

ORIGINAL ARTICLE

Primary malignant epithelial salivary gland tumors in an Iranian population: A retrospective study of 81 cases

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ABSTRACT

Background: Salivary gland tumors of epithelial origin are rare lesions. Few epidemiologic studies on prevalence of such condition in Iranian population have been published. This study with the aim of determining the relative frequency of epithelial salivary tumors was performed in Yazd city from 2001 to 2012. **Materials and Methods:** Cases diagnosed as primary malignant epithelial salivary gland tumor were collected from the Pathology Department of main hospitals and Health Department of Medical Science Yazd University from 2001–2012. Histopathologic type, tumor location, age, gender and whether patients were native or non-native were analyzed. **Results:** Eighty-one cases of primary malignant epithelial salivary gland tumors were recorded. Male to female ratio was 1:1.3. The most common malignancy was adenoid cystic carcinoma (35.8%) and the most common effected site was the parotid gland. Mean age for malignancy was 52.57 ± 18.25 years. **Conclusion:** According to the findings of this study, predilection of adenoid cystic carcinoma was more in non-natives as compared to natives (from Yazd). This could suggest the influence of racial and environmental factors on prevalence of such malignancies.

Key words: Adenoid cystic carcinoma, epithelial origin, salivary gland tumors

INTRODUCTION

Epithelial Salivary gland neoplasms are relatively uncommon accounting for less than 1% of all tumors and 3–10% of all head and neck tumors.^[1-3] According to epidemiological studies, the annual incidence of these tumors is 0.4 to 13.5 cases in 100,000 persons.^[4-8] These neoplasms are a diverse group of benign and malignant neoplasms with different clinical behaviors and histopathological features.^[9-11]

Worldwide reports show differences in incidence, prevalence and histological types of these neoplasms.^[11-13] Tumor location, age and sex distribution of salivary neoplasms varies depending on race and geographical conditions.^[9-11]

Based on our review of the English^[14-17] and Persian literature^[18,19] few scattered reports of epidemiological characteristics of salivary gland tumors in Iranian population exist.

This study examines the prevalence of salivary gland neoplasms of epithelial origin from 2001–2012 in Yazd city. Yazd is a medical hub in the center of Iran, which provides services to many patients from south and southeast neighboring provinces. This offers a mixture of cases with regards to histopathological nature of lesions, anatomical location, age, sex and whether patients were native or non-native. These factors were evaluated for all cases.

MATERIALS AND METHODS

In this cross-sectional study, data were collected from records available in the Pathology Department of main hospitals and Health Department of Medical Science from 2001–2012. Any diagnosis of primary malignant head and neck salivary gland tumor in major or minor salivary glands with the exception of metastatic tumors were gathered and decoded to protect the identity of patients. Using SPSS 17 software, statistical

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analysis was performed on histopathological diagnosis, tumor location, age, gender and whether patients were native or non native.

RESULTS

From 2001–2012, 15,391 cases of malignancies were reported in the city of Yazd. Of those, 81 (0.52%) cases were primary salivary gland neoplasms of epithelial origin. The Most common tumor was adenoid cystic carcinoma (35.8%), followed by mucoepidermoid carcinoma (27.16%) [Table 1].

Age of patients ranged from 10–100 years with the mean age of 52.57 ± 18.25 years. Peak incidence for salivary gland tumors was between fourth and sixth decades of life and adenoid cystic carcinoma was most prevalent in this age group (55.2%) [Table 1].

With regards to gender distribution, 43.3% were male and 56.8% were female. The male to female ratio was 1:1.3. The Most common tumor reported in males was mucoepidermoid carcinoma (13.58%) and in females was adenoid cystic carcinoma (23.45%) [Figure 1].

As to anatomical location, 54.3% of cases developed in parotid gland, 32.1% were in minor salivary glands, 11.1% in submandibular gland and 2.5% formed in sublingual gland. In minor salivary glands, palate was the most common site (38.5%), followed by sino-nasal tract (19.2%) and finally floor of the mouth (15.3%) [Figure 2].

Most common malignant tumor of parotid gland, submandibular gland, minor salivary gland were mucoepidermoid carcinoma (36.36%), adenoid cystic carcinoma (77.77%)

and acinic cell carcinoma (50%), respectively. In sublingual gland, both adenoid cystic carcinoma and primary squamous carcinoma were equally prevalent [Table 2].

