

## CLINICOPATHOLOGICAL ASSESSMENT OF MAJOR SALIVARY GLANDS TUMORS IN SAMPLE OF IRAQI PATIENTS

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### ABSTRACT

**Background:** salivary gland tumors comprise about 6% of head and neck neoplasms and about 0.5% of all malignancies in humans. Most SGTs are located in major salivary glands approximately 80% in the parotid gland, and are rare in the sublingual glands <1%, majority of tumors arising from submandibular, sublingual and minor salivary glands are malignant. **Objective:** The aim of this study is to assess pathological types of major salivary glands tumors and their clinical correlation in a sample of Iraqi patients. **Methods:** A retrospective study including analysis of 100 randomly selected cases with major salivary gland tumors collected from Al-Emamain Al-Kadhmain Medical city and Baghdad medical city from October 2017 to January 2023. **Results:** In this study Mean age of patients was  $44.19 \pm 15.72$  years, (41-60y years) was the most common age group for developing salivary gland tumors. Male patients were predominant 65% and female 35% with male to female ratio 1.8:1. Malignant tumors were accounted 39% while benign tumors were 61%. As for histological types, pleomorphic adenoma was the most common benign tumor 47% followed by warthin tumor 11%, basal cell adenoma 2%, myoepithelioma 2%, oncocytoma 2%, cystadenoma 2%, hemangioma 2% and lipoma 2%. Mucoepidermoid carcinoma was the most common malignant tumors 17% followed by acinic cell carcinoma 3%, squamous cell carcinoma 3%, poorly differentiated carcinoma 2%, carcinoma ex pleomorphic adenoma 2%, basal cell carcinoma 2%, adenoid cystic carcinoma 1% and metastasis (breast) 1%. However, No significant association was found between age, sex, and site with major salivary gland tumors. There was a significant association between gross feature and nature of salivary gland lesions since most solid lesion were malignant and most cystic lesion were benign (with p value of 0.035). **Conclusion:** Benign tumors were more common than malignant tumors with Pleomorphic adenoma was the most common benign tumor in parotid gland followed by warthin tumor, Mucoepidermoid tumor was the most common malignant tumor follow by acinic cell carcinoma. Male patients were the most commonly diagnosed with MSGTs and parotid gland was most common site for both malignant and benign tumors. Most common age group (41-60 years). According to clinicopathological features, Gross features of the lesions were the most significantly associated with the nature of major salivary gland tumors.

### INTRODUCTION

Salivary gland tumors are the exocrine organs for the production and secretion of saliva, there are three groups of major salivary gland parotid, submandibular and sublingual. There are hundreds of minor salivary glands located in the mucosal lining of aerodigestive tract.<sup>[1]</sup>

According to the World Health Organization (WHO), salivary gland tumors comprise about 6% of head and neck neoplasms and about 0.5% of all malignancies in humans.<sup>[4]</sup>

The exact etiological factor of these tumors have not been identified however smoking, sunlight, ionizing

radiation chemotherapy and deficiency of vitamin A has been identified by some researchers, occupations like working in asbestos or rubber, woodwork and plumbing had been reported as occupational risk factors for developing salivary gland tumors.<sup>[2]</sup>

Most salivary gland tumors are located in major salivary glands approximately 80% in the parotid gland, and are rare in the sublingual glands <1%. Majority of tumors arising from submandibular, sublingual and minor salivary glands are malignant.<sup>[2]</sup>

The malignant tumors constitute 15%-30% of all parotid glands tumors, 40%-45% of submandibular tumors,

70%-90% of sublingual tumors and 70-80% of minor salivary tumors.<sup>[3,21,22]</sup>

Mucoepidermoid carcinoma (MEC) is the most common malignant neoplasm of parotid gland, comprising approximately 30% of all salivary malignancies.<sup>[5,12]</sup>

Classifying salivary gland tumors may be difficult, as the majority of the tumors arise from epithelial and myoepithelial cells that have the ability to undergo variety of metaplastic changes (squamous, mucinous, sebaceous, oncocytic and chondroid) and the diagnosis is complicated by the fact that some of these neoplasms are of heterogenous composition that varies from field to field in the same lesion, accordingly small biopsies can lead to misdiagnosis.<sup>[4,10]</sup>

