

THE MORPHOLOGICAL SPECTRUM OF SALIVARY GLAND TUMOURS AT KEMU AND MAYO HOSPITAL, LAHORE

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ABSTRACT

Objective: Salivary gland tumours constitute an important aspect of oral and maxillofacial pathology. The aim of this study was to classify and analyse the diverse spectrum of major and minor salivary gland tumours according to the revised WHO Classification (2005) of Salivary Gland Tumours (SGT).

Materials and Methods: This was a 4 year descriptive cross – sectional study (from 1st July 2008 – 30th June 2012) on 259 salivary gland tumours reported at the Department of Pathology, King Edward Medical University, Lahore.

Results: In a total of 259 salivary gland tumours, 162 tumours (62.54%) were classified as benign and 97 tumours (37.45%) as malignant. The male to female ratio was almost equal and patients ranged in age from 8 years to 80 years. Maximum number of tumours were diagnosed in the 3rd to 5th decade of life. The commonest benign SGT was pleomorphic adenoma PA which constituted a total of 146 cases (90.12%) followed far down in frequency by Warthin tumour which comprised of 8 cases (4.93%). The commonest malignant SGT was mucoepidermoid carcinoma which constituted 43 cases (44.32%) followed by adenoid cystic carcinoma constituting 30 cases (30.92%). A total of 200 tumours (77.22%) were reported in the major salivary glands of which 134 cases (67%) were classified as benign and 66 cases (33%) were malignant. The commonest benign tumour in the major salivary glands was pleomorphic adenoma constituting 118 cases (80.05%) out of 134 benign tumours and the commonest malignant tumour was mucoepidermoid carcinoma constituting 37 cases (56.06%) out of 66 malignant tumours. Fifty nine tumours (22.78%) were reported in the minor salivary glands of which 28 cases (47.45%) were benign and 31 cases (52.54%) were malignant. Pleomorphic adenoma was the sole benign tumour reported in the minor glands and adenoid cystic carcinoma was the commonest malignant tumour of minor salivary glands constituting 20 cases (64.51%) followed by mucoepidermoid carcinoma constituting 6 cases (19.35%). The palate constituted the commonest site of minor salivary gland tumours harbouring 35 cases (59.32%) followed by the lips containing 10 cases (16.94%). Other sites of minor salivary gland tumours included the buccal region (10.16%), pharynx-geal wall (5.08%), nasal cavity (3.39%), maxillary sinus (3.39%) and tongue (1.69%).

Conclusion: In the major salivary glands, benign tumours are much more common than the malignant tumours with the parotid being the most common location of both benign and malignant tumours. The sublingual gland harbours only a minor fraction of salivary tumours of which malignant tumours are more common than the benign. In the minor salivary glands, malignant tumours outnumber the benign tumours and the palate constitutes the most common location of minor salivary gland tumours. In fact the palate harbours more tumours than the sub-mandibular and the sublingual glands thus constituting the 2nd most common site of salivary gland tumours after the parotid gland.

Key Words: Salivary gland tumours (SGT's), major salivary glands, minor salivary glands, parotid, Pleomorphic adenoma (PA), Adenoid Cystic Carcinoma (ACC), palate, Mucoepidermoid carcinoma (MEC), sublingual gland.

INTRODUCTION

The major salivary glands are parotid, submandibular and sublingual glands. In addition innumerable small, minor salivary glands are distributed in the sub-mucosa of the upper aerodigestive tract which includes the lips, gingiva, buccal region, floor of the mouth, cheek, palate, tonsillar areas, tongue, nose and paranasal sinuses, pharyngeal area, trachea and bronchi.¹ Despite their relatively simple morphology the 3 major paired salivary glands and the

hundreds of minor salivary glands can give rise to a bewildering array of neoplasms constituting the most complex and heterogenous spectrum of tumours in the field of oral and maxillofacial pathology.² The revised WHO Classification of Salivary Gland Tumours (2005) recognizes more than 35 histologically distinct tumours.³ These tumours comprise 3 – 10% of all head and neck neoplasms demonstrating complex and variable clinico-pathological and biological characteristics stemming from their morpho-

gical diversity.⁴

Worldwide epidemiological series demonstrate geographical and ethnic variation in the relative incidence of these tumours with an estimated global incidence of 0.4 – 13.5 per 100,000 persons annually.^{2,5,6} Little is known about their aetiology and some studies have suggested a link between salivary gland tumours and occupational exposures, viruses, tobacco, alcohol and ultraviolet light, however only radiation exposure seems to be the only well established risk factor.^{6,7} An increased incidence of benign mixed tumour and other neoplasms has been observed following therapeutic childhood radiation and a possible increase in Mucoepidermoid carcinoma has been noted among atomic bomb survivors.^{7,8}

The vast majority of major SGT's occur in the parotid gland where 70% – 80% of these tumours are located, followed by the submandibular gland which harbours 7% – 10% of the tumours.^{9,10} Tumours of the sublingual gland are rare comprising less than 1% of all SGT's.¹¹ Approximately 15% – 30% of the parotid gland neoplasms are malignant and the rest are benign with Pleomorphic adenoma being the commonest benign tumour and mucoepidermoid carcinoma being the commonest malignancy at this location.⁹ In contrast, approximately 40% – 45% of the sub-mandibular gland tumours and 70% – 90% of the sublingual gland tumours are cancers.^{10,11} Of all salivary gland neoplasms 10% – 15% are located in the minor salivary glands with the posterior third of the palate being the most common site⁽¹²⁾. These minor glands are important because the incidence of malignancy increases with the decreasing size of the salivary gland.^{9,10} Almost 50% of the minor salivary gland tumours are malignant.^{9,12} Muco-epidermoid carcinoma and adenoid cystic carcinoma are the commonest cancers of the oral minor salivary glands although polymorphous low grade adenocarcinoma is also becoming recognized as a common minor salivary gland malignancy.⁹ Pleomorphic adenoma constitutes the commonest benign tumour of the minor salivary glands.¹²

MATERIALS AND METHODS

This descriptive, cross – sectional study on salivary gland tumours (SGT's) was conducted at the Department of Pathology, King Edward Medical University, Lahore, Pakistan in collaboration with the 4 General Surgical Units and the Department of Oral and Maxillofacial Surgery of Mayo Hospital, Lahore.