Adenoid cystic carcinoma occurred most frequently in minor salivary glands (44.8% of cases). mucoepidermoid carcinoma was more prevalent in the parotid gland (72.7% of cases) and all of acinic cell carcinomas were found in the parotid gland (100% of cases). This was the same for polymorphous low grade adenocarcinomas which were all found in minor salivary glands (100% of cases) [Table 3].

Among the patients, 65.5% were native (from Yazd) and 34.5% were non-native, mostly from neighboring provinces of Kerman and Hormozgan [Figure 3]. The relative frequency of adenoid cystic carcinoma to mucoepidermoid carcinoma as the most common malignant tumors in natives was 1 to 1.1 and in non-natives was 1.8–1, respectively.

DISCUSSION

Primary salivary gland neoplasms with epithelial origin comprised 0.52% of all malignancies. This finding is consistent with studies done by Mendenhall *et al.*, (0.52%) and Speight *et al.*, (0.52%) and somewhat lower than Hashemi Pour's *et al.*, results (0.66%).^[7,15,20] The higher reported frequency in Hashemi Pour's study is possibly due to the inclusion of the non-epithelial malignant tumors and metastatic tumors as a part of salivary malignant tumors database.^[15]

Although the overall incidence of salivary gland malignancies compared to other salivary gland diseases is low,^[3,21] they are an important part of oral cancers after squamous cell carcinoma.^[22-28]

Table 1: Histopathological diagnosis and relative frequency of Primary epithelial malignant salivary gland tumors according to age

Tumor	Diagnosis	No (%)				Total	Mean age±SD
		20-40 years	40-60 years	60-80 years	>80 years		
Adenoid cystic carcinoma	29 (35.8)	7 (24.1)	16 (55.2)	5 (17.2)	1 (3.4)	29 (100)	49.55±16.2
Mucoepidermoid carcinoma	22 (27.2)	8 (36.4)	7 (31.8)	7 (31.8)	0 (0)	22 (100)	49.40±16.66
Acinic cell carcinoma	7 (8.6)	22 (28.6)	1 (14.3)	4 (57.1)	0 (0)	7 (100)	60.14±21.72
Polymorphous low grade adenocarcinoma*	4 (4.9)	1 (33.3)	0 (0)	1 (33.3)	1 (33.3)	3 (100)	60.00±30.8
Primary squamous cell carcinoma	4 (4.9)	0 (0)	1 (25)	2 (50)	1 (25)	4 (100)	67.00±13.63
Carcinoma ex-pleomorphic adenoma	3 (3.7)	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	3 (100)	51.33±14.22
Clear cell carcinoma	2 (2.5)	0 (0)	0 (0)	0 (0)	1 (50)	1 (100)	50.00±45.25
Basal cell adenocarcinoma:	2 (2.5)	0 (0)	0 (0)	2 (100)	0 (0)	2 (100)	74.50±4.94
Adenocarcinoma not otherwise specified	2 (2.5)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)	44.50±0.7
Myoepithelial carcinoma	1 (1.2)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	50.00
salivary duct carcinoma	1 (1.2)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	80.00
Lymphoepithelial carcinoma	1 (1.2)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	51.00
Small cell undifferentiated carcinoma	1 (1.2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10.00
Large cell undifferentiated carcinoma	1 (1.2)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	53.00
Sebaceous Carcinoma	1 (1.2)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	77.00
Total	81 (100)	19 (23.8)	31 (38.8)	24 (30)	4 (4.9)	80 (100)*	52.57±18.52

*One patient with polymorphous low grade adenocarcinoma did not provide age

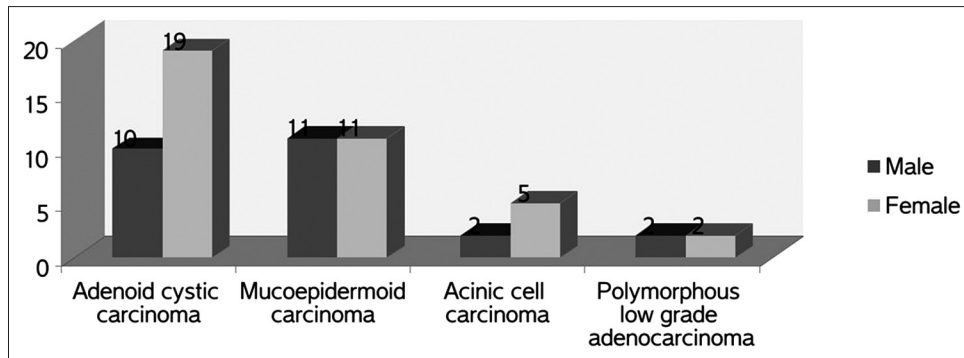


Figure 1: Relative frequency of four most common primary epithelial malignant salivary gland tumors according to gender

