Histopathological Analysis of Neoplastic and Non Neoplastic Lesions of Salivary Gland – A Retrospective Study in a Tertiary Care Hospital

Sheela K.M.¹, Priya V.S.², Lali K. Rajan³, Ashida M. Krishnan⁴

^{1, 2, 3, 4} Department of Pathology, Government Medical College, Thiruvananthapuram, Kerala, India.

ABSTRACT

BACKGROUND

Salivary gland lesions constitute less than 1 % of tumours and about 4 % of all epithelial neoplasms of head and neck region. These comprise of a wide variety of benign, malignant and non-neoplastic lesions which exhibits a difference in histological behaviour. There are no reliable criteria to differentiate on clinical grounds the benign from malignant ones. So morphological evaluation is necessary. We aim to study the frequency of various salivary gland lesions in sialoadenectomy specimens and categorise them into neoplastic and non-neoplastic lesions.

METHODS

It is a record based retrospective 5-year study carried out in the Government Medical College, Thiruvananthapuram, Kerala, from January 2014 to December 2018.

RESULTS

In this study a total of 329 histopathologically proven cases of salivary gland lesions were included. Neoplastic lesions and non-neoplastic lesions constituted 78.42 % and 21.58 % respectively. Pleomorphic adenoma was the most common neoplasm (50.54 %) trailed by Warthin's tumour (9.73 %). Most common malignant neoplasm encountered in our study was mucoepidermoid carcinoma (9.73 %) among which low grade tumours showed predominance. We observed significantly higher incidence of benign and malignant lesions in the 5th to 6th decade while non neoplastic lesions were seen more in the 4th to 5th decade. Average age of the patients with salivary gland tumours was 46.12 \pm SD 15.57. Majority of cases of salivary gland lesions in our study were from parotid gland (75.68 %) followed by submandibular gland 24.01 %.

CONCLUSIONS

Pleomorphic adenoma was the most common benign tumour in our study and mucoepidermoid carcinoma the most common malignant tumour. Neoplastic lesions showed a predominance over non neoplastic lesions. Histopathological examination is the mainstay for diagnosis and clinical management.

KEYWORDS

Histopathology, Pleomorphic Adenoma, Mucoepidermoid Carcinoma

Corresponding Author: Dr. Lali K. Rajan, 3C, Marutham Gateway, Pallimukku, Pettah P.O., Thiruvananthapuram-695024, Kerala, India. E-mail: dr.lalileven@gmail.com

DOI: 10.18410/jebmh/2021/45

How to Cite This Article: Sheela KM, Priya VS, Rajan LK, et al. Histopathological analysis of neoplastic and non-neoplastic lesions of salivary gland – a retrospective study in a tertiary care hospital. J Evid Based Med Healthc 2021;8(05):236-240. DOI: 10.18410/jebmh/2021/45

Submission 11-10-2020, Peer Review 15-10-2020, Acceptance 12-12-2020, Published 01-02-2021.

Copyright © 2021 Sheela K.M. et al. This is an open access article distributed under Creative Commons Attribution License [Attribution 4.0 International (CC BY 4.0)]

BACKGROUND

Salivary gland tumours are relatively uncommon and account for approximately 3 - 6 % of all neoplasms of the head and neck. ^{1.2} Annual incidence of salivary gland tumours is 0.4 - 13.5 per 100000 persons. ^{3,4.5} Salivary gland lesions comprise a wide variety of benign and malignant neoplasms and non-neoplastic lesions which demonstrates a difference in biological behaviour. Non neoplastic lesions include inflammatory disorders of infectious, granulomatous or autoimmune aetiology and other conditions like obstructive, developmental and idiopathic disorders which often present as tumours. ⁶ Salivary gland lesions present with clinical and morphological diversity which makes it difficult for histopathological interpretation. ⁷

It can show morphological diversity between different tumours and also within an individual tumour. Of the salivary gland tumours, 80 % are found in the parotid and 10 - 15 % in the submandibular gland. Majority of the salivary gland tumours show benign histology with pleomorphic adenoma being the most common type. 8

Most common malignant tumour in the salivary gland is mucoepidermoid carcinoma followed by adenoid cystic carcinoma. 9,10.11 Common presenting symptom in these patients is a mass in the gland followed by pain, facial palsy and skin ulcers. There are no reliable criteria to differentiate on clinical grounds the benign from malignant ones, so morphological evaluation is necessary. This study was undertaken to analyse the histopathological profile of various salivary gland lesions in sialoadenectomy specimens received in our department and categorise them into neoplastic and non-neoplastic lesions.

