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## Prevalence of salivary gland neoplasms in the head and neck in educational hospitals in Cairo Governorate

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**Abstract**--Background: Salivary gland neoplasms are morphologically diverse neoplasms with variable histology, clinical behavior, and tumor grade. Moreover, specific gene translocations and fusions are associated with some types of SGNs. Aim: To evaluate the prevalence of salivary gland neoplasms diagnosed in Cairo's educational hospitals and to compare the results with findings in the literature. Materials and Methods: Data of salivary gland neoplasms diagnosed between 2010 and 2019 were collected from the files of the Cairo's educational hospitals. Results: Salivary gland neoplasms in the present study constituted 2.4% of all the 9609 registered oral and maxillofacial biopsies. A total of 231 cases of SGNs were collected and reviewed. Of these, (61.1%) were benign and (38.9%) were malignant. Minor salivary glands (51.94%) were more involved than major ones (45.02%). Pleomorphic adenoma was the most frequent type of benign SGNs (68.8%) while Mucoepidermoid carcinoma was the most frequent type of malignant SGNs (46.7%). The mean age of SGNs was 41.14 ±15.43 years with a slight male predilection. Conclusion: In this study we observed a marked geographic variation in the relative frequency of various salivary gland neoplasms in Cairo government.

**Keywords**--Salivary gland neoplasms, epidemiology, world health organization, oral pathology.

## Introduction

Salivary gland neoplasms (SGNs) are morphologically diverse as they originate from different glandular cell types. The incidence of SGNs has slowly increased during the last four decades. The etiology of SGNs is mostly unknown; however, specific gene mutations are associated with some types of salivary tumors (**Lin et al., 2018**). Salivary gland neoplasms generate considerable interest because of their heterogeneous nature and variable histology, clinical behavior and tumor grade. More than 30 malignant and benign histologic subtypes were classified by the World Health Organization (WHO) with more concern in defining translocations and gene fusions in monomorphic salivary gland tumors (**Seethala and Stenman, 2017**).

The incidence of SGNs is variable worldwide with regional differences, **Živković et al., 2021** documented an incidence ranging from 3% to 6% of all tumors of the neck and head region, with an annual incidence of 0.05 to 2 newly discovered tumors in 100000 individuals. Benign SGNs are more frequent than malignant ones (**Quiriny et al., 2017**). On the contrary, malignant SGNs are infrequent, heterogeneous representing less than 1% of all malignancies. MEC and ACC are the most common ones. Although ACC and MEC account for about half of overall cases, 24 distinct malignant types are included in the 2017 WHO Classification (**Schvartsman et al., 2019**).

Most of neoplasms occurring in the major salivary glands are benign, most frequently occurring in the parotid gland. On the other hand, most neoplasms of the minor salivary glands are located in the palate with high incidence of malignancy. Furthermore, metastatic tumors and lymphomas constitute a percentage of malignant salivary neoplasms thus should be considered during differential diagnosis (**Kane et al., 2020**).

Salivary gland neoplasms histopathology and cytology are extremely sophisticated, even for experienced pathologists as they demonstrate a highly diverse mix of cell types, growth patterns and overlapping morphologic features which represents a great diagnostic challenge. Fine needle aspiration cytology (FNAC) is considered the first diagnostic method for salivary neoplasms in major glands. However, it is not always reliable and should be used in conjunction with other investigations such as incisional biopsy (**Pfeiffer and Ridder, 2012 and Peravali et al., 2015**).

## Method

### Study design

Retrospective descriptive cross sectional study.

### Participants

Patient adhering to all following criteria were included:

### Inclusion criteria:

- Age: All age groups.
- Gender: Both genders.

- Site: Head and neck region.

All salivary gland neoplasms in the head and neck region that fitted the histological classification of the 2017 WHO were included in the study. All reports were included in period between (2010 and 2019).

**Exclusion criteria:**

- Any patient's reports that were not archived in educational hospitals in Cairo Governate.
- Any reports not found in period between (2010 and 2019).
- Any salivary gland lesion found in areas other than head and neck region i.e., DIFFERENT SITE.