The majority of salivary gland tumors benign and/or malignant, irrespective of site, presented as a painless mass. definitive symptoms and sign of malignancy is the presence of nerve palsy and/or the presence of cervical lymphadenopathy.<sup>[6]</sup>

Comprehensive diagnosis of an Salivary gland tumors requires a through understanding of the anatomy and history of the disease. Magnetic resonance imaging, computed tomography, and ultrasonography are the diagnostic tools of choice for diagnosing location, extend, and presence of perineurial invasion.<sup>[1]</sup>

The 2017 World Health Organization (WHO) salivary gland tumor classification guidelines distinguish 31 different primary neoplasms. The most common histological types are pleomorphic adenoma (PA), Warthin’s tumor (WT), mucoepidermoid carcinoma (MEC), and adenoid cystic carcinoma (ACC). However, large histological heterogeneity with a wide range of tumor locations may cause diagnostic and therapeutic problems in some cases.<sup>[5]</sup>

This study aimed to asses histopathological type of major

salivary gland tumors in a sample of Iraqi patient in correlation with clinicopathological parameters (age, sex, location, clinical presentation, gross features of tumors and whether they are benign or malignant).

**MATERIAL AND METHODS**

A retrospective study including analysis of 100 randomly selected patients with major salivary gland tumors collected from Al-Emamain Al-Kadhmain Medical city, Baghdad medical city from October 2017 to October 2023.

The clinicopathological data included:

1. Age
2. Sex
3. Clinical presentation
4. Location
5. Gross features of the tumors
6. Histopathological diagnosis ( benign or malignant, exact subtypes)

Exclusion criteria include minor salivary gland tumors, salivary gland cyst and non neoplastic lesions.

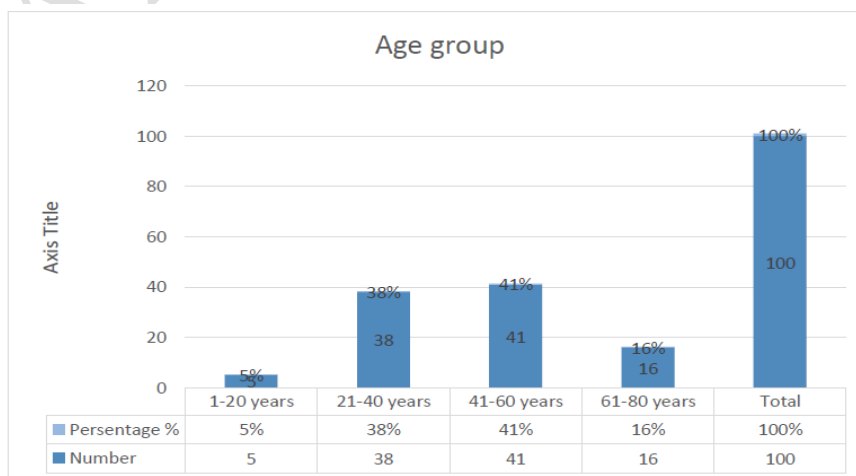
Formalin-fixed paraffin-embedded tissue blocks were collected,then, sections4-6 microns stained routinely with hematoxylin and eosin and the diagnosis was revised by two pathologists.

All statistical analyses were performed utilizing SPSS, version 23 and including mean, standard deviation, frequency and percentage using Yates Chi square with p. value <0.05 regarded as statistically significant.

**RESULTS**

**1- Distribution of the lesions according to the age of presentation**

Mean age of patients in this study was 44.19 ± 15.72 years with maximum and minimum age 74 and 1 years, Major salivary gland tumors were most common at age group 41-60 year (41%); as illustrated in chart (1).