METHODS

This retrospective study was done in the Department of Pathology, Govt. Medical College, Thiruvananthapuram. The study period was one year from January 2018 to December 2018. The study was approved by the research and ethical committee. In this retrospective study, all the histopathology proven cases of salivary gland lesions for a period of five years which constitute 329 cases were included. The clinical information and the required data of the selected patients were recorded from archived case sheets. Final histopathological diagnoses were obtained from the records. In all the selected cases the standard tissue protocols were followed. The tissues were already processed, and sections were cut at 4 to 5-micron thickness and stained with haematoxylin & eosin stain. Special stains immunohistochemistry were carried out in relevant cases.

All histopathologically proven cases of salivary gland lesions were analysed according to the age of distribution, nature of specimen and histopathology. Salivary gland tumours were broadly classified into neoplastic and nonneoplastic. Neoplasms again classified into benign and malignant. The neoplastic lesions were classified according to World Health Classification (WHO) classification 2017. Mucoepidermoid carcinoma was graded according to Armed

Forces Institute of Pathology (AFIP) grading. The data's collected was analysed using descriptive statistics. All histopathologically proven cases of salivary gland lesions received during the study period were included in the study. Cases which were inadequate for a definite histopathological diagnosis were excluded from the study.

Statistical Analysis

All the data were analysed using SPSS Version 25 Software. Quantitative variables were expressed in mean and standard deviation. Qualitative variables were expressed in percentage.

RESULTS

In the present study, a total of 329 sialoadenectomy specimens received in the Department of Pathology, Government Medical College, Thiruvananthapuram, for a period of 5 years were analysed. There were 51.06 % of males (n = 168) and 48.9 % (n = 161) of females with male female ratio of 1.07:1. Female preponderance was seen in benign lesions with M:F ratio of 0.87:1. Sex wise distribution of lesions is depicted in Table 1.

Lesions	Female	Male	Grand Total				
Benign	110	96	206				
Basal cell adenoma	2	1	3				
Intra ductal papilloma	1		1				
Lymphangioma	1		1				
Monomorphic adenoma		1	1				
Oncocytoma		1	1				
Pleomorphic adenoma	103	63	166				
Sialolipoma	1		1				
Warthin's tumour	2	30	32				
Malignant	19	33	52				
Acinic cell carcinoma	2	2	4				
Adenoid cystic carcinoma	1	1	2				
Epithelial myoepithelial carcinoma	1	1	2				
Hodgkin's lymphoma		1	1				
Invasive pleomorphic adenoma	2		2				
Metastasis from well differentiated carcinoma	1		1				
Mucoepidermoid carcinoma	11	21	32				
Myoepithelial carcinoma	1	1	2				
Polymorphus low grade adeno carcinoma		1	1				
Salivary duct carcinoma		2	2				
Well differentiated squamous cell carcinoma		3	3				
Non neoplastic	32	39	71				
Benign cystic lesion	2		2				
Chronic sialadenitis	24	29	53				
Lymphoepithelial cyst	2	4	6				
Parotid abscess	1		1				
Sialolithiasis	2	2	4				
Chronic calcific sialadenitis	1	3	4				
Submandibular abscess		1	1				
Grand total	161	168	329				
Table 1. Distribution of Lesions According to Sex							

In the malignant lesions male predominance were seen with M:F ratio of 1.73:1. Non-neoplastic lesions were more common in males with male female ratio 1.21:1. The age of the patients ranged from 2 yrs. to 82 yrs. The average age of patients with salivary gland lesions was $46.12 \pm SD 15.57$. Most of the cases of salivary gland lesions included in this study were from parotid gland 75.68 % (n = 249) while involvement of submandibular gland was seen in 24.01 % (n = 76) and minor salivary gland in 0.30 % (n = 1) cases. Most favoured sites for benign, malignant and non-neoplastic lesions in our study was parotid gland. Site of

involvement of salivary gland lesions are depicted in Table 2.

