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ORIGINAL ARTICLE

Clinicopathological Patterns of Salivary Gland Neoplasms in Al-Ramadi, Iraq: A Five-Year Retrospective Study

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ABSTRACT

Tumors of the salivary glands are rare, making up 1.2% of cancers and 2–5% of head and neck cancers. Approximately 80–85% of all salivary gland tumors arise in the parotid glands, where 70–80% are benign. Pleomorphic adenoma is the most common benign tumor. It is difficult to distinguish neoplastic tumors from non-neoplastic tumors based on clinical findings. Histopathology is considered the gold standard. To determine the frequency and clinicopathological pattern according to age, gender, and histopathological distribution of salivary gland tumors in Al-Ramadi, Iraq, as compared to available literature from Iraq and abroad. Cross sectional study over a five-year duration (January 2020 until December 2024) conducted in Al-Ramadi Teaching Hospitals. 43 cases of major salivary gland neoplasms were studied according to their age, gender, site and histopathologically WHO defined type. Non-neoplastic tumors were not included. There were 25 males and 18 females (ratio of male to female being 1.4:1) ranging from ages 10 to 70 years, with an average age of 37 years. The most affected site is the parotid gland, comprising 67.44%; the submandibular gland is 32.56%. The predominating tumors are the benign ones (74.42%), while the malignant ones comprise 25.58%. Malignancy is 20.7% of the parotid gland, but 35.7% of the submandibular gland is malignant. Pleomorphic adenomas are the commonest among the benign tumors (62.79%). Among the malignant tumors, acinic cell carcinoma (9.30%) and mucoepidermoid carcinoma (6.97%) are the commonest. Conclusion: From the results of our study group, we observe similarities with international trends in regards to the sites and gland involved as well as histology types. However, the increased malignancy rate of the submandibular gland and male predominance of the mucoepidermoid carcinoma require continuous monitoring. Histopathologic classification is very important; and any patient having painless swelling of the salivary gland not due to inflammation should be referred to surgery.

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1- INTRODUCTION

Salivary gland tumors represent a rare but highly challenging entity in head and neck oncology. Tumors of salivary glands represent approximately 1.2% of all human neoplasms and 2%-5% of head and neck tumors, though their prevalence continues to increase in some parts of the world, including the Middle East [1,2,3]. One of the factors justifying the high level of attention towards this type of tumors is related to their deceptive

symptomatology: the asymptomatic slow-growing parotid mass is often neglected, while only symptoms like involvement of facial nerve or regional lymphadenopathy indicate the malignant nature of the disease [4,5]. The true challenge in the treatment of salivary gland neoplasms lies in the heterogeneity of these cancers. In fact, the World Health Organization classification published in 2017 (fourth edition) included over 20 epithelial subtypes of salivary gland cancer, which number increased even more in the fifth edition in 2022, from a non-aggressive pleomorphic adenoma to the very aggressive undifferentiated carcinoma, exhibiting such varied biological behavior that a uniform treatment approach is impossible.[3,6] Heterogeneity also complicates the epidemiologic comparison, as a number could include many other factors than simply the population differences [6]. Even the anatomical location is a diagnostic factor. The association between gland size and cancer risk is known to be inverse – about 20–25% of parotid cancers are malignant, while 40–50% of submandibular gland masses and 70–80% of those of minor salivary glands and sublingual areas are malignant [5,7]. This is not just a statistical fact but has practical meaning since a hard lump in the submandibular region in an adult patient implies almost double the likelihood of a cancer than the similar parotid lump [8]. There are some deficiencies with the etiological data. Exposure to ionizing radiation is the only one risk factor that has been consistently reproduced; increased incidences of mucoepidermoid carcinoma have been noted decades after exposure among atomic bomb survivors from Hiroshima and Nagasaki in a dose-dependent manner [9]. Epstein-Barr virus has been linked to development of lymphoepithelial carcinomas that occur much more commonly in individuals hailing from South East Asia and the Inuit region of the Arctic [10]. Occupation-based exposures have been hypothesized, but have never been proven [2,9]. It is unclear whether any of the environmental risk factors apply to the Iraqi population in question and that epidemiological gap is one reason regional audit data carry value. Pleomorphic adenomas merit discussion not because they are the commonest salivary tumors, as is clear [11] but because their recurrence pattern is often misinterpreted. This tumor's pseudocapsule is misleadingly structured: satellite nodules penetrate through capsular perforations in up to 30% of cases, and enucleation surgery cannot remove these satellites and leaves them behind, resulting in recurrences of 20-45% [12,13]. The game changed when it was discovered that superficial parotidectomy with sufficient cuff of normal tissue results in recurrence less than 2%, which cannot be achieved by enucleation surgery [14]. The transformation into cancer, often reported at the lifetime risk of up to 5% (according to Andreasen *et al*., about 1.6% within 20 years in Danish population [12]), occurs only in tumors with the history of more than 15 years; therefore, watch-and-wait management of asymptomatic older patients is a valid option that should be explicitly discussed [15]. The survival rate for malignant cancers is determined by the grade and not the subtype. Acinic cell carcinomas have 10-year survival rates exceeding 90% among patients who have low-grade tumors without nodes. Undifferentiated carcinomas have 10-year survival rates of about 44% [1,16]. Intermediate mucoepidermoid carcinoma represents a difficult clinical dilemma, in that there is considerable observer variability associated with the grading process. Thus, what may be intermediate grade cancer to one pathologist is high grade cancer to another, and therapy is changed from observation to radiotherapy [17,18,19].