A total of 259 previously reported and diagnosed cases of salivary gland tumours were included in this 4 – year retrospective study commencing from 1st July 2008 to 30th June 2012. Patients of all ages and both sexes were included in the study. Inflammatory conditions like sialadenitis and cystic lesions were excluded from this study. Detailed record compris-

ing of computer data files, biopsy reports, slides and relevant tissue blocks of these tumours were retrieved and all relevant information was recorded in a proforma. These details included patient's age, sex, address, occupation, smoking history, brief medical and surgical history including history of previous salivary gland surgery (recurrent tumour) or a fine needle aspiration (FNAC) procedure if performed. Additional information like exact anatomical location of the tumour, per operative findings and gross descriptive details of the specimen like size and dimensions, status of cervical lymph nodes etc were also retrieved from the computerised histopathology reports. Eosin / Haematoxylin stained slides and paraffin embedded tissue blocks were retrieved and reviewed again. Results and data were compiled using Statistical Package for Social Sciences 10 (SPSS Version 10) and presented in the form of tables and charts with calculations, percentages and ratios. Results and findings so obtained were compared with other similar local and international studies.

RESULTS

A total of 259 Salivary Gland Tumours (SGT's) were included in this 4 – year study commencing from 1st July 2008 to 30th June 2012. These cases had been submitted and reported at the Histopathology Department of King Edward Medical University, Lahore – Pakistan. These cases included 130 tumours from male patients and 129 tumours from females giving an almost equal sex ratio. Patients ranged in age from 8 years to 80 years with a mean of 44 years. The youngest patient in this study was an 8 year old girl with a Pleomorphic adenoma and there were 3 patients aged 80 years. One was an elderly man with a NHL of the parotid gland, one man had Warthin tumour and one female had a mucoepidermoid carcinoma of the parotid gland.

In a total of 259 salivary gland tumours, 162 cases (62.55%) were categorized as benign and 97 cases (35.45%) were reported as malignant giving a B : M ratio of 1.67 : 1.0. Table I depicts the relative frequency of the various histological subtypes of benign and malignant SGT's. Pleomorphic adenoma (PA) was the commonest benign salivary gland tumour constituting 146 cases i.e. 90% of the benign tumours and 56.36% of the total number of SGT's (Fig. 1). This was followed far down in frequency by Warthin tumour which constituted only 8 cases (4.93%) of the benign tumours and 3.08% of the total cases (Fig. 2). Other benign entities and their frequencies are shown in Table 1.

Regarding the malignant tumours, mucoepidermoid carcinoma (MEC) was the commonest cancer constituting 43 cases (44.32%) in the malignant category and 16.60% of the total number of SGT's, (Fig. 3). This was followed by adenoid cystic carcinoma

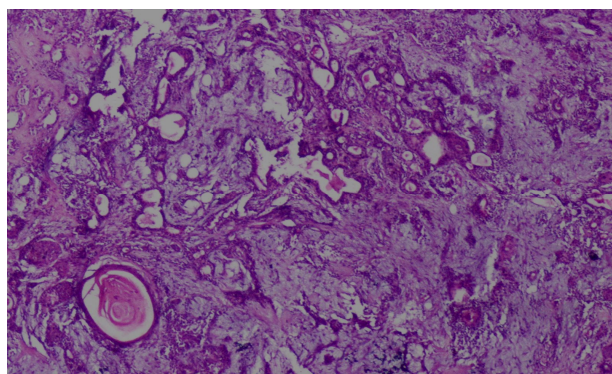


Fig. 1: Microscopic appearance of a Pleomorphic adenoma showing epithelial and myoepithelial cells embedded in a chondromyxoid stroma.

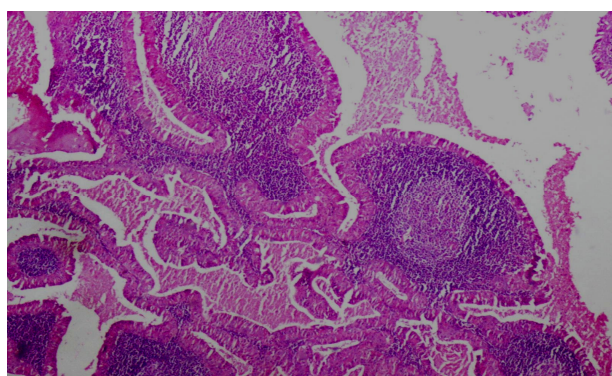


Fig. 2: Warthin tumour showing epithelial and lymphoid elements. Note the prominent lymphoid follicles with germinal centres.

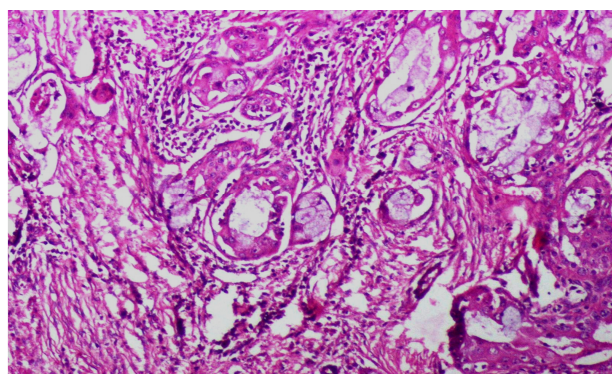


Fig. 3: Muco-epidermoid carcinoma showing squamoid cells and clear vacuolated mucous cells enclosing cystic spaces filled with mucinous material.