Lesions	Parotid	Submandibular Gland	Palate	Grand Total				
Benign	177	28	1	206				
Basal cell adenoma	3			3				
Intra ductal papilloma	1			1				
Lymphangioma		1		1				
Monomorphic adenoma	1			1				
Oncocytoma	1			1				
Pleomorphic adenoma	138	27	1	166				
Sialolipoma	1			1				
Warthin's tumour	32			32				
Malignant	46	6		52				
Acinic cell carcinoma	4			4				
Adenoid cystic carcinoma	1	1		2				
Epithelial myoepithelial carcinoma	1	1		2				
Hodgkin's lymphoma		1		1				
Invasive pleomorphic adenoma	2			2				
Metastasis from well differentiated carcinoma	1			1				
Mucoepidermoid carcinoma	32			32				
Myoepithelial carcinoma	2			2				
Polymorphous low-grade adenocarcinoma	1			1				
Salivary duct carcinoma	1	1		2				
Well differentiated squamous cell carcinoma	1	2		3				
Non neoplastic	26	45		71				
Benign cystic lesion	2			2				
Chronic sialadenitis	15	38		53				
Lymphoepithelial cyst	5	1		6				
Parotid abscess	1			1				
Sialolithiasis	1	3		4				
Chronic calcific sialadenitis	2	2		4				
Submandibular abscess		1		1				
Grand total	249	79	1	329				
Table 2. Distribution of Lesions According to Site								

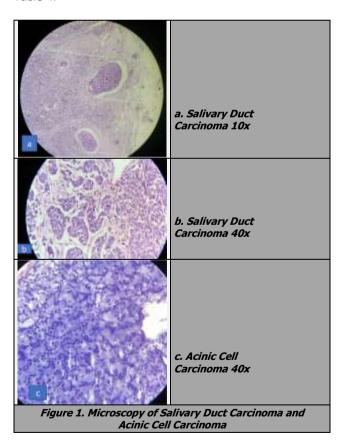
Histopathological	Number	Percentage				
Diagnosis	of Patients	of Total				
Benign	206	62.6				
Basal cell adenoma	3	0.91				
Intra ductal papilloma	1	0.30				
Lymphangioma	1	0.30				
Monomorphic adenoma	ī	0.30				
Oncocytoma	1	0.30				
Pleomorphic adenoma	166	50.45				
Sialolipoma	1	0.30				
Warthin's tumour	32	9.72				
Malignant	52	15.80				
Acinic cell carcinoma	4	1.21				
Adenoid cystic carcinoma	2	0.60				
Epithelial myoepithelial carcinoma	2	0.60				
Hodgkin's lymphoma	1	0.30				
Invasive pleomorphic adenoma	2	0.60				
Metastasis from well differentiated	1	0.30				
carcinoma	1	0.30				
Mucoepidermoid carcinoma	32	9.72				
Myoepithelial carcinoma	2	0.60				
Polymorphous low grade adeno	1	0.30				
carcinoma						
Salivary duct carcinoma	2	0.60				
Well differentiated squamous cell	3	0.91				
carcinoma						
Non neoplastic	71	21.58				
Benign cystic lesion	2	0.60				
Chronic sialadenitis	53	16.10				
Lymphoepithelial cyst	6	1.82				
Parotid abscess	1	0.30				
Sialolithiasis	4	1.21				
Chronic calcific sialadenitis	4	1.21				
Submandibular abscess	1	0.30				
Grand total	329	100				
Table 3. Histopathological Spectrum of Salivary Gland Lesions						

The histopathological spectrum of salivary gland lesions is depicted in Table 3. The lesions were broadly classified into neoplastic and non-neoplastic lesions. Neoplasms were again categorised into benign and malignant. Neoplastic lesions constituted 78.42% (n = 258) and non-neoplastic

lesions 21.58 % (n = 71). Pleomorphic adenoma was the most common benign neoplasm constituting 50.45 % (n = 166) trailed by Warthin tumour 73 % (n = 32). Other benign lesions in our study were basal cell adenoma, intraductal papilloma, lymphangioma, monomorphic adenoma, oncocytoma, sialolipoma. Malignant lesions accounted for 15.8 % (n = 52) of the total cases in our study. Out of the malignant lesions mucoepidermoid carcinoma 9.73 %, (n = 32) trailed by acinic cell carcinoma 1.21 % (n = 4). Other malignant tumours in our study were adenoid cystic carcinoma, epithelial myoepithelial carcinoma, Hodgkin's lymphoma, invasive pleomorphic adenoma, metastasis from well differentiated squamous cell carcinoma, myoepithelial carcinoma, polymorphous low-grade adeno carcinoma, salivary duct carcinoma and well differentiated squamous cell carcinoma.