**Data sources**

Data for the study was obtained from the reports of patients diagnosed histopathologically with salivary gland neoplasms in the head and neck region between January 2010 to December 2019.

Cases were reviewed from the archives of:

- Cairo University, Faculty of dentistry, Oral and Maxillofacial Pathology Department.
- Cairo University, Faculty of medicine, General Pathology Department.
- Ain Shams University, Faculty of dentistry, Oral Pathology Department.
- Al-Azhar University, El-Sayed Galal Hospital, General Pathology Department.
- Ahmed Maher Teaching Hospitals.

**Outcome:**

Prevalence rate of salivary glands neoplasms (Benign and malignant) in the head and neck region.

**Statistical analysis**

Categorical variables were expressed in proportions or percentages; Chi square and Fisher's exact tests were applied as appropriate. Continuous variables were examined for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test. We were expressed using range, mean, median± standard deviation (normal variables); range, median and interquartile range (non-normal variables).

**Results**

From an estimated total of 9609 oral and maxillofacial biopsies registered during the 10 years' period from January 2010 to December 2019. After exclusion of incomplete medical records and indefinite histopathological reports, only 231 (2.4%) were salivary gland neoplasms (SGNs). Of the 231 cases, the majority were benign accounting for 141 (61.1%), while the remaining 90 (38.9%) were malignant.

### 1. Variable Prevalence rates of Salivary gland neoplasms:

Regarding benign SGNs, Pleomorphic adenoma was the most frequent type of benign SGNs, accounting for 97 (68.8%) followed by warthin tumor 20 (14.2%) and Myoepithelioma 8 (5.7%) Figure (1).

Regarding malignant SGNs, Mucoepidermoid carcinoma was the most frequent type of malignant SGNs, accounting for 42 (46.7%) followed by adenoid cystic carcinoma 26 (28.9). Both polymorphous adenocarcinoma and acinic cell carcinoma had similar percentage (4.4 %), and also, myoepithelial carcinoma and adenocarcinoma NOS (3.3%) Figure (1).

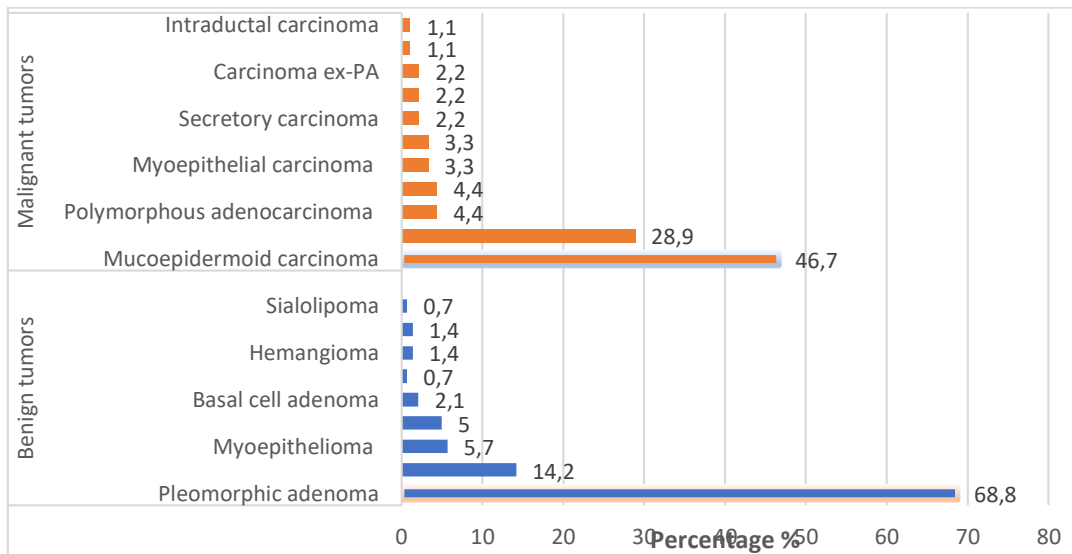


Figure (1): Bar chart representing the percentage of benign and malignant salivary gland neoplasms in relation to the group (benign or malignant) collected in this study.

