

***Original Article***

## **Malignant Salivary Glands Tumors in Kerman Province: A Retrospective Study**

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### **ABSTRACT**

**Introduction:** Malignant salivary glands tumors (MSGTs) are uncommon cancers. The most common site of these cancers is the parotid gland. Some investigations show these cancers preference for males than females. The majority of MSGTs arise in sixth decade of human life. According to the literature review for the present work, there is a few epidemiological researches about MSGTs in Iran and especially there isn't any study in Kerman province. So the aim of this study was investigation the incidence, sex, age, histological types, and site distribution of MSGTs in the Kerman province during the time period from March 1991 to March 2002.

**Methods and Materials:** Documents and records of 70 patients with MSGTs diagnosed from March 1991 to March 2002 were reviewed. The patients' records were analyzed based on gender, age, location, and histopathological type of the tumor. Data were analyzed by SPSS-13.5 statistical software using t-test, chi-square, and ANOVA tests.

**Results:** During this period of time, 70 cases (43 men, 27 women) of MSGTs had been diagnosed. Mucoepidermoid carcinoma was the most common cancer (30%) and the parotid was the most affected site (70%). The age range was 10-86 years old with the overall mean age of  $50.18 \pm 17.97$ .

**Discussion:** Despite a considerable volume of literatures written about MSGTs in many countries, the incidence of these cancers haven't as yet been thoroughly documented or analyzed in Iran. However, comparison between the findings of this study with the results of other investigations showed a relative consistency.

**Key words:** Salivary Glands, Malignant, Kerman.

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### **Introduction**

The three major salivary glands are parotid, submandibular, and sublingual ones. There are also thousands of minor salivary glands throughout the mouth, most of which are named based on their anatomic location (labial, buccal, etc)<sup>1,2,3</sup>. Different diseases such

as infections, inflammation, obstruction, functional disorders, and neoplasms affect the efficiency and normal function of the salivary glands<sup>4</sup>. Malignant tumors of the salivary glands represent a diverse group of neoplasms with varied biological behavior<sup>1,5</sup>.

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Although in a general population, the incidence of salivary gland cancers is relatively low, in comparison to the other salivary gland diseases<sup>4,6</sup>, they constitute a significant proportion of oral tumors after squamous cell carcinoma<sup>7-13</sup> and it has been estimated that they are about 0.3% of all cancers<sup>13</sup>. The annual incidence of MSGTs in different countries ranges from about 1 to 6.5 cases per 100000 people<sup>1,6,7,9,10,11,13</sup>. The MSGTs account for 5-9% of all oral cancers<sup>1,9,14</sup> and about 1-7% of all cancers diagnosed in the head and neck region<sup>15,16,17</sup>.

Approximately 13-30% of parotid gland tumors and 50% of submandibular gland tumors are malignant. In contrast, more than 60% of tumors in the sublingual and minor salivary glands are malignant<sup>6,14</sup>, although the parotid gland is the most common location of malignant salivary gland tumors<sup>3,7,13,17</sup>.

The age of patients with MSGTs is widely distributed<sup>4</sup>. In many studies it was reported that MSGTs are more common in 5<sup>th</sup> to 7<sup>th</sup> decades<sup>16,18</sup>. MSGTs are uncommon in children<sup>19,20</sup>. Approximately 2.5-5% of all MSGTs occur in children and adolescents<sup>10,19,20</sup>.

The sex distribution of these neoplasms is also reported differently by different authors. A Jordanian study shows a slight male preponderance<sup>8</sup>. In another study by Saki and Nik Akhlagh in Ahvaz, it was reported that the male to female ratio is about 4.1 to 1 in the patients with MSGTs<sup>21</sup>. Although, some researches show that the malignant tumors are more frequent in women than in men<sup>8,9</sup>, but in other studies, malignant tumors have an equal sex distribution of<sup>12</sup>.

Etiology of MSGTs hasn't been known yet. There are many factors affecting the development of tumors. Ionizing radiation, breast cancer, alcohol abuse, exposure to sunlight, chemotherapy, the history of previously diagnosed benign salivary gland tumors in young age, and infection with herpes virus and human immunodeficiency virus are the main factors. Several different factors are also mentioned in literatures such

as use of hair dye, hair sprays, and low intake of vitamin A<sup>12,15</sup>.

There are a few epidemiological researches about MSGTs in Iran. Since the prevalence of MSGTs depends strongly on the etiological factors and geographical conditions, therefore it is necessary to do similar studies in different parts of the world. So, the goal of this study was to analyze the prevalence of 70 malignant primary cancers of the major and minor salivary glands in Kerman province retrospectively between March 1991 and March 2002.

## Methods and Materials

This work is a retrospective analysis that represents the first population-based study about the status of MSGTs in Kerman province from March 1991 to March 2002. Since in the time period of doing the present research, there was not any so established cancer registry center for getting accurate data, consequently, the data included in this study were collected from all of the 18 histopathology laboratories around the Kerman province. These laboratories had received almost all biopsy specimens from Kerman province. Because of accessibility to diagnostic tools around the province, and long distances between the crowd centers in Kerman province and the major cities in neighboring provinces, we believe that few cases might be missed. Cases with grossly incomplete information, repeated biopsies, or double registered cases were carefully excluded from the study. Also only cases of primary MSGTs were considered in this study; no recurrent, in situ, or benign lesions were included. In the present research, the patients information were analyzed based on sex, age, histopathological type, and site of the tumor. This data were analyzed by SPSS-13.5 statistical software using t-test, chi-square, and ANOVA tests.