The variety of diagnostic modalities has increased. The sensitivity of FNAC is 85-90%, and specificity exceeds 95% in expert centers for malignancy; however, the rate of false-negatives in case of cystic lesions and low-grade mucoepidermoid carcinoma stays relatively high [20,21]. Dynamic contrast-enhanced MRI replaces CT in the evaluation of perineural invasion and deep lobe involvement of the parotid gland, which dramatically influences surgical approach [22,23]. US guided core biopsy is becoming more popular for the submandibular glands in comparison with FNAC due to less yield in the latter group; however, the risk of tumor cell seeding is considered purely theoretical by most experienced centers [21,24]. The current study provides information on clinicopathological characteristics of salivary gland tumors in Al-Ramadi Teaching Hospitals during the past five years and compares local data with data obtained in other regions of Iraq and abroad.

2- MATERIALS AND METHODS

This is a cross-sectional study that included a cohort of 43 patients undergoing surgical removal of major salivary glands in Al-Ramadi Teaching Hospitals; between January 2020 and December 2024. In this study, we only included the patients whose tumors were surgically removed and their records collected from the operative and pathology logs. Patient's record includes age, gender, location of the gland harboring the tumor, and histopathological diagnosis. Specimens were processed and classified based on the 4th edition of World Health Organization Classification of Head and Neck Tumours (2017). These specimens were not re-classified based on the 5th edition (2022) that published within the scope of this study. Only diagnosis based on the 4th edition criteria were considered. There was no data about fine-needle aspiration for comparison with surgical histopathology reports only.Non-neoplastic lesions such as sialadenitis, sialolithiasis, tuberculosis, and retention cysts were excluded. One

benign vascular lesion (hemangioma) and two lymphoma cases involving the salivary gland region met the operative inclusion criteria for this cohort. Consistent with the 5th edition WHO reclassification of vascular/mesenchymal and hematolymphoid entities outside the core salivary gland epithelial tumor chapter, these three cases are reported separately from the epithelial neoplasms in the Results below rather than analyzed as primary salivary gland tumors [9].

Statistical Analysis

This research is descriptive. IBM SPSS v26.0 (p) software was used to summarize data. Frequency distribution and percentage were used to present results for categorical variables while mean ± SD and range were used for continuous variables. No inferential statistical analyses were performed, as the purpose of the research was descriptive. Future studies should apply chi-square testing or Fisher's exact test to subgroup comparisons (e.g., sex by gland site, benign vs. malignant by age group) to allow meaningful statistical inference.

