic. The 2017 World Health Organization classification system recognizes 20 malignant and 12 benign salivary gland epithelial tumors. The incidence of salivary gland tumors is estimated to be 1-2/100,000. The burden of salivary gland lesions in sub-Saharan countries, particularly in Ethiopia, is not well studied and neglected. In one study in Ethiopia, of all salivary gland tumors, parotid gland accounts 43,2 % submandibular gland for 25 % and the rest of all minor salivary glands contributes. Pleomorphic adenoma forms 58.5% of all tumors¹. This pattern of salivary gland tumors closely resembles other sub-Saharan countries²; However, the epidemiology of salivary gland lesions relatively not well documented. In many studies, data are limited to parotid gland. The etiologies are diverse including Genetically, viruses, bacteria, radiation and an idiopathic cause.

Accurate pre-surgical diagnosis of salivary gland lesions is very important because most non-neoplastic lesions and some neoplastic conditions do not require surgery. Additionally, to make an accurate and effective surgical intervention, it is essential to make a preoperative assessment of the nature of these lesions. Fine Needle Aspiration cytology(FNAC), Core Needle Biopsy(CNB), clinical and radiologic modalities are important tools to reach diagnosis. In recent decades, FNAC has been established as efficient diagnostic tool for superficial mass including salivary gland lesions. It is technically simple, safe and cost-effective. The added advantage of fistula formation and recurrence following capsular disruption, which is common with incisional biopsy makes it favorable for initial assessment.

Fine needle aspiration cytology for salivary gland disease has not gained universal acceptance because of reported complications of hemorrhage, turnout seeding within the needle tract, infection and lack of confidence in diagnostic accuracy. Errors may occur in sampling tumors such as carcinoma arising in a pleomorphic adenoma where FNAC can miss the malignant component. However, in resource constrained area FNAC remain the mainstay primary diagnostic modality for salivary gland lesions.

FNAC diagnosis in each discipline has its own pitfalls and setbacks. Diagnosing salivary gland become more difficult due to the following reasons¹³.

1. Shared cytomorphologic findings Among Salivary gland neoplasms.
2. Circumscription, Encapsulation, and Invasive Growth cannot be assessed on cytology
3. Interpersonal variability in technique of performing FNAC
4. Immunohistochemistry a little role in differentiating these lesions

Therefore, while performing FNAC the basic things to be needed are the experience of pathologist or clinician and familiarity of pathologist with details of the clinical history, physical examination and the results of laboratory investigations. For example, False positive diagnoses can be caused by regenerative epithelial hyperplasia and squamous metaplasia in sialadenitis or Warthin's tumor. While epithelial atypia and high cellularity can occasionally be worrying in pleomorphic adenoma. False negative diagnoses can be due to faulty technique, Central cystic, hemorrhage or necrotic area devoid of diagnostic cells, Small lesions and Uncooperative patients. The site and type of salivary gland and specimen adequacy may also have significant role in the accuracy of FNAC. Assessing specimen adequacy is quit subjective as it depends on type of lesion².

Due to significant overlap between of histologic features of salivary gland tumor and diagnosis with FNAC needs experience and qualified expertise and inter-observer variability. Our objecties are to do histotyping of salivary gland lesions on study period of time and to find out the accuracy of FNAC in diagnosing salivary gland lesion in our institution. Our department is one of the youngest department in the hospital. Started in 2005, it made tremendous progress in term of giving quality services for the patients and physicians. The department has set different measure to assure diagnostic accuracy of any pathologic specimen including slide sessions, clinico-pathology sessions, and extra-departmental consultations. However, beside instant case review, we could not set mechanisms to check our diagnostic accuracy; Perhaps no research had been conducted issuing correlation of any of sub-division related to the patient outcome or inter-observer variability. Therefore, the current study will have the following impact and implications

1. As a prime study, it gives background for future research on salivary gland
2. It will point out diagnostic weakness on salivary gland lesions
3. Since we discuss common discordant cases, it has educational value for the fellow readers.
4. It helps to set a possible diagnostic guideline for salivary gland lesions by collaborating with maxillofacial department.