(ACC) which constituted 30.92% of the malignant tumours and 11.58% of the their relative frequencies are shown in Table 1.

Considering the anatomical location of these 259 tumours, 200 cases (77.22%) were reported in the major salivary glands and 59 cases (22.78%) in the Minor salivary glands (Table 2). Amongst the major

salivary glands the parotid contained the vast majority i.e. 165 cases (82.5%) out of 200 tumours and in the minor salivary glands the palate harboured the maximum number of cases i.e. 35 cases (59.32%) out of 59 minor SGT's. The exact number of tumours and their localisation in each salivary gland is seen in Table 2.

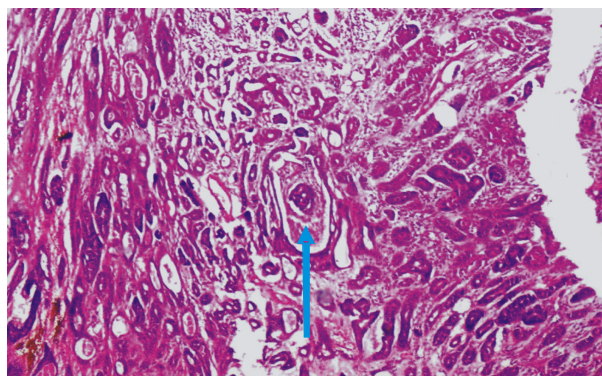


Fig. 4: Adenoid Cystic carcinoma with a predominant tubular pattern. Centre of the field shows neural invasion by tumour cells (arrow).

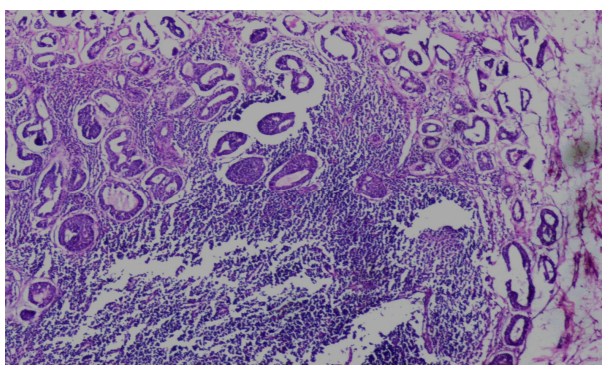


Fig. 5: Adenoid Cystic Carcinoma of the tubular type showing lymph node invasion.

Considering other important and relevant pathological aspects of pleomorphic adenomas as seen in this study. In a total of 146 PA's, 100 cases (68.49%) were located in the parotid gland, 17 cases (11.64%) in the submandibular gland and only a single case of PA was located in the sublingual gland (Table 3). Twenty eight cases (19.17%) were reported in the minor salivary glands with the palate and lips being the favoured sites where 16 cases and 9 cases of PA's were reported respectively. Other sites of PA's in the minor SGT's are shown in Table 4.

Regarding age distribution, PA's were seen in all age groups, the youngest patient being 8 – year old girl and the oldest being a 75 – year old female. In a total of 146 PA's, 23 cases (15.75%) were reported in children and adolescents ≤ 20 years. Maximum number of cases amounting to 68 cases (46.5%) of PA's

Table 1: *Histological categorization of various benign and malignant salivary gland tumours (n = 259).*

<i>A – Benign Tumours (n = 162)</i>			
<i>Histological Subtype</i>	<i>Number of Cases</i>	<i>Percentage of Benign Tumours</i>	<i>Percentage of Total Number of SGT's.</i>
1. Pleomorphic adenoma (PA)	146	90.12	56.37
2. Warthin tumour	08	4.93	3.08
3. Lipoma	03	1.85	1.15
4. Hemangioma	01	0.61	0.38
5. Basal Cell adenoma	01	0.61	0.38
6. Oncocytoma	01	0.61	0.38
7. Myoepithelioma	01	0.61	0.38
8. Sebaceous Lymphadenoma	01	0.61	0.38
Total Benign Tumours	162	100	62.55
<i>B – Malignant Tumours (n=97)</i>			
<i>Histological Subtype</i>	<i>Number of Cases</i>	<i>Percentage of Malignant Tumours</i>	<i>Percentage of Total Number of SGT's.</i>
1. Mucoepidermoid carcinoma (MEC)	43	44.32	16.60
2. Adenoid Cystic Carcinoma (ACC)	30	30.92	11.58
3. Carcinoma Ex Pleomorphic adenoma (Ca exPA)	04	4.12	1.54
4. Adenocarcinoma NOS	04	4.12	1.54
5. Acinic Cell Carcinoma	03	3.09	1.15
6. Salivary Duct Carcinoma	03	3.09	1.15
7. Non-Hodgkin Lymphoma	03	3.09	1.15
8. High Grade Undifferentiated Malignant Neoplasm	02	2.06	0.77
9. Polymorphous Low Grade Adenocarcinoma (PLGA)	02	2.06	0.77
10. Carcinosarcoma	01	1.03	0.38
11. Neuroendocrine Carcinoma	01	1.03	0.38
12. Epithelial Myoepithelial Carcinoma	01	1.03	0.38
Total Malignant Tumours	97	100	37.45

were seen in the age range of 30 – 50 years. As regards the sex distribution, there were 76 females and 70 males giving a female to male ratio of 1.08:1.00.