Non neoplastic lesions constituted 21.58 % (n = 71). The commonest non-neoplastic lesion was chronic sialadenitis 16.1 % (n = 53) trailed by lymphoepithelial cyst 1.82 % (n = 6). Other non-neoplastic lesions in our study were benign cystic lesion, parotid abscess, sialolithiasis, chronic calcific sialadenitis and submandibular abscess.

The three categories of salivary gland lesions were analysed with the age to study whether there is any age predilection for different types of salivary gland lesions. Age wise distribution of salivary gland lesions are depicted in Table 4.



We observed significantly higher incidence of benign and malignant lesions in the 5th to 6th decade while non-neoplastic lesions were seen more in the 4th to 5th decade. Mucoepidermoid carcinoma was graded according to AFIP grading to grade 1, grade 2 and grade 3. Grade 1 cancer was seen in most cases of mucoepidermoid carcinoma which

constituted 62.5 % (n = 20) and least observed were grade 3, 12.5 % (n = 4) and 25 % (n = 8) showed grade 2. Gross and microscopy of some of the lesions are depicted in Figure 1 & 2.

Name of the Lesion	1-10 yrs.	11-20 yrs.	21-30 yrs.	31-40 yrs.	41-50 yrs.	51-60 yrs.	61-70 yrs.	71-80 yrs.	81-90 yrs.	Total
Benign	3	12	34	26	49	54	23	5	0	206
Basal cell adenoma	-	-	-	-	1	-	2	-	-	3
Intra ductal papilloma	-	-	-	-	-	1	-	-	-	1
Lymphangioma	1	-	-	-	-	-	-	-	-	1
Monomorphic adenoma	-	-	-	-	-	-	1	-	-	1
Oncocytoma	-	-	1	-	-	-	-	-	-	1
Pleomorphic adenoma	2	12	33	26	40	33	15	5	-	166
Sialolipoma	-	-	-	-	1	-	-	-	-	1
Warthin's tumour	-	-	-	-	7	20	5	-	-	32
Malignant	2	-	5	5	9	14	15	1	1	52
Acinic cell carcinoma	-	-	1	2	- 1	1	- 1	-	-	4
Adenoid cystic carcinoma	-	-	-	-	1	-	1	-	-	2
Epithelial myoepithelial carcinoma	-	-	-	-	-	-	2	-	-	2
Hodgkin's lymphoma	-	-	-	-	-	-	1	-	-	1
Invasive pleomorphic adenoma	-	-		1	1	-	-	-	-	2
Metastasis from well differentiated carcinoma	-	-	-	-	-	-	1	-	-	1
Mucoepidermoid carcinoma	2	-	4	2	6	9	7	1	1	32
Myoepithelial carcinoma	-	-	-	-	1	1	-	-	-	2
Polymorphus low grade adeno carcinoma	-	-	-	-	-	1	-	-	-	1
Salivary duct carcinoma	-	-	-	-	-	1	1	-	-	2
Well differentiated squamous cell carcinoma	-	-	-	-	-	1	2	-	-	3
Non neoplastic	-	5	7	9	18	17	13	2	_	-
Benign cystic lesion		-	-	-	1	1	-	-	_	2
Chronic sialadenitis	_	4	6	8	11	13	10	1	-	53
Lymphoepithelial cyst	-	1	1	-	1	2	1	-	-	6
Parotid abscess	-	-	-	-	1	-	-	-	-	1
Sialolithiasis	-	-	-	-	2	-	1	1	-	4
Chronic calcific sialadenitis	-	-	-	1	1	1	1	-	-	4
Submandibular abscess	-	-	-	-	1	-	-	-	-	1
Grand total	5	17	46	40	76	85	51	8	1	329
Table 4. Age Wise Dis	Table 4. Age Wise Distribution of Salivary Gland Lesions							15		

DISCUSSION

The salivary gland disorders represent a distinct group of disorders affecting both major and minor salivary glands. Only a few recorded analyses of salivary gland lesions based on a significantly large number of cases are published from India. This present study was done over a period of 5 years in a tertiary care hospital in South Kerala from January 2014 to December 2018 which included 329 cases.