Literature review

Since the introduction of FNAC by German hematologist, Hans hirshfield, 1912; It has been used for diagnostic tool for variety of clinical entities (Aristidis et al). Its feasibility and cheap price makes it a preferable choice for physicians especially in developing countries³. However, it has pitfalls and set back in terms of giving accurate and reliable diagnosis. These depend on inter-observer variability and the site of the lesion. FNAC is widely used in the head and neck swellings frequently encountered in general practice, such as in the lymph nodes, thyroid, major salivary glands, and other neoplastic lesions⁴⁻⁷. FNAC is very helpful in the diagnosis of salivary gland tumors, where it can differentiate between a malignant and a benign tumor. It could differentiate the infective process from neoplastic one and avoids unnecessary surgeries. Many Studies have shown that FNAC correlates with histopathology and therefore can provide a preoperative cytological diagnosis which can influence management of patients of salivary tumors in terms of whether to operate or not, and If a patient should be operated then what would be the extent of surgery and would the facial nerve be spared or not. It's not only diagnostic but can also be therapeutic especially in cystic lesions⁸⁻¹².

There are similar researches conducted in sub-Saharan countries, for instance in Zambia Kazuma *et al* had done retrospective study of 28 parotid gland lesions. They found FNAC correlated with histopathology with a sensitivity of 100% and specificity of 66.7%; positive and negative predictive values of 95.7% and 100% respectively. All Parotid tumors were neoplastic with 76% benign and 24% malignant tumors on histopathology. FNAC accurately diagnosed 68% benign and 20% malignant tumors. Finally, they recommended FNAC provides a preoperative diagnosis that influences management by either avoiding surgery (inflammatory lesion) and limiting the extent of surgery for benign and malignant Parotid tumours².

Elagoz and Gulluoglu selected 56 cases of FNAC with biopsy diagnosis. The sensitivity and specificity for benign and malignant lesion were 72 and 100% respectively. There is diagnostic sensitivity for all neoplastic and non-neoplastic lesion was 84% and the specificity 92%, with the overall finding, they conclude FNAC is a useful and reliable tool in diagnosing of salivary gland mass performed by radiologist and clinical. Similarly, Khandekar M.M. and Kavatkar A.N. conducted prospective study of salivary aspirations on 70 patients. Histopathological correlation was done whenever possible. Specimens received in the surgical pathology section of B.J. Medical College, Pune, over a period of two years. FNAC has a sensitivity of 94.5 % and specificity of 80.95% for neoplastic lesions⁹.

In Italy, Similar research was conducted by Lopez- pazor et al. over the period of 13 years with total number 433 salivary gland cases. The FNAC sensitivity and specificity was 77% and 96% respectively, A positive predictive value of 82.35% and a negative predictive value of 94.8%. In their study FNAC show relatively high sensitivity and specificity and the level of agreement between the FNAC diagnosis and the final biopsy diagnosis is good. Tushar and Banyameen conducted 2 years' study selectively to parotid gland tumoral lesion, they found Parotid gland was commonest affected site. Out of 46 neoplastic lesions 39 (84.7%) were benign and 07 (15.3%) were malignant. An overall of 86.9% (40/46) concordance between FNAC and final histological diagnosis was established. A sensitivity of 97.4% and specificity was 71.4%, were observed with 93.4 % of accuracy. The positive and negative predictive values were 95% and 83.3%, respectively.