The second commonest benign salivary gland tumour in this study was Warthin tumour, which constituted only a minor fraction (4.94%) of the benign SGT's as compared with PA (90%) as shown in Table I. All cases of Warthin tumour were located in the parotid gland with 6 cases seen in males and 2 in females. Youngest patient was an 18 year old boy and the oldest patient was an 80 year old woman.

Other benign tumours included 3 cases (1.85%) of lipomas all seen in the parotid, and 1 case (0.61%) each of haemangioma, basal cell adenoma, oncocytoma, myoepithelioma and sebaceous lymphadenoma (Table 1 and Table 3).

Analysing the data regarding malignant SGT's which constituted 97 cases (37.45%), mucoepidermoid carcinoma (MEC) was the commonest salivary cancer constituting 43 cases (44.32%) of the malignant tumours and 16.60% of the total number of cases in our study (Table 1). Thirty cases (69.76%) of

MEC were reported in the parotid gland, 5 cases (11.62%) in the submandibular gland and 2 cases each in the sublingual gland, palate, buccal region and pharyngeal wall respectively (Table 3 and Table 4). Ten cases (23.25%) of this salivary cancer were seen in children and adolescents ≤ 20 years of age, the youngest patient being an 11 year old boy with a low grade MEC in the parotid and the oldest patient being an 80 year old female with a high grade MEC also located in the parotid. Fifteen cases of MEC were seen in the age range between 50 – 80 years and 18 cases were diagnosed between the ages of 20 – 50 years.

Table 1 shows adenoid cystic carcinoma to be the 2nd commonest salivary gland cancer constituting

Table 2: *Anatomic Distribution of Major and Minor Salivary Gland Tumours (n = 259).*

Site	Gland Name	Number of Tumours	Percentage	Total (a+b)
Major Salivary Glands	Parotid	165	82.5	259 (100%)
	Submandibular	29	14.5	
	Sublingual	06	3.0	
Total (Major Salivary Glands)		200 (a)	77.22 (a)	
Minor Salivary Glands	Palate	35	59.32	
	Lips	10	16.94	
	Buccal Region	06	10.16	
	Pharynx	03	5.08	
	Nose	02	3.38	
	Maxillary Sinus	02	3.38	
	Tongue	01	1.69	
Total (Minor Salivary Glands)		59 (b)	22.78 (b)	

Table 3: *Histological Categorization of Various Benign and Malignant Major Salivary Gland Tumours (n = 200).*

Gland Name	Benign (n = 134) Tumours			Malignant (n = 66) Tumours			Total (n = 200)
	Category	No. of Cases	Total	Category	No. of Cases	Total	
Parotid Gland	PA	100		MEC	30		
	Warthin tumour	08		ACC	06		
	Lipoma	02		Adenoca (NOS)	04		
	Basal Cell Adenoma	01		Acinic Cell Ca	03		
				Ca ex PA	03		
				Salivary duct carcinoma	03		
	Oncocytoma	01		NHL	02		
	Seb. Lymphadenoma	01		High Grade Undiff. Malignant Neoplasm	01		
	Total:		113	Total:		52	165
Submandibular Gland	PA	17		MEC	05		19 + 10 (14.5%)
				ACC	02		
	Lipoma	01		Ca. ex PA	01		
	Myoepithelioma	01		High Grade Undiff. Malignant neoplasm	01		
				NHL	01		
	Total:		19	Total:		10	
Sublingual Gland	PA	01		MEC	02		
	Haemangioma	01		ACC	02		
	Total:		02	Total:		04	
Total	Total Benign Tumours		134 (67%)	Total Malignant Tumours		66 (33%)	200 (100%)

Table 4: *Histological Categorization of Various Benign and Malignant Minor Salivary Gland Tumours (n = 59).*

Gland Name	Benign Tumours (n = 28)		Malignant Tumours (n = 31)			Total (n = 59)
	Category	No. of Cases	Category	No. of Cases	Total	(%)
Palate	PA	16 (45.71%)	ACC	13	19 (54.28%)	16 + 19 = 35 (59.32%)
			MEC	02		
			PLGA	02		
			Neuroendocrine Ca	01		
			Epithelial Myoepithelial Ca	01		
Lips	PA	9	ACC	01	01	9 + 1 = 10 (16.94%)
Buccal Region	PA	02	MEC	02	04	02+04 = 06 (10.16%)
			ACC	01		
			Carcinosarcoma	01		
Pharyngeal Wall	PA	01	MEC	02	02	01 + 02 = 03 (5.08%)
Nasal Cavity	o	o	ACC	02	02	02 (3.39%)
Maxillary Sinus	o	o	ACC	02	02	02 (3.39%)
Tongue (Posterior)	o	o	ACC	01	01	01 (1.69%)
Total	Benign Tumours	28 (47.45%)	Malignant Tumours	31	31 (52.54%)	59 (100%)

30 cases (30.92%) out of 97 salivary gland cancers (Fig. 4), Twenty cases (66.66%) of this malignant entity were reported in the minor salivary glands with the palate being the commonest site where 13 cases (43.33%) were located (Table 4). Ten cases (33.34%) of ACC were located in the Major Salivary glands with parotid containing 6 tumours (Table 3). Distribution of adenoid cystic carcinomas in other major and minor salivary glands is shown in Table 3 and 4. Regarding age, only 1 case of ACC was seen in a 23 year old female; all others were reported in patients older than 40 years of age. Majority of cases showed perineural invasion and lymph node involvement with a male to female ratio of 1.5:1. (Fig. 5).