In the present study out of 329 cases of salivary gland lesions, neoplastic lesions (78.42 %) showed a predominance over non neoplastic lesions (21.58 %). This observation was comparable to the study done by Nepal et al, 12 Ali et al 13 and Atarbashi Moghadam et al. 14

Among the neoplastic lesions maximum incidence was seen in benign neoplasms. Pleomorphic adenoma 50.45 % (n = 166) was the major common benign tumour trailed by Warthin's tumour 9.72 % (n = 32). Mucoepidermoid carcinoma 9.72 % (n = 32) was the most common malignant tumour trailed by acinic cell carcinoma. This was in concordance with the study conducted by Kalburge et al 15 and Ochicha et al 16 who found mucoepidermoid carcinoma as the most frequent tumour. Mucoepidermoid carcinoma was reported on a grading system based on AFIP grading to grade 1, grade 2 and grade 3. 17,18 Grade 1 tumours

constituted 62.5 %, grade 2 tumours 25 % and grade 3 tumours 12.55 % respectively.

Acinic cell carcinoma constituted 1.21 % (n = 4) of all tumours and 7.69 % of all malignant ones and it is the second most common malignant tumour in our study. Chronic sialadenitis 16.1 % (n = 53) was the most common among the non-neoplastic lesion followed by lymphoepithelial cyst 1.82 % (n = 6). Males show a slight predominance with 51.06 % (n = 168) over females 48.9 % (n = 161) in our study with M:F ratio 1.07:1. In the benign lesions female preponderance was seen and M:F ratio was 0.87:1. Malignant lesions were seen predominantly in males with M:F ratio 1.73:1. Non neoplastic lesions were more common in males with M:F ratio of 1.21:1.

In the present study the commonest age group with benign lesions was in the 5^{th} to 6^{th} decade of life while study carried out by Chatterjee et al observed increased proportion of benign cases in the 3^{rd} to 4^{th} decade. Malignant tumours in this study were predominant in the 5^{th} to 6^{th} decade. Nonneoplastic lesions were seen more common in the 4^{th} to 5^{th} decade.

Most of the cases of salivary gland specimens included in the study were from parotid gland 75.68 % (n = 249). Submandibular gland was involved in 24.015 (n = 76) and minor salivary gland 0.30 % (n = 1). These findings were comparable to other studies conducted by Chatterjee et al, 19 Bashir et al 20 Erik G. Cohen et al. 21

The most favoured site for benign, malignant and non-neoplastic lesions in our study was parotid gland. Among 206 benign lesions in our study 33.43 % (n = 110) cases were seen in females and 29.17 % (n = 96) were seen in males. Pleomorphic adenoma was predominantly seen in females 62.04 % (n = 103). Out of 32 cases of Warthin's tumour 30 cases were seen in males with 2 cases in females. Mucoepidermoid carcinoma was seen predominantly in males 65.62 % (n = 21). Non neoplastic lesions showed a slight male predominance 54.92 % (n = 39).

Pleomorphic adenoma was the commonest benign neoplasm and mucoepidermoid carcinoma was the commonest malignant neoplasm. Acinic cell carcinoma, adenoid cystic carcinoma, epithelial myoepithelial carcinoma, Hodgkin lymphoma, invasive pleomorphic adenoma, metastasis from well differentiated squamous cell carcinoma, polymorphous low-grade adeno carcinoma, Salivary duct carcinoma and myoepithelial carcinoma were the other malignancies seen in our study. Chronic sialadenitis was the most common non-neoplastic lesion which was predominantly seen in submandibular gland.

Thus, the present study gives valuable epidemiological and demographical information about various salivary gland lesions that was incident over 5 years in a tertiary care hospital in South India.

CONCLUSIONS

Salivary gland tumours are a subject of considerable interest since these are not very rare, present with varied histology and clinical features. Even though FNAC provide a diagnosis in most cases, histopathological examination of

sialoadenectomy specimens is the main stay for definitive diagnosis. Neoplastic lesions of salivary gland were more common in our study which was in concordance with the study done elsewhere.

Pleomorphic adenoma was the most common benign neoplasm and mucoepidermoid carcinoma was the most common malignant neoplasm and chronic sialadenitis was the common non-neoplastic lesion. Among mucoepidermoid carcinoma, grade 1 tumours showed predominance. We observed higher incidence of benign and malignant neoplasms in the 5th to 6th decade and non-neoplastic lesions were more in the 4th to 5th decade. Male female ratio was 1.07:1.