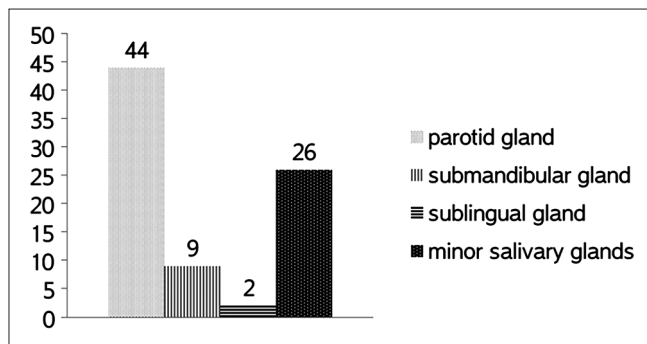


Figure 2: Relative frequency of primary epithelial malignant salivary gland tumors according to anatomical location

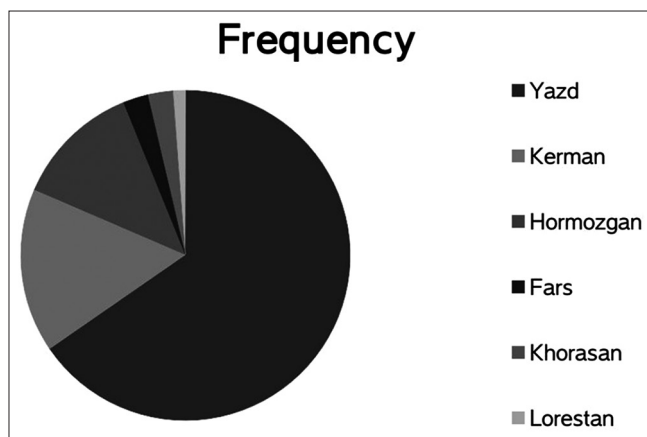


Figure 3: Relative frequency of primary epithelial malignant salivary gland tumors according to province of origins

The mean age and standard deviation for this study was 52.57 ± 18.52 years and most of salivary gland tumors were seen in patients between 40 and 60 years of age. In this age group, adenoid cystic carcinoma was the most common tumor. The mean age for the patients with malignant salivary gland tumors in Hashemi Pour *et al.*, study, in Kerman, was 47.33 years.^[15] In Vargas *et al.*, study, in Brazil, the mean age for such tumors was 48.8 years.^[3] Based on study of Oti *et al.*, in Africa, the mean age was 53.5 years and similarly Fonseca *et al.* result was 54 years for the same types of tumors. These results suggest that these malignant tumors are formed in late fourth decade to early fifth decade of life.

Comparison of the mean age of patients showed that minimum age belonged to Small cell undifferentiated carcinoma (10 years) and maximum age belonged to salivary duct carcinoma (80 years). Additionally, acinic cell carcinoma occurred in older population (60.14 years) compared to adenoid cystic carcinoma (49.55 years) and mucoepidermoid carcinoma (49.4 years).

In this study, the mean age of patients with adenoid cystic carcinoma was 49.55 years which was similar to Chau’s study (50 years).^[29] Similarly, other studies have shown that peak incidence of adenoid cystic carcinoma is in the fifth decade of life.^[19,30] Spafford *et al.*, in 1991, noted in their study that the mean age of patients with acinic cell carcinoma is a decade less compared to other parotid malignancies.^[31] While in this study acinic cell carcinoma’s mean age (60.14 years) occurred almost a decade later than adenoid cystic carcinoma (49.55 years) and mucoepidermoid carcinoma (49.4 years). This difference might be due to the differences in etiological factors of salivary gland tumors such as ionizing radiation, solar radiation, chemotherapy, smoking and vitamin A deficiency; even though these factors are not well recognized.^[28]

Results from this study revealed a higher incidence of malignant salivary gland tumors in females, with a ratio of 1:1.3. Similarly most studies showed that females are more frequently affected.^[7,31-34] Conversely in Oti *et al.* study in Ghana, male to female ratio was 1.8–1 and In Hashemi Pour *et al.*, study done in Kerman this ratio was 1.6–1.^[15,35]