### 2. Age distribution of 231 salivary gland neoplasms cases:

The age of patients ranged from 4 to 80 years with mean age of  $41.14 \pm 15.43$  years. The mean age of benign salivary gland neoplasms  $40.24 \pm 14.87$  years was while the mean age of malignant ones was  $42.54 \pm 16.26$  years. The distribution of benign salivary gland neoplasms according to age was, 8 (5.7%) patients within the age group of 0–20 years, 71 (50.4%) patients within the age group of 21–40 years. 48 (34%) patients within the age group of 41–60 years. 12 (8.5%) patients within the age group of >61 years Figure (2).

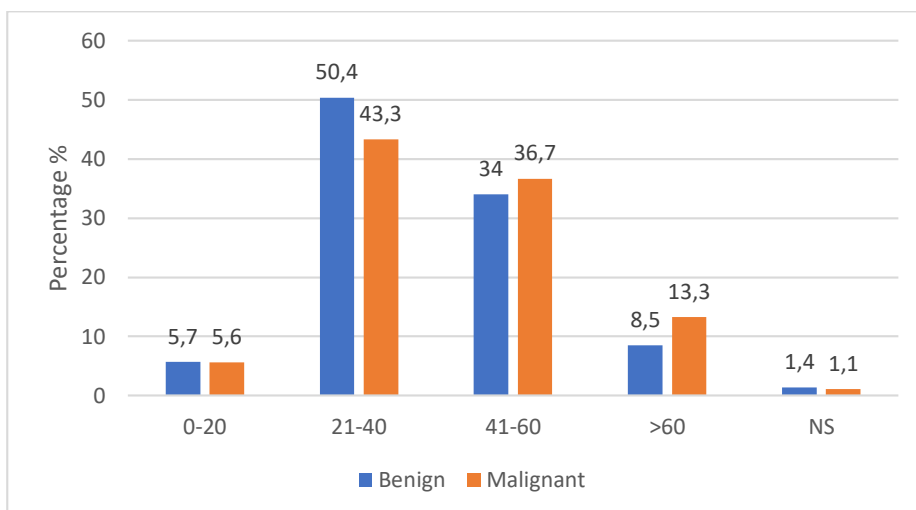


Figure (2): Bar chart representing distribution of benign and malignant salivary gland neoplasms according to the age range.

### 3. Gender distribution of 231 salivary gland neoplasm cases

From the 231 salivary gland neoplasms cases, 117 (50.64%) were males, while 114 (49.35) were females Figure (3). Benign salivary glands were more common in females which accounted for 71 (50.35%) while malignant ones were more common in males which accounted for 47 (52.22%) Figure (4).

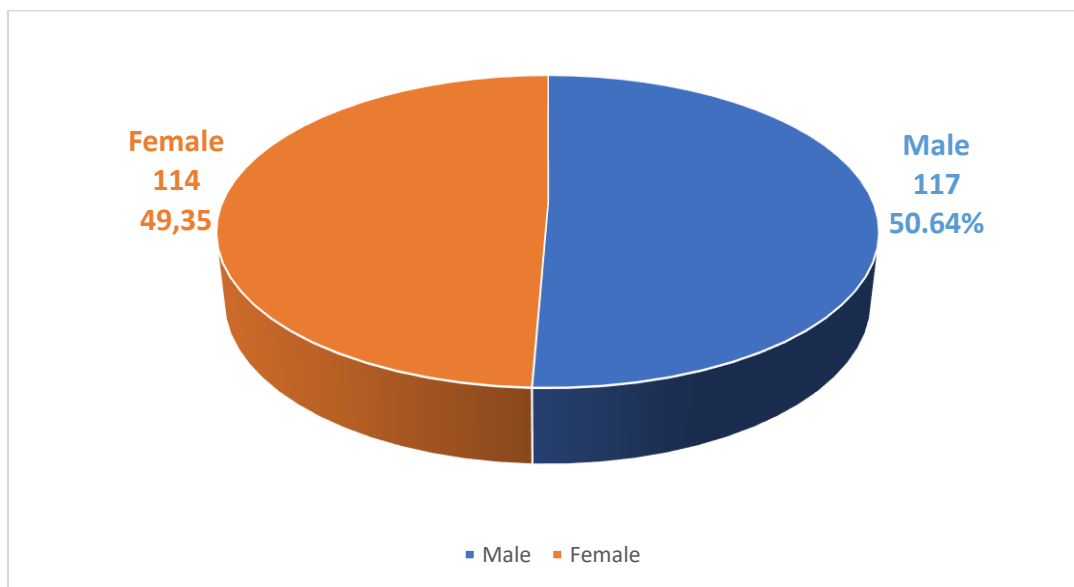


Figure (3): Pie chart representing gender distribution among salivary gland neoplasm cases.