3- RESULTS AND DISCUSSION

3.1 Demographic Profile

Patients treated during the study period were 43 in number. Out of which 25 were male patients (58.14%) and 18 were female patients (41.86%), male to female ratio of 1.4:1. Patients' ages varied from 10 years to 70 years having an average of 37 years. There were more males aged between 30 years and 70 years, whereas more females were of ages between 20 years and 50 years. (Table I; Figure 1).

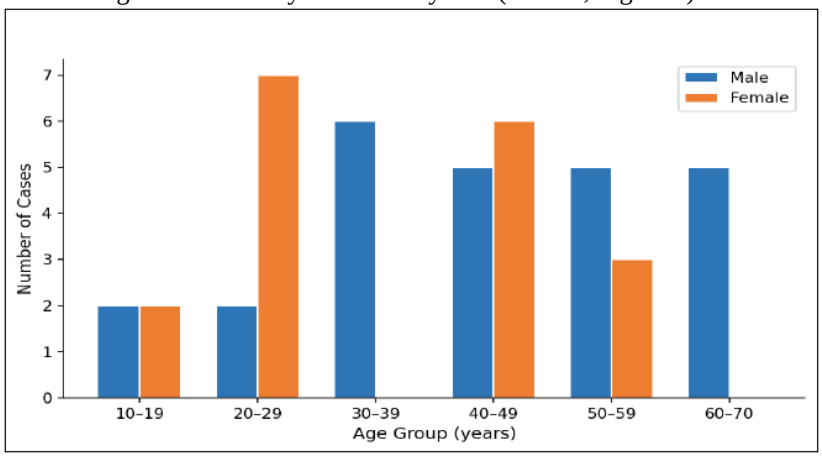

Fig (1): Age and sex distribution of salivary gland tumor cases (n=43). Female cases peak in the 20–29 decade; male cases are distributed across the 30–70-year range

Table (1): Age and Sex Distribution of Salivary Gland Tumors

Age Group	Male (n)	Male (% of N=43)	Female (n)	Female (% of N=43)	Total (n)	Total (%)
10–19	2	4.65%	2	4.65%	4	9.30%
20–29	2	4.65%	7	16.28%	9	20.93%
30–39	6	13.95%	0	0.00%	6	13.95%
40–49	5	11.63%	6	13.95%	11	25.58%
50–59	5	11.63%	3	6.98%	8	18.60%
60–70	5	11.63%	0	0.00%	5	11.63%
Total	25	58.14%	18	41.86%	43	100.00%

3.2 Benign Tumors

Benign tumors made up 32 out of 43 cases (74.42%). Among all types of tumors studied, pleomorphic adenoma was the most common one, affecting 27 individuals (62.79%). The male to female ratio among those patients was 1.25:1. The age range during which pleomorphic adenomas occurred most commonly was between the second and the fourth decades [25]. The second most common tumor was Warthin tumor, occurring in four individuals (9.30%), with the male to female ratio being 3:1, which can be explained by the fact that Warthin tumor is linked to tobacco usage [26]. One hemangioma was identified in a female patient (2.33%) (Table II). As a vascular/mesenchymal lesion, it is reported separately from the epithelial tumors in keeping with the 5th edition WHO reclassification; its inclusion here reflects that it met operative criteria and was managed surgically within this cohort.

Table (2): Benign Pathological Diagnosis by Sex

Pathological Type (Benign)	Male (n)	Male (%)	Female (n)	Female (%)	Total (n)	Total (%)	Ratio (M:F)
Pleomorphic Adenoma	15	34.88%	12	27.90%	27	62.79%	1.25:1
Warthin Tumor	3	6.97%	1	2.33%	4	9.30%	3:1
Hemangioma	0	0.00%	1	2.33%	1	2.33%	0:1
Total Benign	18	41.86%	14	32.55%	32	74.42%	1.29:1