Frequency ratio of male to female for adenoid cystic carcinoma and acinic cell carcinoma was 1:1.9 and 1:2.5, whereas for mucoepidermoid carcinoma and polymorphous low-grade adenocarcinoma this ratio was 1:1. Most studies performed in the west show equal gender presentation, whereas results from Africa show salivary gland tumor predilection for females.^[7,34] These different reports of malignant salivary gland tumors incidences between sexes could be due to limitations of females in some societies to seek medical treatment or conversely in other regions females paying more attention to

Table 2: Relative frequency of primary epithelial malignant salivary gland tumors according to types of salivary glands

Site	No (%)							
	Adenoid cystic carcinoma	Mucoepidermoid carcinoma	Acinic cell carcinoma	Polymorphous low grade adenocarcinoma	Primary squamous cell carcinoma	Carcinoma ex-pleomorphic adenoma	Clear cell adenocarcinoma	Basal cell adenocarcinoma
Parotid gland	8 (18.18)	16 (36.36)	7 (15.9)	0 (0)	3 (6.81)	2 (4.54)	1 (2.27)	1 (2.27)
Submandibular gland	7 (77.77)	1 (11.11)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11.11)	0 (0)
Sublingual gland	1 (50)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)
Minor salivary gland	13 (50)	5 (19.23)	0 (0)	4 (15.38)	0 (0)	1 (3.84)	0 (0)	1 (3.84)
Total	29 (35.8)	22 (27.16)	7 (8.64)	4 (4.93)	4 (4.93)	3 (3.7)	2 (2.46)	2 (2.46)

	No (%)							
	Adenocarcinoma (NOS)	Myoepithelial carcinoma	Salivary duct carcinoma	Lymphoepithelial carcinoma	Small cell undifferentiated carcinoma	Large cell undifferentiated carcinoma	Sebaceous Carcinoma	Total
Parotid gland	2 (4.54)	1 (2.27)	0 (0)	1 (2.27)	1 (2.27)	1 (2.27)	0 (0)	44 (54.32)
Submandibular gland	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	9 (11.11)
Sublingual gland	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (2.26)
Minor salivary gland	0 (0)	0 (0)	1 (3.84)	0 (0)	0 (0)	0 (0)	1 (3.84)	26 (32.1)
Total	2 (2.46)	1 (1.23)	1 (1.23)	1 (1.23)	1 (1.23)	1 (1.23)	1 (1.23)	81 (100)

Table 3: Relative frequency of salivary glands according to types of primary epithelial malignant salivary gland tumors

Tumor	No (%)				
	Parotid gland	Submandibular gland	Sublingual gland	Minor salivary gland	Total
Adenoid cystic carcinoma	8 (27.6)	7 (24.1)	1 (3.4)	13 (44.8)	29 (100)
Mucoepidermoid carcinoma	16 (72.7)	1 (4.5)	0 (0)	5 (22.7)	22 (100)
Acinic cell carcinoma	7 (100)	0 (0)	0 (0)	0 (0)	7 (100)
Polymorphous low grade adenocarcinoma	0 (0)	0 (0)	0 (0)	4 (100)	4 (100)
Primary squamous cell carcinoma	3 (75)	0 (0)	0 (0)	1 (25)	4 (100)
Carcinoma ex-pleomorphic adenoma	2 (66.7)	0 (0)	0 (0)	1 (33.3)	3 (100)
Clear cell carcinoma	1 (50)	1 (50)	0 (0)	0 (0)	2 (100)
Basal cell adenocarcinoma	1 (50)	0 (0)	0 (0)	1 (50)	2 (100)
Adenocarcinoma not otherwise specified	2 (100)	0 (0)	0 (0)	0 (0)	2 (100)
Myoepithelial carcinoma	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)
salivary duct carcinoma	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Lymphoepithelial carcinoma	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)
Small cell undifferentiated carcinoma	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)
Large cell undifferentiated carcinoma	1 (100)	0 (0)	0 (0)	0 (0)	1 (100)
Sebaceous Carcinoma	0 (0)	0 (0)	0 (0)	1 (100)	1 (100)
Total	44 (54.3)	9 (11.1)	2 (2.5)	26 (32.1)	1 (100)

their health. On the other hand these differences could suggest a role of hormones in histogenesis of salivary gland tumors.