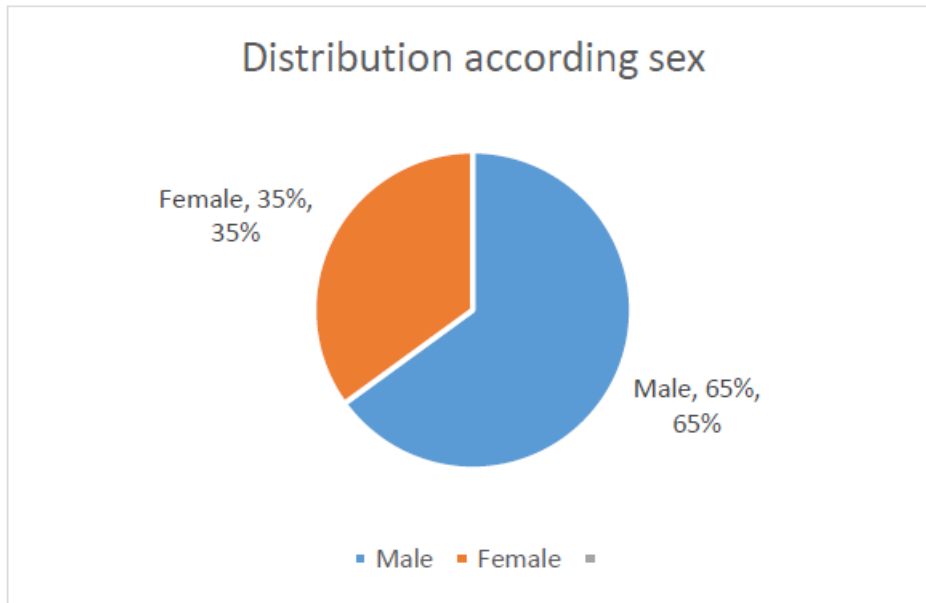


**Chart (1): distribution of the lesions according to age group.**

**2- Distribution of the lesions according to sex**

Major salivary gland tumors were most frequently in

male patients 65% and 35% for female patients, the male to female ratio was 1.8:1; as illustrated in chart(2).



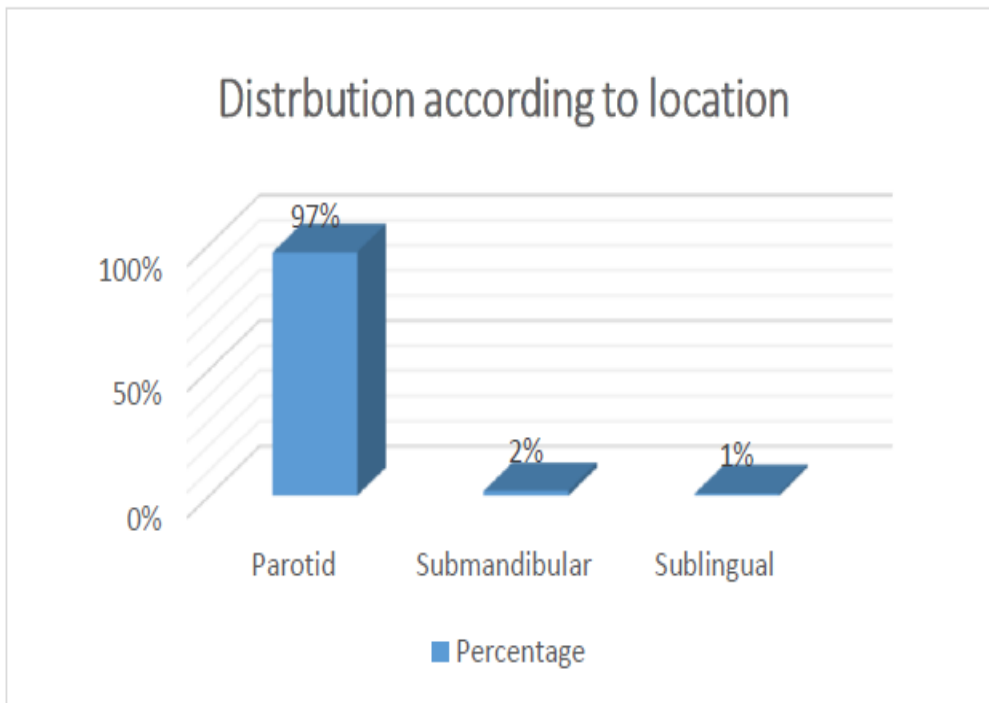
**Chart (2): Distribution of major salivary gland tumors according to sex.**

**3- Distribution according to location and types of major salivary gland tumors**

Regarding location, most Major salivary gland tumors were located in the parotid gland (97%) followed by submandibular glands(2%) and sublingual glands( 1%);

as illustrated in chart (3).

According to types of tumors 61% were Benign tumors and 39% were malignant as illustrated in chart (4).