3.3 Malignant Tumors

Malignancies were found in eleven (25.58%) patients with the male:female ratio being 1.75:1. Acinic cell carcinoma was the most common type of malignancy (four cases, 9.30%), while the next common was mucoepidermoid carcinoma (three cases, 6.97%). In all the three cases of mucoepidermoid carcinoma, males were found, which an interesting finding is since there is a preponderance of females in this type of carcinoma in world literature [7]. Due to the small sample size (n=3), this finding may not reflect a true biological trend and requires validation in larger cohorts. Adenocarcinoma and squamous cell carcinoma occurred in one patient each (2.33%), while there were two cases of salivary lymphoma occurring in females (4.65%) (Table III; Figure 2) [27]. The available pathology material did not permit definitive distinction between a primary lymphoma arising in the salivary parenchyma and secondary involvement of an intraparotid or periparotid lymph node [27]. Both cases are therefore reported here as salivary-region lymphoid malignancies rather than as primary epithelial salivary gland neoplasms, in keeping with the 5th edition WHO framework, which classifies hematolymphoid tumors separately from the epithelial salivary gland tumor category [9]. The age group when malignancies occur more frequently was between the fourth and sixth decades [7,8,28].

Table (3): Malignant Pathological Diagnosis by Sex

Pathological Type (Malignant)	Male (n)	Male (%)	Female (n)	Female (%)	Total (n)	Total (%)	Ratio (M:F)
Acinic Cell Carcinoma	3	6.97%	1	2.33%	4	9.30%	3:1
Mucoepidermoid Carcinoma	3	6.97%	0	0.00%	3	6.97%	3:0
Adenocarcinoma	1	2.33%	0	0.00%	1	2.33%	1:0
Squamous Cell Carcinoma	0	0.00%	1	2.33%	1	2.33%	0:1
Lymphoma	0	0.00%	2	4.65%	2	4.65%	0:2
Total Malignant	7	16.28%	4	9.30%	11	25.58%	1.75:1

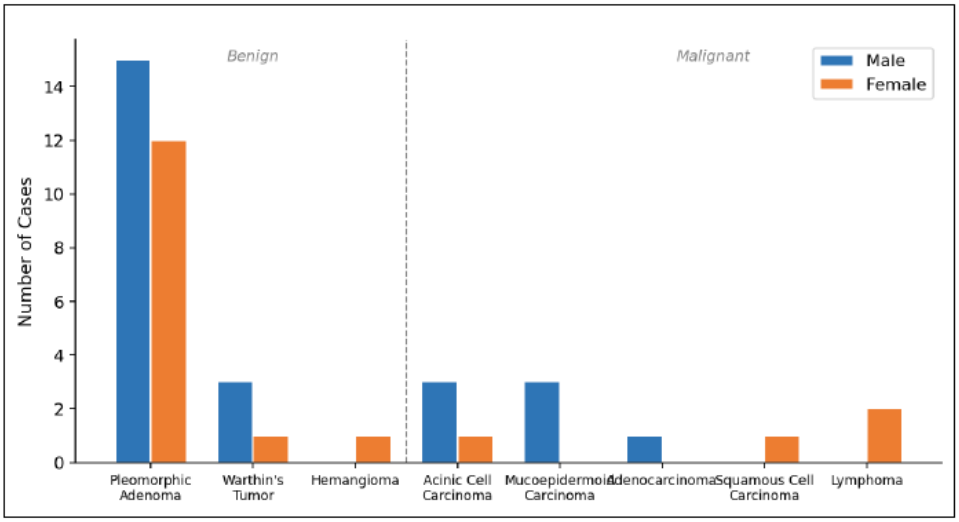

Fig (2): Histopathological tumor types by sex. The dashed line separates benign (left) from malignant (right) diagnoses

3.4 Anatomical Site Distribution

The tumor arose from the parotid gland in 29 patients (67.44%), whereas the remaining 14 tumors (32.56%) arose from the submandibular glands. No cases arising from sublingual and minor salivary glands were present, likely reflecting referral patterns at this institution, where minor gland lesions are preferentially directed to oral and maxillofacial surgery departments rather than general surgical units. In the parotid gland, 20.7% of tumors were malignant. On the other hand, in the submandibular gland, 35.7% of the tumors were malignant. This reflects the inverse correlation of size of the gland with the probability of malignancy (Table IV; Figure 3) [29].