Ritu et al took 80 cases over a period of 3 years' majority (67.5%) involved the parotid gland. Eight cases (10%) were non-neoplastic lesions, comprised of sialadenitis, retention cyst and sialadenosis. Of a total of 72 neoplasms, 58 were benign and 14 were malignant salivary gland tumors. A cyto-histologic concordance of benign diagnosis was achieved in 85.7% of cases and for malignant lesions in 92.8% of the malignant tumors. FNAC showed a sensitivity of 92.8%, specificity of 93.9%, a positive predictive value of 81.2% and negative predictive value of 98.4% for malignant salivary gland tumors. There was one false-negative diagnosis and four false-positive cases diagnosed on FNAC¹¹. Research conducted in Nepal Pleomorphic adenoma was the most frequent lesion in this study. Parotid gland was the most common site affected by salivary gland lesions. The sensitivity, specificity and accuracy for non-neoplastic lesions was 100%, 89.28%, 91.67%; For benign neoplasms was 100%, 86.95%, 91.67% and for malignant neoplasms was 57.14%, 100%, 83.33% respectively¹¹.

Tessy PJ *et al* obtained 130 cases of salivary gland lesions on which FNAC was done. The age range of the group varied from 1 year to 88 years with a mean age of 45 years. Biopsy confirmation of diagnosis was available in 61 cases. Benign tumors constituted the largest category followed by malignant tumors and inflammatory lesions. Pleomorphic adenoma was the most common benign tumor and mucoepidermoid carcinoma was the most common malignant tumor in our study. The overall diagnostic accuracy of FNAC was 86.7% with a sensitivity of 56.3% and a specificity of 97.7% for detecting malignancy. Other research extended their correlation to clinical findings¹⁴. In another study, Manish et al, out of 23 cases diagnosed as benign on FNAC, only 20 cases were confirmed as benign on histology and 3 cases turned out to be malignant. In case of malignant tumors, all the 5 (15.6%) cases diagnosed on FNAC as malignant were confirmed on biopsy. 3 cases which were misdiagnosed on FNAC as benign came out to be malignant on final diagnosis. Chronic sialadenitis was the most common non-neoplastic lesion whereas amongst benign tumors, pleomorphic adenoma was frequently

encountered.

Methodology

The research is retrospective descriptive study conducted at pathology department of St Paul hospital. All Biopsies and FNACs from major and minor salivary gland over period of 4 years [Sept 2008 to April 2011] were carefully selected from medical record. Those biopsy cases who has pre-surgical cytology diagnosis were selected & recorded beside FNAC diagnosis. Metastasis of primary tumor in other location and uncertainly diagnosed cases were excluded from the study statistics. The selected FNAC cases grouped according to Millan cytology diagnostic classification.

FNAC- based diagnose was compared with histological examination of specimens and calculated the sensitivity regarding the presence of malignancy [true positive/ true positive + false negative], specificity regarding absence of malignancy [true negative / true negative + false positive], Negative predictive value [true negative / true negative + false negative] and accuracy of FNAC [true positive + true negative / total]. Other Statistical analysis were carried by using SPSS version 20.

RESULT

The patients under study were of age group ranging from 5-78 years. Maximum numbers of patients were in the age group of 21-30 years 39 (25%) (Table 1). According to sex, females were 94(60.3%) and males were 62 (39.7%) (Table 2). In the present study out of 156 lesions, 77 (49.4%) were more common in the parotid gland. These were followed by submandibular gland 69 (44.2%). 5 cases (3.2%) occurred in the minor salivary glands. The remaining nine (5.8%) case was unspecified on the request form (Table 3). Salivary gland lesions were classified into 3 diagnostic classes: Non-neoplastic lesions 34(21.8%), benign lesions 78(50%), and malignant lesions 44(28.2%).

Non-neoplastic lesions 6(18%) were most common in the age group of 51-60 years. Benign lesions 24 (30.7%) were common in 21-30 age group (Table 4). Malignant lesions 9 (20.5%) were common in 31-40 age group. (Table 5). Among the non-neoplastic (34) lesions of salivary glands, chronic sialadenitis 27 cases (77.1%) were the most common and of these 24(88.8%%) seen in the submandibular gland and 3(11.2%) in the parotid gland.