**Chart (3): Distribution of major salivary gland tumors according ti location.**

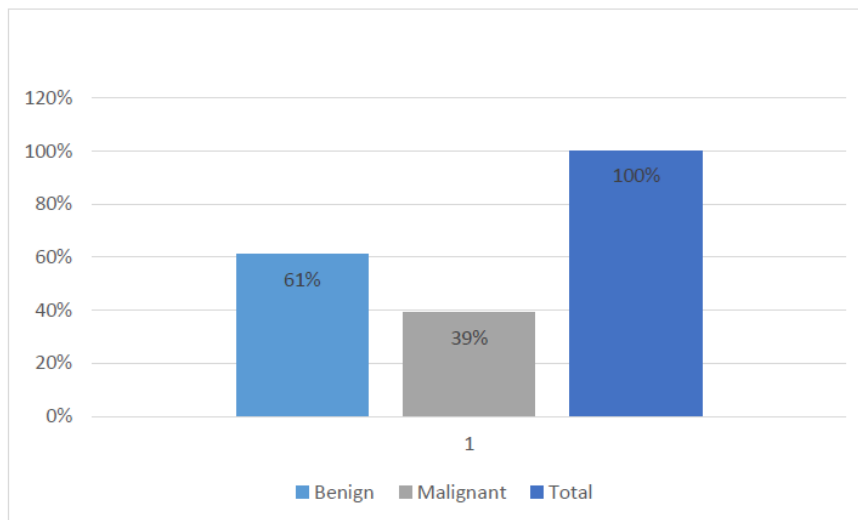


Chart (4): Distribution of major salivary gland tumors according to types of the tumors.

**4- Clinicopathological feature of major salivary gland tumors**

The clinicopathological characteristics of the study sample are illustrated in tables.(1). Mass was the most common presenting symptoms 100% of the malignant and benign major salivary gland tumors, lymph node enlargement was found in 5% of presenting symptoms associated with malignant lesions, whereas Pain was found only in one case (mucoepidermoid carcinoma).

According to gross features; Regarding cut section color of the tumor, brown color was the most common 34.3% follow by grey color 30.5%, variegated and pink color

were 4.8% for each, yellow 3.6% and black color 1.9%.

Regarding consistency of the lesions, solid lesions were account for 65% while cystic lesions were found in 28% and 82% of cystic lesions were benign tumors, While 61% of solid lesions were malignant tumors. Concerning side, Right side was effected slightly more than left side with 54% and 46% respectively. Regarding size of tumors, most frequent tumors size was 4-6 cm with (38%) and mostly was benign tumors , followed by 1-3 cm (30%), 7-10cm(27%) and mostly were malignant tumors, tumors with <1cm were (3%) and tumors with >10 cm were (2%).

Table (1): 1 clinicopathological features of MSGTs.

Clinicopathological feature	Number	Percentage
Mass	100	100%
Pain	1	1%
Facial nerve palsy	0	0%
Change clour of the skin	3	3%
Reccurent tumor	5	5%
Lymph node enlargement	5	5%
<b>Gross feature</b>		
Solid	65	65%
Cystic	28	28%
Lobulated	25	25%
Multiple mass	4	5%
<b>Size</b>		
<1cm	3	3%
1-3 cm	30	30%
4-6 cm	38	38%
7-10cm	27	27%
>10cm	2	2%
<b>Right side</b>		
Right side	54	54%
<b>Left side</b>		
Left side	46	46%

Table (1): 2 surgical procedure.

Surgical procedure	Number	Percentage%
True cut Biopsy	2	2%
Excision biopsy	96	96%
Neck dissection	2	2%
<b>Total</b>	<b>100</b>	<b>100%</b>