Table (4): Anatomical Site Distribution and Malignancy Rate

Gland Site	Total Cases	% of Total	Benign (n)	Benign (%)	Malignant (n)	Malignancy Rate
Parotid Gland	29	67.44%	23	79.31%	6	20.69%
Submandibular Gland	14	32.56%	9	64.29%	5	35.71%
Total	43	100%	32	74.42%	11	25.58%

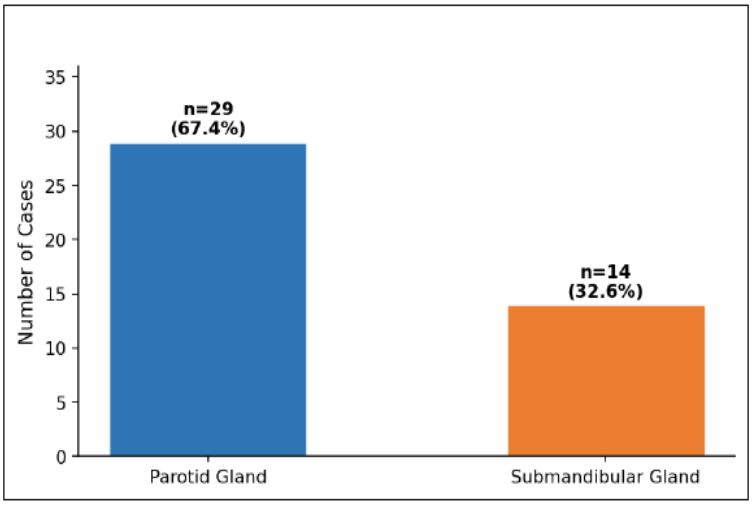

Fig (3): Anatomical site distribution of salivary gland tumors. The parotid gland was involved in 67.44% of cases; the submandibular gland in 32.56%

While the 74.42% rate of benign neoplasia in this study series fits the 70-80% expected range in institutional salivary gland series, the malignancy rate of 25.58% refers to surgically treated cases in our series, which is higher than the general population prevalence due to referral and selection bias, as many benign lesions are observed and not excised. Nevertheless, this proportion underscores the need for timely action when shifting from watchful observation to surgery. The composition of the series, namely 62.79% pleomorphic adenomas accounting for 84.4% of all benign tumors, is fully within the world standards, where the incidence of pleomorphic adenoma is estimated at 60-75% among salivary neoplasias [5,25]. Bimodal age/sex distribution seen in this series – male dominance in the older age categories and female dominance in the 20-29 age category – is similar to the distribution shown in studies of the North African and Middle Eastern populations [3,6]. Thus, in practice, a pleomorphic adenoma should be assumed in a case of a slow-growing and painless mass in the parotid gland of a patient aged 20-50, but this presumption should be dropped in case the tumor grows rapidly, becomes hard and is accompanied by facial nerve symptoms.

Warthin tumor with male predominance 3:1 and incidence in the fifth decade coincides with its well-known association with smoking and parasympathetic function in older males [26]. Warthin tumor occurs bilaterally in 10% of the cases worldwide; in our series, none of the four patients had this type bilaterally because systematic ultrasonic search bilaterally is not done routinely in this region, and thus bilateral Warthin tumors may have been missed. Of note, smoking history was not recorded in this study, limiting our ability to confirm the known association between Warthin tumor and tobacco use in this patient population. The rate of malignancy in the submandibular glands at 35.7% was significantly higher than that in the parotid glands at 20.7% in accordance with the inverse relationship between gland size and malignancy rates. The threshold for biopsy or excision of a submandibular mass should be lower than that for a morphologically similar parotid lesion. The comparative figures from international literature series are provided in Table V [7,8,30,31].

Table (5): Comparison with Published International Studies

Study (Country, Year)	n	Parotid (%)	Benign (%)	Pleo. Adenoma (%)	Malignant (%)
Present Study (Al-Ramadi, Iraq)	43	67.44%	74.42%	62.79%	25.58%
Aldelaimi *et al.* (Iraq, 2022)	159	~63%	~79%	~58%	~21%
Lukšić *et al.* (Croatia, 2012)	573	~72%	~73%	~58%	~27%
Fonseca *et al.* (Brazil, 2012)	493	~68%	~77%	~56%	~23%

Note: Values for published studies are approximate, derived from reported series. Pleo. Adenoma = Pleomorphic Adenoma. †Aldelaimi *et al*. (2022) is from the same institution (Al-Ramadi Teaching Hospital) and includes 159 salivary gland disease cases (neoplastic and non-neoplastic); values shown are for the neoplastic subset. AlSalem *et al*. (Ref 2), a carcinoma-only study of 571 malignant cases, was excluded from this table because its overall benign/malignant proportions would necessarily have been extrapolated rather than directly observed.