Other less frequent but pathologically and diagnostically important malignant SGT's included carcinoma Ex pleomorphic adenomas (Ca ex PA) and Adenocarcinoma (NOS) which constituted 4 cases (4.12%) each (Table 1). All 4 adenocarcinomas (NOS) and 3 Ca ex PA's were located in the parotid. One Ca ex PA was reported in the submandibular gland (Table 3). All cases were seen in patients above 45 years of age and all Ca ex PA's were seen in females.

In addition, we reported 3 cases each (3.09%) of salivary duct carcinoma and acinic cell carcinoma all

located in the parotid gland and seen in patients older than 45 years of age. One case of acinic cell carcinoma was a huge cheek mass measuring 12 × 11 × 5 cm, and one case of salivary duct carcinoma showed tumour involving the branches of facial nerve with cervical lymph node metastasis. Primary Non-Hodgkin lymphoma also comprised of 3 cases (3.09%), 2 were seen in the parotid and 1 in the submandibular gland of a 17 year old boy. As already stated one of our oldest male patient had a NHL of the parotid gland. One case of NHL (MALT lymphoma) was seen in the parotid of a 40 year old female (Table 3).

Other malignant SGTs included 2 cases (2.06%) of polymorphous low grade adenocarcinoma (PLGA) both located on the palate and two cases of high grade undifferentiated malignant neoplasm (Table 1). One was seen in the parotid of a 70 year old male and the other in the submandibular gland of a 35 year old man. Other salivary cancers included a single case of neuroendocrine carcinoma located in the hard palate of a 55 year old male and a carcinosarcoma (True Malignant Mixed Tumour) presenting as a huge pedunculated buccal mass in a 37 year old female (Table 1). This tumour showed widespread

invasion into the facial bones, mental nerve involvement, and cervical lymph node metastasis. A single case of Epithelial – Myoepithelial Carcinoma was seen in the palate (Table 4).

The histological categorisation, location and number of tumours in each major and minor salivary gland is shown in Table 3 and 4. In the major glands there were 134 benign tumours (67%) and 66 malignant tumours (33%) with Pleomorphic adenoma being the commonest benign tumour constituting 118 cases (88.05%) out of 134 benign tumours. The commonest malignant tumour in the major salivary gland was MEC which constituted a total number of 37 cases (56.06%). Other benign and malignant tumours and their numbers are depicted in Table 3. The parotid gland contained 165 tumours (82.5%) of which 113 cases (68.48%) were benign and 52 cases (31.51%) were malignant. The submandibular gland contained 29 cases (14.5%) of which 19 tumours (65.51%) were benign and 10 tumours (34.48%) were malignant. The sublingual gland contained only 6 cases (3%) of which 4 cases were malignant and 2 tumours were benign. The various benign and malignant tumours and the exact numbers located in each major gland are shown in Table 3.

As regards the minor SGT's which numbered 59 cases (22.78%), there were 28 benign (47.45%) and 31 malignant (52.54%) tumours. All 28 benign tumours were PA's, and the commonest malignant tumour was ACC constituting 20 cases (64.56%) out of 31 malignant tumours (Table 4). Other malignant tumours comprised of 6 cases (19.35%) of MEC, 2 cases (6.45%) of PLGA. 1 case (3.22%) each of neuroendocrine carcinoma, carcinosarcoma and epithelial Myoepithelial carcinoma. Maximum cases numbering 35 (59.32%) were located in the palate (Table 4) of which 16 tumours (45.71%) were benign and 19 (54.28%) were malignant (Table 4). The lips ranked at 2nd position containing 9 PA's and 1 ACC. Other minor SGT's, their location and numbers are depicted in Table 4.

DISCUSSION

Tumours of the salivary glands constitute an important area in the field of oral and maxillofacial pathology. Although uncommon they are by no means rare constituting 3% of all human tumours and 3 – 10% of all head and neck neoplasms.⁴ They pose a significant diagnostic and therapeutic challenge for both histopathologists and surgeons because of their varied clinical, morphological and biological characteristics and the difficulties involved in their management.¹³ Many benign and malignant salivary gland tumours may resemble each other grossly as well as histologically. The histological bland features of some malignant salivary tumours and the aggressive biological nature of the benign tumours as typified

by the high rate of recurrence, repeated surgical failures and locally invasive and metastatic characteristics may lead to misdiagnosis and consequent mismanagement.^{5,6,13}

Because of their great morphological diversity and the lack of uniform diagnostic criteria, many classifications have evolved over time and the establishment of an adequate clinic – histological correlation proves difficult. The 1st edition of the WHO Histological Classification of Salivary Gland Tumours was published in 1972.¹⁴ The proposed nomenclature was widely accepted and adopted leading to considerable ease and uniformity in diagnosis. This was revised under the supervision of Prof. Seifert¹⁵ and the 2nd Edition of the WHO Histological Classification of Salivary Gland Tumours was published in 1991. This new classification was based on data regarding newly described tumour entities and the prognosis and behaviour of the previously classified tumours. It suppressed the concept of "Monomorphic adenoma" as this was considered a diagnostic dustbin and historically this designation included several distinct entities some of which were not even benign.¹⁶ This gave origin to several more distinct and histologically independent benign entities. Among the cancers, various types were distinguished and the term 'tumour' was replaced by 'carcinoma' for 2 entities namely acinic cell carcinoma and mucoepidermoid carcinoma.^{15,16} Polymorphous low grade adenocarcinoma (PLGA) was first identified in 1983 as "Terminal Duct Carcinoma" and included in the 1991 classification. Clinicians now recognise that it is one of the more common cancers of the minor salivary glands.⁹ Due to their great morphological diversity and the need to establish a precise diagnosis, subsequent refinements were made leading to the most recent WHO Classification published in 2005.³ This current classification has proved to be extremely useful in daily practice and its nomenclature further assists in understanding the biological behaviour of these tumours in relation to their histological patterns.