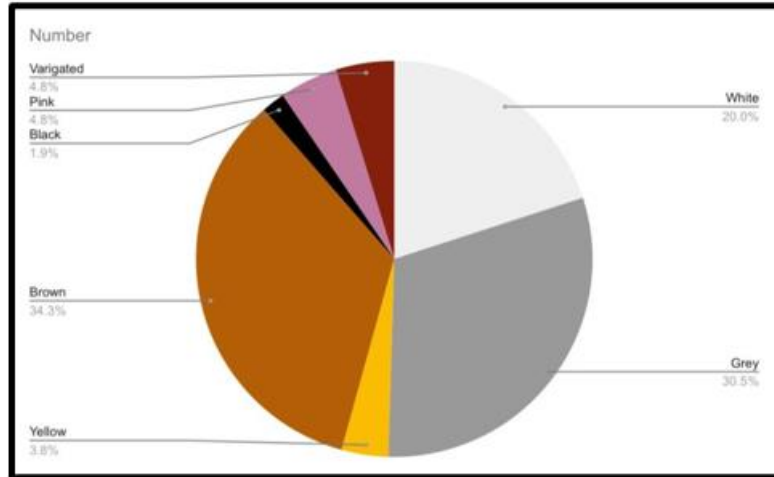


Chart (5): Distribution according to color of the gross section of the tumors

**5- Distribution of the lesions according to Diagnosis**  
Parotid gland was the most common location of benign and malignant tumors of major salivary glands tumors

follow by submandibular gland and the lowest was sublingual gland. The distribution of major salivary gland tumors is illustrated in table (2).

Table (2): Distribution of major salivary glands lesions according to histological types and location.

	Parotid	submandibular	sublingual
<b>BENIGN (61%)</b>	Pleomorphic adenoma		
	warthin tumor	cystadenoma	
	basal cell adenoma		
	cystadenoma		
	myoepithelioma		
	oncocytoma		
	hemangioma		hemangioma
	lipoma		
<b>Malignant (39%)</b>			
	Mucoepidermoid carcinoma		
	acinic cell carcinoma		
	squamous cell carcinoma		
	Adenoid cystic carcinoma		
	Papillary cystadenocarcinoma	poorly differentiated carcinoma	
	carcinoma ex pleomorphic adenoma		
	basal cell carcinoma		
	poorly differentiated carcinoma		
	metastasis		
<b>Total</b>	<b>97</b>	<b>2</b>	<b>1</b>

**6- Distribution of histological types of major salivary gland tumors according to age groups and sex**

As for histological types pleomorphic adenoma were the most common benign tumor in major salivary gland (27%) which was found most frequently in male 57.4% and frequently at age group (21-40year), followed by warthin tumor (11%), whereas Mucoepidermoid carcinoma was the most common malignant tumor(17%)

which was found most frequently in male 82.35%, followed by acinic cell carcinoma (3%).

The distribution of major salivary gland tumors according to most frequent age group and sex was illustrated in table (3).

Table (3): Distribution of salivary gland tumors according to age group and sex.

DIAGNOSIS	Total	Most frequent Age group	Sex
pleomorphic adenoma	47	(21-40 year)	Male 57.4%
Mucoepidermoid carcinoma	17	(21-40 year)	Male 82.35%
Warthin tumor	11	(41-60 year)	Male 100%
Acinic cell carcinoma	3	(41-60 year)	Male 66.67%
Myoepithelioma	3	(41-60 year)	Male 66.67%
squamous cell carcinoma	2	(21-40 year ), (41-60 year)	Female 50%, male 50%
basal cell adenoma	2	(41-60 year)	Female 100%
Oncocytoma	2	(41-60 year), (61-80 year)	Male 100%
Cyst adenoma	2	(21-40 year) (41-60 year)	Female 50%, male 50%
Hemangioma	2	(1-20 year)	Female 50%, male 50%
Lipoma	2	(41-60 year) , (61-80 year)	Male 100%
Poorly differentiated carcinoma	2	(41-60 year)	Female 50%, male 50%
papillary cyst adenocarcinoma	1	(21-40 year)	Female 100%
Adenoid cystic carcinoma	1	(41-60 year)	Female 100%
Basal cell carcinoma	1	(21-40 year)	Female 100%
Carcinoma ex pleomorphic adenoma	1	(41-60 year )	male 100%
metastasis (breast)	1	(41-60 year)	Female 100%

7- Relation between age, sex, site and gross feature with the benign and malignant tumors

There was no significant relation between age, sex, site and size of tumors as illustrated in table (4). However

There was a significant correlation between gross features and nature of the salivary gland lesions with most benign tumors were cystic and most malignant tumors were solid (with p value =0.035).

Table 4: Relation between age and sex with benign and malignant lesions.