Two additional regional series published after the design of the present study, one from Iraq (Ali, 2024; n=715) and one from southern Iran (Ghaderi *et a*l., 2023; n=405), further support the generalizability of these findings: the Iranian series reported benign and malignant proportions of 74.5% and 25.4% respectively, closely matching the present cohort, while the Iraqi series similarly identified pleomorphic adenoma as the predominant benign diagnosis (64.90% of cases) [32,33]. The exclusive male prevalence of mucoepidermoid carcinoma (3: 3 male, 0 female) is contrary to the slightly higher female prevalence seen in most international reports. This could either be due to the referral bias that is characteristic of a small single centre study or a possible regional sex difference that should be prospectively evaluated. There is no conclusion on the cause of this difference. Applying the 5th edition WHO classification (2022) to this cohort would carry two main implications. First, several epithelial entities were formally recognized only in the 2022 update, including microsecretory adenocarcinoma; because specimens here were classified solely under 4th edition (2017) criteria, some tumors labelled broadly as adenocarcinoma in this series cannot be excluded from potential reclassification under these newer entities on re-review. Second, the 5th edition explicitly removed vascular/mesenchymal tumors and hematolymphoid neoplasms such as lymphoma from the core salivary gland epithelial tumor [9]. Under this framework, the hemangioma and the two lymphoma cases in the present series are best regarded as non-epithelial salivary-region lesions rather than primary epithelial salivary gland

neoplasms, as reflected in how these cases are reported above. Acinic cell carcinoma was observed in 9.30% of the cases. This is in accordance with the fact that this type of cancer presents at a younger age with lower-grade lesions compared to other types of salivary gland cancers [34]. Its 10-year disease specific survival of greater than 90% for patients without lymph nodes is in sharp contrast to the 10-year survival rate of 44% of undifferentiated carcinoma, and underlines the clinical necessity of precise histological subtyping. The prognosis of survival for these tumors on the basis of histology varies by almost 50% within 10 years [35]. Proper stratification in treatment demands accurate histological grading and subtyping [36]. Any painless salivary gland mass not attributable to inflammation should be referred promptly for surgical evaluation, since timely intervention is one of the modifiable factors affecting the prognosis [24].

There are some major limitations in this study. One is the single centre study and the small sample size (n=43), which reduce the power of statistics and generalization. Another limitation is that the five-year span is adequate enough to determine the trend of prevalence, but not enough to determine survival. Lack of FNAC information makes it impossible to do a pre/post-surgical diagnostic agreement test; future studies should include FNAC and core biopsy data. Additionally, tumor size, clinical stage, surgical margins, and adjuvant therapy data were not collected, which further limits prognostic analysis. Future studies need to include multi-centre, prospective registries with standardization of data collection including grading, margin status, adjuvant treatment, and follow-up to enable survival analysis by histotype and meaningful international comparison.

4- CONCLUSION

Retrospective analysis was done at Al-Ramadi Teaching Hospitals of 43 salivary glands neoplasms that have been surgically treated. About 75% of the neoplasms were benign, acinic cell carcinoma being the most frequent malignancy, while the parotid gland was the frequent location for neoplasms occurrence. There are two interesting findings obtained from the study, which need to be further surveilled: firstly, 35.7% of the malignancies in the submandibular region, which was twice the frequency in the parotid gland and shows the necessity for timely detection of the neoplasms at the particular location; secondly, mucoepidermoid carcinoma observed only in males, which differs from most previously published groups and requires further confirmation in order to make any etiological conclusions. Histopathological classification using WHO guidelines still forms the cornerstone of management in this category of tumors; no clinical, radiological, or cytological characteristic can take its place.

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