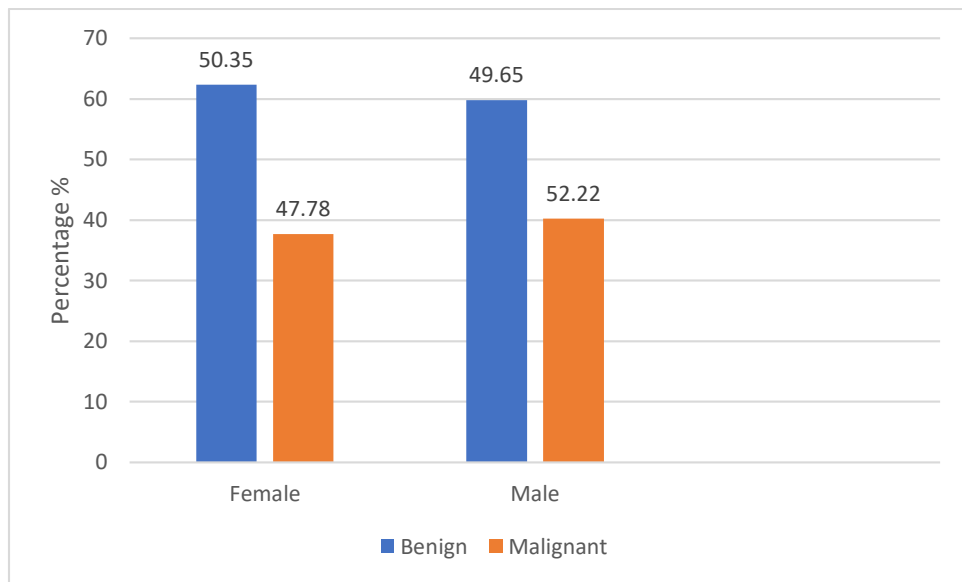


Figure (4): Bar chart representing gender distribution of among benign and malignant salivary gland neoplasms.

#### 4. Distribution of salivary gland neoplasms cases in relation to location

Minor salivary glands were more involved than major ones comprising 120 (51.94%) and 104 (45.02%) Figure (5). Parotid gland was the most frequent location among major salivary glands which accounted for 81 (36.61%). On the other hand, the palate was the most frequent location among minor salivary glands which accounted for 77 (34.37%).

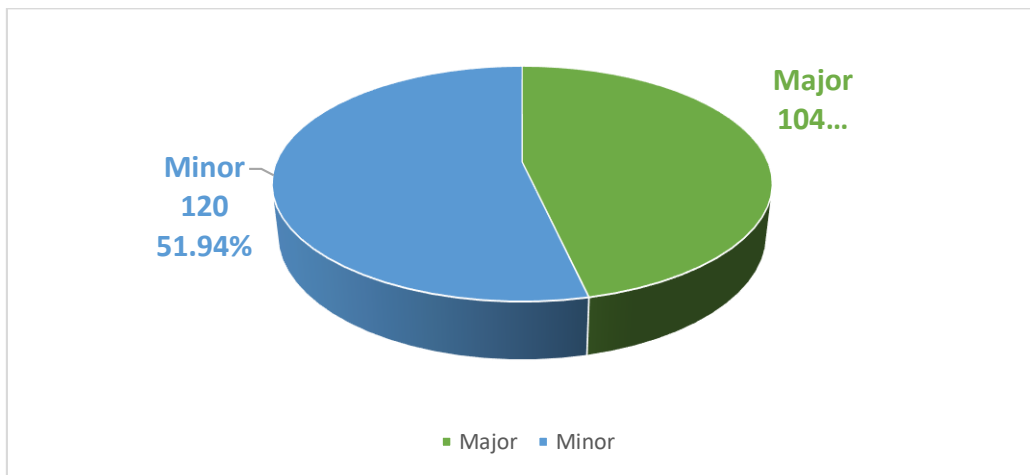


Figure (5): Pie chart representing location distribution among salivary gland neoplasm cases