	Bengin	Malignant	P value
Age	Most common age group (41-60 years)	Most common at age group(41-60 years)	0.818
Sex	More common in male (46%)	More common in male (19%)	1
			0.888
Sit	Mostly at parotid gland (71.13%)	Mostly at parotid gland (28.86%)	
Size	Most common at size (4-6cm)	Most common at size (7-10cm)	0.277
Gross	Most tumor was cystic 82%	Mostly solid tumor 61%	0.035

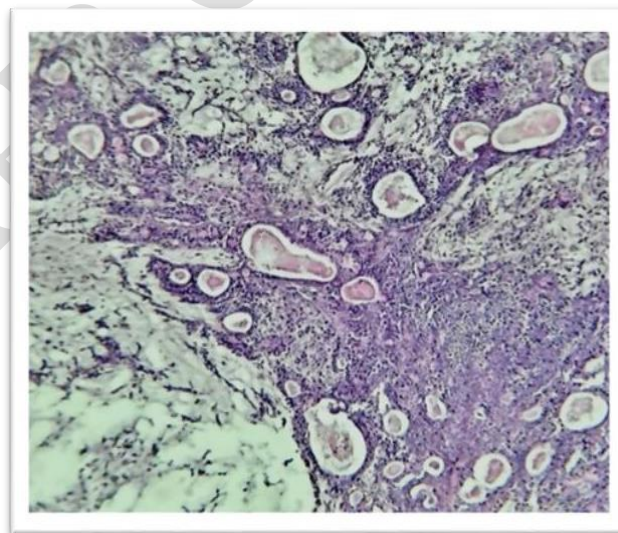


Figure-1: Pleomorphic adenoma show triphasic tumor with epithelial, myoepithelial and stromal component which is typically myxoid.(H&E stain, power 10x).

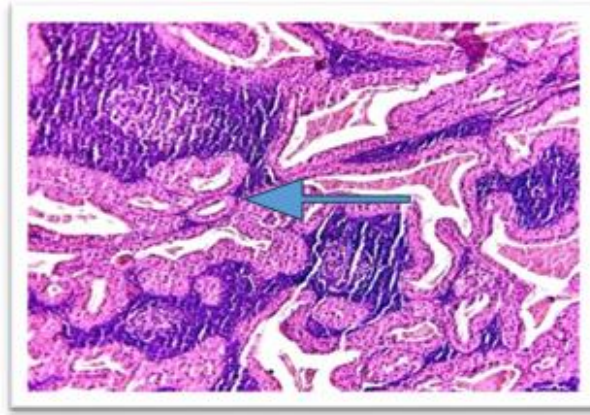


Figure-2: Warthin tumor bilayered oncocytic epithelium (arrow) with lymphoid background (H&E stain, 10X).

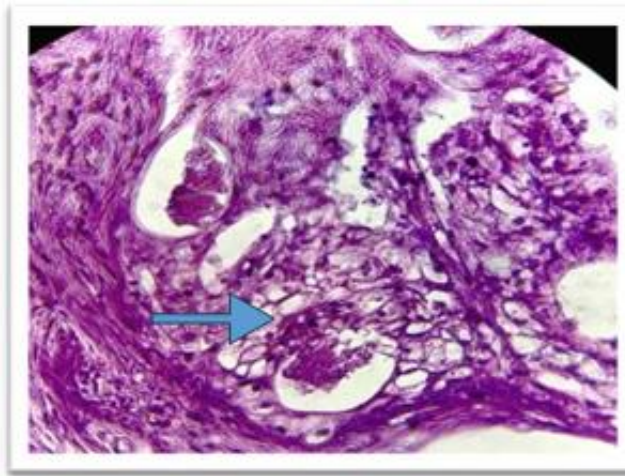


Figure-3: Mucoepidermoid carcinoma, Malignant glandular epithelial neoplasm characterized by mucous (arrow), intermediate and epidermoid cells. (H&E, 40X).