Variables that impact conduct and prognosis of salivary gland tumours should be researched further. More population-based surveys are needed to define the epidemiology of salivary gland neoplasms.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

- [1] Eveson JW, Cawson RA. Salivary gland tumours: a review of 2410 cases with particular reference to histological types, site age & sex distribution. J Pathol 1985;146(1):51-58.
- [2] Eveson JW, Cawson RA. Tumours of minor (oropharyngeal) salivary glands: a demographic study of 336 cases. J Oral Pathol 1985;14(6):500-509.
- [3] Jones AV, Craig GT, Speight PM, et al. The range and demographics of salivary gland tumours diagnosed in a UK population. Oral Oncol 2008;44(4):407-417.
- [4] Ma'aita JK, Al-Kaisi N, AL-Tamimi S, et al. Salivary gland tumours of Jordan: a retrospective study of 221 patients. Croat Med J 1990;40(4):539-542.
- [5] Jaber MA. Intraoral minor salivary gland tumours: a review of 75 cases in a Libyan population. Int J Oral Maxillofac Surg 2006;35(2):150-154.
- [6] Barnes L, Everson JW, Reuichart P, et al. WHO Classification of tumours: pathology and genetics of head and neck tumours. Vol. 9. Lyon: IARC Press 2005: p. 209-281.
- [7] Luukkaa H. Salivary gland cancer in Finland: incidence histological distribution outcome and prognostic factors. Turku Finland: University of Turku 2010.

- [8] Spiro JD, Spiro RH. Salivary gland tumours. In: Shah JP, Decker SB, eds. Cancer of Head and Neck. Hamilton: Decker BC Inc., 2001: p. 240-250.
- [9] Pinkston JA, Cole P. Incidence rates of salivary gland tumours: results from a population based study. Otolaryngol Head and Neck Surg 1991;120(6):834-840.
- [10] Yu GY, Ma DQ. Carcinoma of the salivary gland: a clinico pathological study of 405 cases. Semin Surg Oncol 1987;3(4):240-244.
- [11] Pires FR, de Almeida OP, de Araufo VC, et al. Prognostic factors in head and neck mucoepidermoid carcinoma. Arch Otolarangol Head Neck Surg 2004;130(2):174-180.
- [12] Nepal A, Chettri ST, Joshy RR, et al. Primary salivary gland tumours in Eastern Nepal tertiary hospital. J Nepal Health Res Counc 2010;8(1):31-34.
- [13] Ali NS, Nawaz A, Rajput S, et al. Parotidectomay: a review of 112 patients treated in a teaching hospital in Pakisthan. Asian PAC J Cancer Pre 2010;11(4):1111-1113.
- [14] Moghadam SA, Moghadam FA, Dadfar M. Epithelial salivary gland tumours in Ahvaz, Southwest of Iran. J Dent Res Dent Clin Dent Prospects 2010;4(4):120-123.
- [15] Kalburge J, Kalburge V, Latti B, et al. Salivary gland tumours: clinicopathologic analysis of 73 cases. J Cranio Max Dis 2014;3(2):111-115.
- [16] Ochicha O, Malami S, Mohamed A, et al. A histopathologic study of salivary gland tumours in Kano, Northern Nigeria. Indian Journal J Pathol Microbiol 2009;52(4):473-476.
- [17] Goode RK, Auclair PL, Ellis GL. Mucoepidermoid carcinoma of the major salivary glands: clinical and histopathological analysis of 234 cases with evaluation of grading criteria. Cancer 1998;82(7):1217-1224.
- [18] Good RK, Nagger AK. Mucoepidermoid carcinoma. In: Barner L, Eveson JW, Reichart P, et al. eds. WHO Classification of tumours: pathology and genetics of head and neck tumours. Lyon: IARC Press 2005: p. 219-220.
- [19] Chatterjee MT, Panda PK. A pathological study of benign and malignant tumours of slivary gland. Med J Armed Forces India 2000;56(4):282-286.
- [20] Bashir S, Mustafa F, Malla HA, et al. Histopathological spectrum of salivary gland tumours: a 10 year experience. Scholars J Appl Med Sci 2013;1(6):1070-1074.
- [21] Cohen EG. Warthin's tumour of the parotid gland in an Asian Population. Br J Surg 1999;86:661-664.