The behavior of the tumors (malignant vs benign neoplasms) was evaluated, the major salivary glands were the most affected mainly by benign neoplasms while

the minor salivary glands were the most affected mainly by malignant neoplasms ( $p < 0.05$ ), results were statistically significant Table (1).

Table (1): Anatomic site, gender, and age group distribution of benign and malignant salivary gland neoplasm cases

		Benign		Malignant		Total		P value
		n	%	n	%	n	%	
Anatomic site	Major salivary glands	82		22		104	45.02	P < 0.05 <sup>a</sup>
	Minor salivary glands	58	48.3	62	51.7	120	52.0	
	NI	1	14.3	6	85.7	7	3.0	
Gender	Female	71	62.3	43	37.7	114	49.4	0.7874 <sup>b</sup>
	Male	70	59.8	47	40.2	117	50.6	
Age	19 ≤	8	61.5	5	38.5	13	5.6	1 <sup>b</sup>
	≥ 20	131	61	84	39	215	93.1	
	NI	2	66.7	1	33.3	3	1.3	

NI: Not informed; %: Percentage; a Pearson's Chi-square test; b Fisher's exact test.

## Discussion

Epidemiological data of benign or malignant SGNs is not well established due to the wide variation in their incidence and prevalence across countries, designating a geographic variation particularly in relation to anatomical location and histological subtypes of these neoplasms (**Cunha et al., 2020**). The dynamic classification of SGNs, recent advances in IHC and application of FISH for molecular cytogenetic analysis result in continuous specific and refined changes in SGNs entities. Thus, ongoing epidemiological studies of SGNs are necessary to improve understanding of their clinical and pathological characteristics and are essential to keep physicians and surgeons up to date (**de Silva et al., 2018**).

Several studies were documented in African populations in addition to European, American and Asian ones. Furthermore, in our knowledge, there are no studies available in the English literature about the relative frequency of salivary gland neoplasms in Egypt or, in particular, Cairo city, according to the 2017 WHO classification. The prevalence of SGNs was found to be 231 cases (2.4 %) out of 9609 oral and maxillofacial biopsies, registered during the 10 years' period from January 2010 to December 2019. Similarly, a closer prevalence of (2.75%), (3%) and (2.6%) were reported in Southern Iran, Iran and Brazil respectively (**Jaafari-Ashkavandi et al., 2013, Taghavi et al., 2016, da Silva et al., 2018**) in addition to a prevalence of (1.5%) reported in a single institutional study in Saudi Arabia (**Al Sheddi, 2016**) and a single private practice study over a 20-year period in Mexico (**Cunha et al., 2021**). Other epidemiological studies performed among African populations in Kenya and Nigeria reported a higher prevalence of (5.4%) and (7.9%) (**Bahra et al., 2012, Fomete et al., 2015**).

In the current study, the majority of SGNs were benign accounting for 141 (61.1%), in accordance with most of the reported studies (**Araya et al., 2015, Bittar et al., 2015, Noel et al., 2018, Reinheimer et al., 2019, Mengi et al., 2020 and Cunha et al., 2020**) suggesting that benign neoplasms predominate among SGNs worldwide, while the remaining 90 (38.9%) were malignant. However, malignant SGNs were reportedly higher than benign ones in studies performed among the African population (**Bahra et al., 2012 and Lawal et al., 2013**) and in Iran (**Taghavi et al., 2016**).

In this study, Pleomorphic adenoma was the most frequent type of benign SGNs, representing (68.8%) followed by warthin tumor (14.2%), in accordance with majority of reported studies (71%; 22%), (79.06%; 18.6%) in United Kingdom, Brazil and Turkey (**Bradley and McGurk, 2013, Vasconcelos et al., 2015 and Mengi et al., 2020**) in addition to other studies in Southern Iran, United Arab Emirates, Cameroon and Ghana (**Jaafari-Ashkavandi et al., 2013, Al Sarraj et al., 2015, Sando et al., 2016, Parkins et al., 2021**).