Based on the results of this study, the most common salivary gland tumor was adenoid cystic carcinoma (35.8%) and the second most common tumor was mucoepidermoid carcinoma (27.2%). These results are consistent with results obtained in several studies.^[8,30,36-38] However, some studies have reported mucoepidermoid carcinoma to be the most common tumor.^[12,15,18,29,39-41]

Our results showed Acinic cell adenocarcinoma as the third most common tumor (8.64%) whereas in the study done

by Stene *et al.* it was the most common tumor.^[42] Fourth common malignant salivary gland tumor in this study was polymorphous low-grade adenocarcinoma (4.93%). Prior to 1991 some cases of this tumor were classified as pleomorphic adenoma or adenocarcinoma not otherwise specified. In addition, because of its similar morphologic features such as cribriform pattern and perineural invasion, the diagnosis may have been wrongly reported as adenoid cystic carcinoma.^[25] This may potentially be the reason as to why the incidence of such adenoid cystic carcinoma may be higher in this study keeping in mind that racial and geographical differences may also have influenced the results.^[43]

As to the anatomical location, 54.3%, 32.1%, 11, 1% and 2.5% of cases were reported to be in parotid gland, minor salivary glands, submandibular gland and in sublingual gland, respectively. These findings were similar to results of earlier studies done by Cawson and Eeson in 1985, Eeifert *et al.*, in 1986 and Spiro in 1986.^[25] In a study conducted by Vuhahala, in Uganda parotid gland, submandibular and minor salivary glands were equally affected. In some studies, palate was the most common site for salivary gland malignancies.^[43-45] These differences could be due to incomplete cancer registration in some communities.

Most common malignant tumors of parotid gland, submandibular gland and minor salivary gland were mucoepidermoid carcinoma (36.36%), adenoid cystic carcinoma (77.77%) and adenoid cystic carcinoma (50%), respectively. In sublingual gland, both adenoid cystic carcinoma and primary squamous carcinoma were equally prevalent. Conversely Oti *et al.*, in Ghana reported adenoid cystic carcinoma as the most common malignancy of parotid gland.^[35] In a study done in Brazil by Ito and colleagues, the most common malignancy of parotid gland was mucoepidermoid carcinoma.^[8]

Adenoid cystic carcinoma mostly occurred in minor salivary glands (44.8%); mucoepidermoid carcinoma was more prevalent in the parotid gland (72.7%) and all cases of acinic cell carcinoma and polymorphous low grade adenocarcinoma occurred in the parotid gland (100%) and minor salivary gland (100%), respectively. These results are consistent with studies done around the world^[14,16,46] and also contents listed in text books.^[25,47] Since the results show that some tumors have a tendency to occur in a specific salivary gland, it seems that attention to anatomical locations of lesions can help in diagnosis and classification of malignant salivary gland tumors.

In this study, 65.5% of patients were natives and 34.5% were non-natives from neighboring provinces of south and southeast of Iran. Based on the results of the study, the incidence of adenoid cystic carcinoma in non-natives was 1.8 times higher than mucoepidermoid carcinoma and in natives, this ratio was 1.1. Likewise, results of Ashkavandi *et al.*, study, in the south of Iran and also Shishegar *et al.*, in Shiraz showed that adenoid cystic carcinoma was the most common malignancy in south of Iran^[14,17] A study done by Atarbashi *et al.*, in Ahvaz located in the south of Iran reported mucoepidermoid carcinoma and adenoid cystic carcinoma, with small differences, as the two most common malignant tumors with 8.03% and 7.14% of cases, respectively. While Rahrotaban *et al.*, in the city of Qazvin located in north of Iran, reported mucoepidermoid carcinoma as the most common salivary malignancy in that region.

Results of the current study suggest that the increased frequency of adenoid cystic carcinoma as compared to mucoepidermoid

carcinoma is probably due to presence of non-native patients (predominantly from south and southeast region of Iran) and could confirm the concept that environmental and racial factors affect prevalence of malignant salivary gland tumors.

CONCLUSION

The most common primary salivary gland malignancy in the present study was adenoid cystic carcinoma and the parotid gland was the most common site of involvement for all salivary gland malignancies. Malignancies were most common in the non-native population. Results of this study suggest the important effects of racial and environmental factors on prevalence of malignant salivary gland tumors.

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