This study on Salivary Gland tumours (SGT's) is a detailed analysis on the frequency and morphological patterns of major and minor SGT's. In a total of 259 SGT's, benign tumours constituted 162 cases (62.55%) and malignant tumours constituted 97 cases (37.45%). This is in exact accordance with a study conducted at the same institution in 2004,⁽¹⁷⁾ where benign SGT's constituted 73 cases (62.4%) and malignant constituted 44 cases (37.6%) in a total of 117 cases. Another similar study on 379 cases, from Pakistan in 2001¹⁸ showed benign SGT's to constitute 277 cases (73.09%) and malignant tumours as 102 cases (26.30%). Similarly in a recently published study from Turkey¹⁹ in a total of 235 SGT's, 62.13% cases were benign and 37.87% were malignant. Another study reported from Brazil,²⁰ also classified

335 (67.5%) benign tumours and 161 (32.5%) malignant SGT's in a total of 496 epithelial and mesenchymal tumours of minor and major salivary glands diagnosed at the Londrina Cancer Institute. A large Chinese study² on 6982 primary SGT's during a 23 – year period constituted 4743 (68%) benign tumours and 2239 (32%) malignant tumours. All these studies highlight the fact that the frequency of benign SGT's is almost twice that of the malignant SGT's.

In the present study, the commonest histological type of benign SGT was Pleomorphic adenoma which constituted 90.12% (146 cases) of the benign tumours and 56.3% of the total number of SGT's including both benign and malignant tumours. This was followed far down in frequency by Warthin tumour which constituted of only 8 cases (4.93%) of benign tumours and 3.08% of the total SGT's. A study by Gill¹⁸ estimated PA to constitute 84.5% of their benign cases and 61.74% of the total number of SGT's. Similarly Warthin tumour ranked far down in frequency constituting 6.13% of their benign cases and 4.49% of the total SGT's. A study by Qureshi and associates¹⁷ estimated PA to constitute 82.1% and Warthin tumour as 6.8% of their benign tumours. A study in Brazil by de Oliveira,⁴ also estimated PA to constitute 86.7% of all benign SGT's and 68.4% of the total SGT's followed by Warthin tumour which constituted 6.4% of the benign tumours. In a recent study conducted on 130 cases in Iran, Shishegar and associates⁵ estimated PA to account for 85% of all benign tumours and 58% of the total number of SGT's followed by Warthin tumour which constituted 8.6% of the benign tumours. In our study PA had a slightly higher frequency as compared to the other studies. Regarding the age and sex distribution of PA, it was seen in all age groups including children and maximum number of cases (46.5%) were seen in the 30 – 50 year old age group and females slightly outnumbered males giving a female to male ratio of 1.08:1.00 which is in accordance with other studies from Brazil⁴ and Iran.⁵ All these studies highlight the fact that there is a striking predominance of a single type of tumour namely the pleomorphic adenoma.

Regarding the anatomic location of the 146 PA's in our study, 118 cases (80.82%) were located in the major salivary glands and 28 cases (19.17%) were seen in the minor salivary glands. These findings are similar to the study of Shishegar⁵ and to the WHO report³ in which approximately 80% of all PA's were seen in the 3 major paired salivary glands and 20% in the minor oral salivary glands. Some authors consider PA to correspond to a low grade malignancy based on its characteristics like poorly defined limits, multifocal presentation, aggressiveness, the capacity to metastasize and relapse and undergo potential malignant change over a long term.^{9,12} Relapse of PA, which is almost always due to incomplete surgical

resection of the lesion manifests in the form of multiple foci and is estimated to occur in 5 – 30% of the cases.¹²

Warthin tumour was the 2nd commonest benign salivary gland tumour of which we had only 8 cases (4.94%), and all were located in the parotid. All cases gave a history of cigarette smoking. Although this tumour may be regarded as exclusively a parotid gland tumour, some rare cases have been reported in the submandibular gland and even in the minor salivary glands.^{1,12} Vicente¹² reported 1 case of Warthin tumour in the posterior third of the hard palate, and Ma'aite²¹ reported 2 cases (3.5%) of Warthin tumour in their exclusive study of 56 submandibular salivary gland masses.

Other benign entities seen in our study included 3 cases of lipoma which constituted 1.85% of the benign tumours. A study by Gill¹⁸ reported 4 cases of lipoma out of 277 benign tumours. Lipomas are rare tumours of the parotid, however, many studies do report occasional cases of lipomas in the salivary glands.²² Musani²³ reported lipomas to constitute 2% of parotid gland tumours in his study. Other less common benign SGT's in our study included 1 case (0.62%) each of Basal cell adenoma, myoepithelioma, oncocytoma, sebaceous lymphadenoma and Haemangioma respectively. Shishegar⁵ reported myoepithelioma, basal cell adenoma and oncocytoma to constitute 4.5%, 1.1% and 0.7% of their benign tumours respectively. Qureshi and coworkers,¹⁷ reported Monomorphic adenoma and Oncocytoma to constitute 4.1% and 2.8% of benign tumours respectively. Basal cell adenoma, capillary haemangioma and lipoma constituted a single case (1.4%) each in their study.