Amongst benign neoplastic lesions (78), pleomorphic adenoma 59 (76.6%) was most commonly encountered in the parotid gland comprising 32(54.2%%) and 23 (38.9%) in the submandibular gland (table 6). Amongst the total 44 cases of malignant neoplastic lesions,13(29.5%) cases were mucoepidermoid carcinoma followed by 11 (25%) cases Adenoid cystic carcinoma and 7(15.9%) cases Acinic cell carcinoma. 33(75%) occur on parotid gland, 10(24%) cases occur on submandibular gland and 1 case (25%) case of polymorphous low grade adenocarcinoma occur in minor salivary gland (Table 6).

For our research we were able to retrieve 60 FNAC cases with histology correlation. 3(5%) non-diagnostic cases, 4(6.6%) Non-neoplastic lesions,31 cases (51.6%) benign lesions, and 22 cases (36.6%)malignant lesions (Table 7). On final analysis of the present series, there were 22 malignant tumours on cytological diagnosis of which histopathological correlation were available in 3 cases with false positive and 19 cases as true positive. Similarly, there were 34 cases of benign lesions (both non-neoplastic lesion and benign tumours) of which histopathological correlation were available in 27 as true negative cases and 7 cases as false negative

		Frequency	Percent
Sex	F	94	60.3
	M	62	39.7
	Total	156	100.0

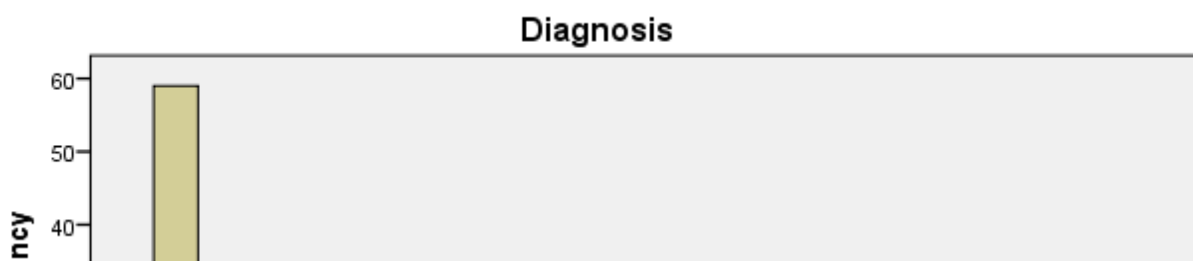
Table 1. Sex distribution

		Frequency	Percent
Age	0-20	24	15.4
	21-30	39	25.0
	31-40	35	22.4
	41-50	17	10.9
	51-60	22	14.1
	>60	17	10.9
	Unspecified	2	1.3
	Total	156	100.0

Table 2. Age distribution of salivary gland lesions

		Frequency	Percent
Site	parotid gland	77	49.4
	submandibular gland	69	44.2
	minor salivary gland	5	3.2
	Unspecified	5	3.2
	Total	156	100.0

Table 3. Salivary gland lesion in terms of site.



<i>I.Non-diagnostic</i>	<i>3(5%)</i>
<i>II.Non-neoplastic</i>	<i>4(6.6%)</i>
<i>III.Atypia of undetermined significance(AUS)</i>	<i>0</i>
<i>IV.Neoplasm</i>	
<i>IVA.Neoplasm: benign</i>	<i>31(51.6%)</i>
<i>IVB:Neoplasm:Salivary gland neoplasm of uncertain malignant potential</i>	<i>0</i>
<i>V.Suspicious for malignancy</i>	<i>0</i>
<i>VI.Malignant</i>	<i>22(36.6%)</i>

		Age					
		0-20	21-30	31-40	41-50	51-60	>60
Diagnosis	PA	10	22	13	4	5	3
	UH	3	1	1	1	0	1
	LEC	1	3	3	0	0	0
	BCA	0	0	2	1	0	0
	MU	1	0	0	0	0	0
	CSA	2	5	5	4	6	5
	SA	0	2	1	1	3	0

Table 4. Distribution of benign salivary gland tumor on different age group. PA,Pleomorphic adenoma; UH, Unremarkable histology; LEC, Lymphoepithelial cyst; BCA, Basal cell Adenoma; MU, Mucele; CSA, chronic Sialadenitis; SA, Sialadenosis.