Mucoepidermoid carcinoma was the most frequent type of malignant salivary gland neoplasms in the present study, representing (46.7%) followed by ACC (28.9) in accordance with reported studies in United Arab Emirates, Valparaíso-Chile, Brazil and Syria (**Al Sarraj et al., 2015, Araya et al., 2015, Bittar et al., 2015 and Alnour, 2017**).

The differences in subtypes of the benign and malignant categories of SGNs in our study in comparison to other reported studies could be linked to the lack of consistent histomorphologic criteria for diagnosis, different classifications and time of experience and acquaintance of pathologists with these lesions (**Cunha et al., 2021**). The mean age of benign SGNs was  $40.24 \pm 14.87$  years while the mean age of malignant ones was  $42.54 \pm 16.26$  years pointing out to the predilection of malignant SGNs for older patients in agreement with different studies conducted in Iran, Nigeria and Brazil with reported mean ages of  $45.87 \pm 17.88$ ,  $44.5 + 15.1$  and  $55 \pm 16$  (**Saghravanian et al., 2013, Fomete et al., 2015 and da Silva et al., 2018**).

According to the WHO 2017, female patients are slightly more affected by SGNs than male patients (**Seethala and Stenman, 2017**) in agreement with the majority of the studies conducted in different countries; India and Valparaiso, Chile (**Laishram et al., 2013 and Araya et al., 2015**), Syria (**Alnour, 2017 and Alsharif and Alhoms, 2020**), However, in the present study, a slight male predominance (50.64%) was reported in accordance with studies conducted in Iran (**Shishegar et al., 2011 and Jaafari-Ashkavandi et al., 2013**), China (**Wang et al., 2015 and Shen et al., 2018**), Turkey (**Kızıl et al., 2013 and Mengi et al., 2020**) and United Arab Emirates (**Al Sarraj et al., 2015**).

In the present series, minor salivary glands (51.94%) were more involved than major ones (45.02%) in accordance with a single private practice study in Mexico where 68.9% were situated in the minor salivary glands (**Cunha et al., 2021**). On the contrary, major salivary glands were more commonly involved in several studies in Nigeria (**Fomete et al., 2015**), Northern China (**Gao et al., 2017**), Brazil (**Cunha et al., 2020**) and Taiwan (**Liao et al., 2020**). Clearly, the

proportion of major and minor SGNs is variable across different types of hospitals where patients with minor SGNs located in the oral cavity first seek treatment at primary care centers unlike patients with major SGNs treated at tertiary care centers.

Finally, it was greatly hard to make an adequate comparison between the published studies from different periods about the relative prevalence of SGNs due to the changes that have occurred over the years in the classification of SGNs, whereas the definitions of some entities have been changed or new ones were introduced. Moreover, most of the international studies reviewed in this study, were conducted before the 2017 WHO classification of SGNs, a situation that does not allow a proper comparison to be made.

### **Conclusions**

Based on this study results the following are concluded: A marked geographic variation in the relative frequency of various salivary gland neoplasms was observed. Some similarities and discrepancies between our study and previous studies from Africa, Asia, Europe, and America were noted. The variations in the relative frequency of salivary gland neoplasms observed among several studies, including the present study, may be related to different elements in the study design, which would require further research. Following 2017 WHO classification, Pleomorphic adenoma remains the most frequent benign salivary gland neoplasm and mucoepidermoid carcinoma, the most common malignant salivary gland neoplasm in our settings. Also, benign salivary gland neoplasms are more common than malignant ones. Minor salivary glands were more commonly involved than major ones. Parotid gland was the most frequent location among major salivary glands while the palate was the most frequent location among minor ones.

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**Conflict of Interest:** The authors have no conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

**Regulatory Statement:** This study was approved by the Research Ethical Committee at Faculty of Dentistry, Cairo University (Approval code: 19 9 30). Permission was obtained from Cairo's educational hospitals and institutions to access the database used for this study.

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