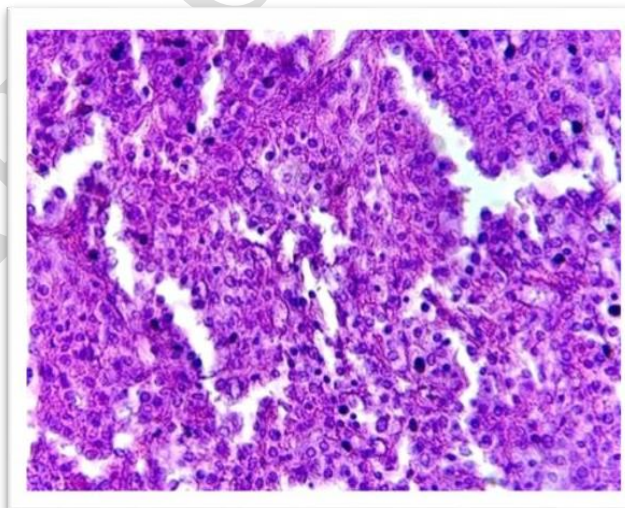
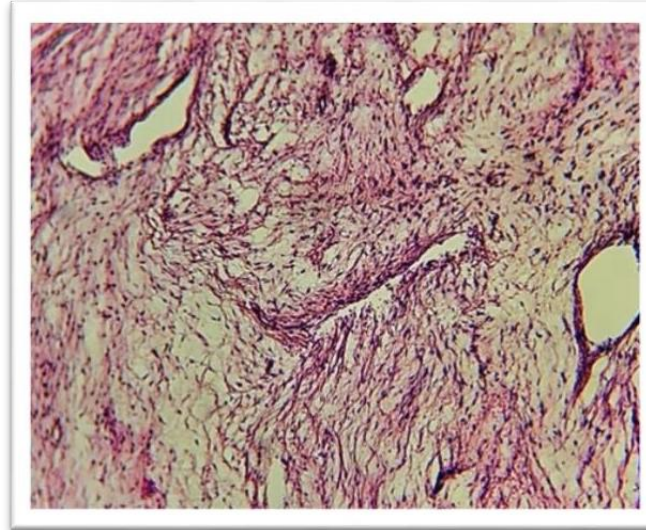


Figure-4: Acinic cell carcinoma, solid growth of acinar cells, with granular to vacuolated cytoplasm and eccentric round nuclei with conspicuous nucleoli. (H&E, 40X).



**Figure-5: Myoepithelioma which is a benign tumor composed almost exclusively of myoepithelial cells in myxoid stroma. (H&E,10X)**

### DISCUSSION

In this study the mean age of patients was  $44.19 \pm 15.72$  year with age range (1-74 year), Age group (41-60 year) was the most frequent age group 41% for both malignant and benign lesions followed by age group (21-40 year) 38%, Regarding sex male patients were most frequently presented with major salivary gland tumors with 65% compare with 35% for female. According to Pakistanis study in Lahore the age range was (11-83 year) with patients most commonly at age group (31-40 years) which is slightly lower than this study and with male predominant which is agree with this study however Brazilian study had shown female percentage 51% and male 49 % and other studies shown also female predominant.<sup>[2,22]</sup>

In this study Benign tumors account 61% and malignant tumors 39% ,this finding is consistent with studies in southern Poland.<sup>[7,11]</sup> however in a study conducted by Ahmed et al, the incidence of malignant and benign tumors were 86% and 14% receptively showing the higher incidence of malignant tumors in this study,<sup>[1]</sup> and the incidence of benign salivary gland lesions which reported in studies conducted in Iran, Congo, the united kingdom, Jorden, Brazil and china accounted more than 50% of all salivary gland lesions, and another study in Mexico showed benign tumors 86.7%, suggested that benign tumors is the most common salivary gland tumors worldwide.<sup>[11,16,19]</sup>

The parotid glands was the most common sit for both benign and malignant lesions with 97% (72.13% benign and malignant 28.86%) follow by submandibular gland 2%(50% malignant 50%benign) and the lowest was sublingual gland 1% (100%benign) and similar result are described in majority of major salivary glands tumors studies including a study done in shanghai, china with majority of salivary gland tumors 85% located in parotid glands.<sup>[2,11,22]</sup>

In this study There was no significant between sex and age groups and with the nature of the lesions (p value 0.818 and 1), and also between site of the glands and nature of the lesions (p value 0.888).