		Age					
		0-20	21-30	31-40	41-50	51-60	>60
	MEC	6	1	0	1	5	0
	EMC	0	0	0	0	0	3
	CPA	0	0	1	0	0	1

The case distribution in our study was as follow: True positive cases 19; false positives cases 3; true negative cases 27; and false negative cases 7. The present study revealed sensitivity of 73%, specificity of 890%, negative predictive value of 79.4%, positive predictive value of 86.3% and overall diagnostic accuracy of 77.19%,. This relative lower than the mean sensitivity and specificity value twenty articles reviewed (Sensitivity 89.8% and specificity 91%).

Litrature review show a wide range of sensitivity and specificity of FNAC for salivary gland swelling in different populations and setups. ZErpa et al, in 93 cases of parotid tumors, revealing a sensitivity of specificity of 57% and and 95% respectively. On the other hand, pastore et al found sensitivity and specificity of 83 % and 93 %. They evaluated 357 cases of salivary gland lesions. Similarly, Jaein et al. revealed 92.8% sensitivity and 93.9% specificity in a study involving 80 cases of salivary gland swelling, out of which 14 cases were of malignant neoplasm. Kim et al found a diagnostic accuracy of FNAC to be 92 % in differentiating malignant from benign lesion. Fakhry et al. evaluated 249 parotid tumor tumors, out of 75 % were benign and 25 % were malignant. The spensitivity and specificity of detecting malignancy was assessed to be 80% and 89.5%. M. Elagoz et al. proposed sensitivity & specificity for benign and malignant salivary gland tumors as 72% & 100%. Diagnostic sensitivity for all neoplastic and non-neoplastic lesions was 84% and specificity was 92%. Christensen et al. study obtained a sensitivity of malignant cases as 83% and specificity of 99%. The positive predictive value was 98%, and the negative predictive value was 97%, the overall accuracy was 93%.

As conclusion, Fine Needle Aspiration Cytology is thus a safe, reliable, quick, convenient and accurate method of diagnosis and should be considered as one of the first line of investigations in the evaluation of salivary gland lesions. However, the accuracy of FNAC can be improved by adopt standard reporting system(milam and adding subspecialty to our department.

Country	Author	Year	Number	M:F	Age Range	Site	Benign	malignant
Kenya	Jyoti et al	2012	132	1:1.3	8-80	Major	PA	ACC
Kenya	Onyango Et al	1992	415	1:1.1	1-91	Major	PA	ACC
Zimbabwe	Chidzonga	1995	282	1:1.3	10-71	Major	PA	ACC
Uganda	Vuhahuhla	2007	261	1:1.3	1-81	Major	PA	ACC
Nigeria	Silas et al	2009	202	1:1.4	4-69	Major	PA	MEC
Tanzania	Masanja	2003	100	1.5:1	20-49	Major	PA	ACC
Current		2019	156	1:1.5	5-78	Major	PA	MEC

Table 9. Comparison of the pattern of SGTs in various countries

Authors	No. of cases	Sensitivity(%)	Specificity(%)
J Akhtor and S.Hirchad	24	90	100
Singn A(murali)	56	76.9	97
Kakoty and Burauh	39	90.91	96.42
Tushar and Banyameen	46	77.7	86.3
Kazume and Muchelog	25	100	66.7
G.Gohe and Krishina	31	90.6	100
M.khardy and Naratkorn	70	94	80.95
Koirala S and Sayami G	28	100	89.28
ARUL and MASILAMANI	146	86.6	96.6
Shubhangi and Nasib	65	89.5	100
Samreen and Atif Ali	36	86.3	77.7
Current study	60	73	90

Table 10. FNAC and Histopathology correlation of salivary gland lesions on various researches