Analyzing the morphological spectrum of the 97 (37.45%) malignant SGT's in our study, MEC was the most common cancer comprising of 43 cases (44.32%). Seventeen cases were of high grade variety consisting predominantly of solid squamoid areas whereas 26 cases were of the intermediate to low grade variety with mixed solid – cystic to predominantly cystic areas with pools of mucin both within the cystic areas as well as in the stroma. The 2nd commonest malignant tumour was adenoid cystic carcinoma (ACC) constituting 30 cases (30.92%). Almost all cases of ACC were of the tubular variety. Perineural invasion, bone invasion and lymph node metastases were observed in 20 out of 30 cases of ACC. Both Ca ex PA and adenocarcinoma NOS ranked at 3rd position with 4 cases (4.12%) each. Other less frequent malignant tumours included acinic cell carcinoma, salivary duct carcinoma and non-Hodgkin lymphoma comprising of 3 cases (3.09%), each. Polymorphous low grade adenocarcinoma (PLGA) and high grade undifferentiated malignant neoplasm comprised of 2 cases (2.06%) each. Carcinosarcoma

(True malignant mixed tumour), neuroendocrine carcinoma and epithelial myoepithelial carcinoma constituted of 1 case (1.03%) each. These figures are more or less in accordance with some local studies by Qureshi¹⁷ and Gill.¹⁸ Another recent study published in 2011 from AFIP (Rawalpindi) by Sarfraz and associates²⁴ on 150 malignant SGT's estimated MEC to constitute 49.3% cases, followed by ACC constituting 31.3% cases. Other malignant SGT's in their study included PLGA (5.3%), acinic cell carcinoma (4.7%), epithelial myoepithelial carcinoma (3.3%), Ca ex PA (2.7%), salivary duct carcinoma (1.3%), myoepithelial carcinoma (1.3%) and oncocytic carcinoma (0.7%).

A study conducted in Uganda¹³ calculated malignant SGT's as 46.6% dominated by ACC having a frequency of 28.8% followed by MEC (20.6%) and acinic cell carcinoma (13.1%). Similarly a study by Shishegar⁵ from Iran on 125 malignant SGT's depicted ACC to constitute 40%, MEC as 24% and SCC as 16% cases. Other less frequent malignant tumours in their series were acinic cell carcinoma (4.8%), adenocarcinoma (NOS) and epithelial myoepithelial carcinoma (3% each). Rare malignant tumours included Ca ex PA, salivary duct carcinoma, PLGA and basal cell adenocarcinoma each of which constituted 2 cases (1%). A large study on 6982 primary SGT's by Tien et al² calculated 2239 (32%) malignant SGT's in which ACC and MEC both had an equal frequency of 30% followed by Ca ex PA (8%), acinic cell carcinoma (8%), adenocarcinoma NOS (6%), lymphoepithelial carcinoma (5%), myoepithelial carcinoma (3%), epithelial myoepithelial carcinoma (2%), squamous cell carcinoma (2%), cyst adeno carcinoma (1%) and large cell neuroendocrine carcinoma (1%). other less common entities in that study included clear cell carcinomas, basal cell adenocarcinomas, sebaceous carcinomas, small cell carcinomas, oncocytic carcinomas, mucinous adenocarcinomas, salivary duct carcinomas and sialoblastomas. the large variety of benign and malignant tumours in that study is due to a very large sample size and the long duration of study spanning 23 years.

Regarding the anatomic location of the 43 cases (44.32%) of MEC in our study, the overwhelming majority of 30 tumours (69.76%) were located in the parotid, 5 cases (11.62%) in the submandibular gland and 2 cases (4.65%) in the sublingual gland. In the minor salivary glands 2 cases each (4.65%) of MEC were seen in the palate, buccal mucosa and pharyngeal wall respectively. These figures correspond to study by Gill¹⁸ and Sarfraz.²⁴

ACC was the 2nd commonest malignant SGT in our study which constituted 30 cases (30.92%) out of 97 malignant tumours. Twenty cases (66.66%) were located in the minor salivary glands with the palate harbouring the maximum number of 13 cases

(43.33%) and 10 cases (33.33%) of ACC were located in the major salivary glands with the parotid containing 6 cases and the submandibular gland and sublingual gland containing 2 cases each. These figures are consistent with the study by Tien² in which ACC constituted 70% (478/681) of the minor salivary gland malignancies with the palate being the commonest site containing 209 cases (43.72%).

"Malignant Mixed Tumour" is a broad term which encompasses 3 entities namely carcinoma ex pleomorphic adenoma (Ca ex PA), True Malignant Mixed Tumour (or carcinosarcoma) and metastasizing mixed tumour.^{9,25} The most common of these tumours is Ca ex PA which is characterised by malignant transformation of the epithelial component of a previously benign PA.^{25,26} This complication occurs in 5 – 10% of these tumours and is seen most commonly in the parotid.⁹ The malignant component most often is a poorly differentiated adenocarcinoma (NOS), a salivary duct carcinoma, an undifferentiated carcinoma or a low grade myoepithelial carcinoma.^{9,25} Carcinosarcoma is a highly lethal biphasic malignant neoplasm composed of both carcinomatous and sarcomatous components.¹ We had 4 cases of Ca ex PA and 1 case of carcinosarcoma all seen in females older than 40 years. The single case of carcinosarcoma showed a mixture of an undifferentiated carcinoma and a high grade spindle cell sarcoma. In Mausani's study²³ on 52 malignant parotid gland tumours there were 3 cases (5.76%) of Ca ex PA (5.76%) and Sarfraz²⁴ reported 4 cases (2.7%) of this malignant tumour.

Adenocarcinoma (NOS) is a diverse group of SGT's that still defy the existing classification schemes and cannot be accommodated within the conventional salivary gland cancers.^{9,15} They exhibit a wide spectrum of differentiation ranging from well differentiated low grade neoplasms to the poorly differentiated high grade malignancies.^{9,27} These tumours constituted 4.12% of our malignancies, all seen in the parotid in patients above 50 years of age. In the study by Tien² and Shishegar⁵ this tumour constituted 6% and 4% of their cases respectively.