Of total 100 cases, most frequent benign tumors were pleomorphic adenoma (which is the most common benign tumor mostly 84% occur in parotid gland composed of epithelial and myoepithelial cells arranged in a large variety of morphological patterns, with area of mesenchymal differentiation) account 47% and commonly found in male patient 57.44%, this result was identical to a study done in mayo hospital Lahore with 60% male predominant and other studies.<sup>[2,16,10]</sup> follow by warthin tumor 11% (occur almost exclusively in parotid gland and mostly in elderly male associated with smoking and microscopically, composed of lymphoid tissue covered by two layers of large epithelial cells with oncocyctic feature) found 100% in male patients.<sup>[4,14]</sup>

In this study myoepithelioma account for 3% of benign lesions (composed of exclusively of myoepithelial cell oncocyctoma 2% (composed of oxyphilic large cells with round nuclei and abundant granular acidophilic cytoplasm rich in mitochondria associated with radiation exposure).<sup>[4]</sup> hemangioma 2%(vascular tumor), basal cell adenoma 2% (usually occur in adult patent slightly female predominant microscopically an important distinguishing feature is the peripheral palisading of epithelial nests giving the tumor basiloid appearance) and lipoma 2%(benign adiposetic tumors).<sup>[21]</sup>

Most frequent malignant tumors found in this study was mucoepidermoid carcinoma (which microscopically composed of four cell types mucin producing, squamous, intermediate and clear and most commonly located in parotid gland and it's the most common malignant Major salivary gland tumors in children and adult),<sup>[19,15,4]</sup> squamous cell carcinoma 2% (histologically identical to



squamous cell carcinoma of the skin), acinic cell carcinoma 3% (majority located in the parotid glands with male predominant show microscopically variation from case to case the most characteristic cell known as acinic, has a cytoplasmic appearance (granular and basophilic) an ultrastructural morphology, and a secretory behavior pattern analogous to that of acinic cells of normal salivary glands),<sup>[4,18,21]</sup> carcinoma ex pleomorphic adenoma 1% (this represented as malignant transformation of a preexisting benign mixed tumor) which found 100% in male patients, poorly differentiated carcinoma 2%, papillary cystadenocarcinoma 2% (papillary Cystadenocarcinoma is a rare malignant tumor histologically characterized by prominent cystic and frequently papillary growth, but lacking features that characterize cystic variants of several more common salivary gland carcinomas: polymorphous low-grade adenocarcinoma, mucoepidermoid carcinoma, and the papillary cystic variant of acinic cell carcinoma),<sup>[9]</sup> Adenoid cystic carcinoma 1%, basal cell carcinoma 1% (it is the malignant counterpart of basal cell adenoma but it differs by virtue of its infiltrative quality, perineurial spread, and vascular invasion),<sup>[4]</sup> and metastasis (breast) was found in one case 1%. This result was equivalent to result reported in studies conducted in Iran, Congo, the united kingdom, Jordan, Brazil and china,<sup>[2]</sup> and most studies reports ,mucoepidermoid carcinoma as the most common malignant tumor follow by adenoid cystic carcinoma,<sup>[19,4]</sup> However in a study by dzaman Ket al, acinic cell carcinoma was the commonest, follow by adenocarcinoma and non-hodgkin lymphoma in decreasing of frequency.<sup>[2,11]</sup>

According to clinical presentation the most common presented feature was mass 100% for benign and malignant tumors this result was equivalent to a study done in Nottingham UK.<sup>[21]</sup> follow by lymph node enlargement 5% and tumor recurrent was found in 5%, However this result was lower than a study done in KSA which had 11.7% lymph node enlargement.<sup>[19,11,12]</sup>

Most lesion was grossly solid 65% (61.5% malignant and 38.5% Benign), follow by cystic 28% (82.1% benign and 17.9% malignant), there was a significant correlation between the gross feature of the masses and the nature of the lesions (with p value 0.035) suggested that most solid tumors were malignant and most cystic tumors were benign.

According to the size, most major salivary gland tumors was at size between (4-6 cm) with 39.4% and 24.13% for benign and malignant tumors receptively, follow by tumor size (1-3cm) (38% malignant and 27% benign), and of p value equal to 0.277 for no significant correlation between the size and malignant or benign lesions.

Some benign salivary gland tumors have propensity to recur such as pleomorphic adenoma and in this study 5%

of total cases presented with recurrent tumor after excision.<sup>[2,13]</sup>

## CONCLUSION

Benign tumors were more common than malignant tumors with Pleomorphic adenoma was the most common benign tumor in parotid gland followed by warthin tumor, Mucoepidermoid tumor was the most common malignant tumor follow by acinic cell carcinoma. Male patients were the most commonly diagnosed with both benign and malignant salivary gland tumors and parotid gland was the sit of majority of tumors. Gross features of the lesions were the most significantly associated with the nature of MSGTs.

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