References

1. Ergicho B, Ergisho B. *Ethiop Med J.* 2003jul;41(3):235-44
2. Zacharie Sandro, Jean valentin Fokouo, Jean Louis. *Pan Afr Med J.* 2016;23:6.
3. Frable WJ. Fine-needle aspiration biopsy: A review. *Hum Pathol* 1983;14:9-28.
4. Himanshu Shekhar, Ashmeet Kaur, Pallav Agrawal. *Int J Res Med Sci.* 2014 Nov;2(4):1667-1671
5. Sneha Kakoty, Tridip Baruah, Ganesh Babu. *Int Surg J.* 2017 Jul;4(7):2148-2152
BMC Research Notes (2015) 8:101
6. Kazuma M, Mucheleng'anga, Hanna H. *East & Central African Journal of Surgery* 2017; Vol. 22 (1)
7. Sheetal G, Mani Krishna, Gautam N. Gole .*National Journal of Medical and Dental Research*, Oct.-Dec. 2016: Volume-5, Issue-1, Page 25-32
8. Hye Song, Joon Seon, Song Chang. *Journal of Pathology and Translational Medicine* 2015; 49: 136-143
9. Khandekar M.M, Kavatkar A.N., Patankar A.Indian. *Journal of Otolaryngology and Head and Neck Surgery* July-September 2006, Vol. 58, No. 3,
10. Tushar Kambale, Banyameen Iqbal, Amar deep. *Indian Journal of Pathology and Oncology*, July-September 2016;3(3);372-375
11. Ritu Jain, Ruchika Gupta, Madhur Kudesia. *CytoJournal* 2013, 10:5
12. Koirala S, Sayami G, Pant AD. *Journal of Pathology of Nepal* (2014) Vol. 4, 654-657
13. Shubhangi Shalley, Nasib Chand, Amit Aggarwal. *The Open Dentistry Journal*, 2018, Volume 12 ,783
14. Tessy PJ, Jayalekshmy PS, Cicy PJ, Usha Poothiode *International J. of Healthcare and Biomedical Research*, Volume: 03, Issue: 04, July 2015, Pages 91-99
15. Arul.P, Akshatha C, Suresh Masilamani, Srivani Jonathahan. *Journal of Clinical and Diagnostic Research.* 2015 Jun, Vol-9(6): EC07-EC10
16. E Wang, Christopher Fundakowski, Jasvir S. *Pathol Lab Med—Vol 139*, December 2015
17. Manish Sharma, Neeru Bala, Sumeet Angral. *Septemeber-October*, Volume 3, Pages 8-12.
18. Shubhangi Shalley, Nasib Chand, Amit Aggarwal.*The Open Dentistry Journal*, 2018, Volume 12 783
19. Orell SR. *Monographs in clinical cytology Salivary gland tumors: 1st edition 2000: S.Karger Publishers* Vol 15:1-2
20. Onyango, J.F., Awange, D.O., Muthamia, J.M. and Muga, B.I.O. (1992) *Salivary Gland tumors in Kenya. East Af- rica Medical Journal*, 69, 525-530.
21. Chidzonga, M.M., Lopez Perez, V.M. and Portilla Alva- rez, A.L. (1995) *Salivary gland tumors in Zimbabwe International Journal of Oral and Maxillofacial Surgery*, 24, 293-29

22. Jones, A.V., Craig, G.T., Speight, P.M. and Franklin, C.D. (2008) The range and demographics of salivary gland tumours diagnosed in a UK population. *Oral Oncology*, 44, 407-417.
23. Tian, Z., Li, L., Wang, L., Hu, Y. and Li, J. (2010) Salivary gland neoplasms in oral and maxillofacial regions: A 23-year retrospective study of 6982 cases in an eastern Chinese population. *International Journal of Oral & Maxillofacial Surgery*, 39, 235-242
24. Speight, P.M. and Barret, A.W. (2002) Salivary gland tumours. *Oral Diseases*, 8, 229-240.