Salivary duct carcinoma is the most aggressive salivary malignancy with an extremely poor prognosis.^{15,16} It morphologically resembles ductal carcinoma of the breast frequently showing comedo type necrosis, an infiltrative growth pattern with marked stromal desmoplasia, vascular and perineural invasion and regional lymph node involvement.^{25,28} There were 3 cases (3.09%) of salivary duct carcinoma in our study all located in the parotid. Gill¹⁸ reported 2 cases (1.9%) and Sarfraz also reported 2 cases (1.3%) of salivary duct carcinoma in their studies.

Lymphomas of the salivary glands may be either a primary process or a secondary involvement by extraglandular disease. Most major salivary gland lym-

phomas arise de-novo and are NHL of B-cell type.^{15,16} We reported 3 cases (3.09%) of NHL, 2 in the parotid and 1 in the submandibular gland. Gill¹⁸ reported 4 cases (3.92%) and Musani²³ reported 3.84% cases of NHL in their studies.

Literature from various studies points out that there are differences in the frequency with which the major and minor salivary glands are involved by tumours.²⁹ Traditionally, the distribution of salivary neoplasms between sites followed the pattern of a 100:10:10:1 ratio for parotid, submandibular, minor salivary glands and sublingual glands respectively.³⁰ Generally speaking 10 – 15% of salivary tumours occur in the minor oral salivary glands and fewer than 1% occur in the sublingual glands.^{11,12} Considering the site – wise categorisation of the 259 SGT's in our study, 200 cases (77.22%) were seen in the 3 major paired salivary glands and 59 cases (22.77%) involved the minor oral salivary glands. The parotid contained 165 tumours (82.5%), submandibular gland contained 29 tumours (14.5%) and the sublingual gland contained only 6 tumours (3%). In the minor glands the palate contained a maximum of 35 tumours (59.32%) followed by the lips containing 10 tumours (16.94%) and the remaining tumours were distributed in the buccal mucosa, pharyngeal wall, nasal cavity, maxillary sinus and posterior tongue. In our study the ratio of salivary tumours was estimated as 100:17.6:35.6:3.6 (or 165:29:59:06) for the parotid, submandibular, minor glands and the sublingual gland respectively. In the study by Tien² the ratio was 100:16:46:2 for the parotid, submandibular, minor salivary glands and the sublingual glands respectively with the palate being the most frequent location for the minor gland tumours containing 57% cases, and the 2nd most common site for all salivary gland tumours in accordance with our study.

Another study by Ito²⁰ on 496 SGT's also concluded that the parotid contained 67.7% tumours, followed by the minor salivary glands containing 22.8% and the submandibular gland containing 9.5% tumours. No tumour was identified in the sublingual gland, and among the minor salivary glands, the palate was the most frequent location containing 67% of minor SGT's.

These studies highlight the fact that the minor salivary glands are the 2nd commonest location of SGT's after the parotid gland. However, in a study by de Oliveira⁴ the sub-mandibular gland was the 2nd most common site for SGT's and the minor salivary glands ranked at 3rd position. No tumour was identified in the sublingual gland in their study. All reports and studies confirm that the palate is the most frequent site of minor salivary gland tumours followed by the upper lip and the buccal mucosa.^{20,29,31}

Out of 200 major SGT's, 134 cases (67%) were benign and 66 cases (33%) were malignant. Pleo-

morphic adenoma was the commonest benign tumour constituting 118 cases (88.05%) and MEC being the commonest malignant tumour constituting 37 cases (56.06%) followed by ACC constituting 10 cases (15.15%). These figures are somewhat in accordance with some local and international studies.^{5,18-20} Regarding the minor SGT's numbering 59 cases, 31 tumours (52.54%) were malignant and 28 cases (47.45%) were benign. All benign tumours comprised of PA's, and the commonest malignant tumour was ACC constituting 20 cases (64.51%) out of 31 cancers with the maximum number (65%) of ACC's located in the palate. The 2nd commonest malignant minor SGT was MEC comprising 6 cases (19.35%), followed at 3rd position by PLGA constituting 2 cases (6.45%). A study by Buchner³² on 380 intra-oral salivary tumours classified 224 cases (59%) as benign and 156 cases (41%) as malignant. Among the malignant tumours MEC was the most common cancer comprising of 21.8% followed by PLGA (7.1%), ACC (6.3%), adenocarcinoma NOS (2.1%), acinic cell carcinoma (1.6%) etc. Another study by Yung³³ on 213 minor salivary gland tumours classified 119 cases (56%) as benign and 94 cases (44%) as malignant. PA was the most common benign tumour and MEC was the most common malignant tumour comprising of 45 cases (47.87%) followed by ACC constituting 22 cases (23.40%) and PLGA at 3rd position (19.14%) with the maximum number of tumours located in the palate.

Studies prior to 1984 did not recognise PLGA as an entity and it was frequently diagnosed as ACC.²⁹ It is a low grade malignancy largely restricted to the minor salivary glands with the palate being the most common location.²⁵ In Tian's study² it comprised of only 1% cases, and in the study by Sarfraz²⁴ it constituted 8 cases (5.3%) out of 150 malignant tumours. In our study PLGA constituted 2 cases (6.45%) out of 31 minor oral gland malignancies and 2.06% of the overall malignant SGT's.

It is **concluded** that SGT's constitute a diverse group of head and neck neoplasms. Their morphology and biological features are an enigma for the surgical pathologists and clinicians. In this study, epidemiological data was compared with other local and international studies regarding the distribution and prevalence of benign and malignant neoplasms of both the major and minor salivary glands. However, there were some racial and geographic variations in the frequency and distribution of tumours between this study and other populations. PA was the most common benign tumour in the major and minor salivary glands. MEC and ACC were the most common malignant tumours of the major and minor salivary glands, respectively. The palate was the most common site for oral minor SGT's followed by the upper lip and the buccal mucosa.

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