## Results

During this eleven years, 10571 new cases of malignancy were diagnosed in Kerman province. The malignant salivary gland tumor was the 26<sup>th</sup> common body cancer.

They comprised 26.61% of all oral neoplasms. MSGTs were about 2.58% (70/2713) of head and neck cancers and 0.66% (70/10571) of body cancers. The incidence of MSGTs was 0.32/100000 per year (0.36/100000 in men, 0.27/100000 in women).

Out of a total number of the 70 cases, 41 cases (61.4%) were male and 27 (38.6%) were female. The male: female ratio was 1.6:1. The relation between sex and the appearance of salivary gland cancers was statistically significant ( $P<0.05$ ). The mean age was  $50.18 \pm 17.97$  (males  $49.86 \pm 19.08$  and females  $50.72 \pm 16.26$ ) with an age range of 10-86 years old. Most of cases were in the third, fourth, and sixth decades of life with a peak incidence in the sixth decade. The age and sex distributions of these cases are shown in Table 1.

**Table 1. Age and sex distribution of malignant salivary gland tumors.**

Age(years)	Male	Female	Total (%)
0-9	-	-	-
10-19	4	2	6(8.8)
20-29	1	1	2(2.9)
30-39	10	5	15(22)
40-49	4	7	11(16.3)
50-59	5	2	7(10.3)
60-69	11	6	17(25)
70-79	5	4	9(13.3)
80-89	1	0	1(1.4)
Total	41	27	68(100)

In 57 patients, the tumors were located in major salivary glands (49 in the parotid, 6 in the submandibular, and 2 in the sublingual salivary glands) and in 13 patients in minor salivary glands. The mean ages of the minor and major malignant neoplasms were  $40.23 \pm 17.76$  and  $52.53 \pm 17.36$ , respectively (Table 2).

Among the MSGTs, mucoepidermoid carcinoma was the most prevalent one (21 cases, 30%), followed by adenocarcinoma (18 cases, 25.7%), and adenoid cystic

carcinoma (15 cases, 21.4%). The distribution of each type of salivary gland neoplasms per site of biopsy is shown in Table 3.

Mucoepidermoid carcinoma cases had a mean age of  $47.6 \pm 22.91$  with a range of 10-75 years old and the male to female ratio was 2:1. It's predominantly seen in the parotid gland (70%). The relation between sex and site of mucoepidermoid carcinoma was statistically significant ( $P<0.05$ ). The distribution of different malignant salivary gland tumors by sex, diagnosis, mean age, male/female ratio, and age range is shown in Table 4.

## Discussion

The results obtained in the present work show that the malignant salivary gland tumors comprised 26.61% of all oral cancers. MSGTs were about 2.58% of head and neck cancers and 0.66% of body cancers. The incidence of MSGTs was 0.32/100000 per year.

Malignant salivary glands are uncommon entities among the patients with head and neck cancers <sup>22</sup>. Their annual incidence appears to be higher in western publications which may be due to the fact that these were based on the centralized treatment centers <sup>16</sup>. Also ethnicity and geographic location of a population apparently have an effect on the frequency of MSGTs <sup>8</sup>. A higher incidence of malignant tumors of salivary glands is reported in Americans compared with the British and a greater incidence has been reported amongst the Eskimos <sup>23</sup>.

Results of this study are in agree with those obtained by Kasangaki & Kamulegeya (2004), Kolude et al (2001), Koivunen et al (2002), Ostemann (1997), and Abiose et al (1990) <sup>4,13,24,25,26</sup>.

In this study, a higher incidence of salivary gland cancers was found in males (61.4%) than in females (38.6%) with the peak incidence in the 6<sup>th</sup> decade. This is a good consistency between the present results with several researches in other countries <sup>27,11</sup>.

**Table 2 . The minor and major malignant salivary gland tumor: distribution by sex, Mean age, M/F ratio, and Age range.**

Diagnosis	Mean age	Age range	Male	Female	M/F ratio	Total (%)
Minor MSGTs	40.23	10-72	6	7	0.86	13(18.6)
Major MSGTs	52.53	10-86	37	20	1.85	57(81.4)
Total	50.18	10-86	43	27	1.6	70(100)

**Table 3. Site distribution of malignant salivary gland tumors.**

Type of tumor	Parotid	Submandibular	Palate	Lip	Sublingual	Cheek	Total (%)
Mucoepidermoid carcinoma	14	2	2	-	-	3	21(30)
Adenocarcinoma	14	1	1	-	1	1	18(25.7)
Adenoid cystic carcinoma	7	1	5	1	1	-	15(21.5)
SCC lymphoma	3	2	-	-	-	-	5(7.15)
Undifferentiated carcinoma	4	-	-	-	-	-	4(5.7)
Acinic cell carcinoma	1	-	-	-	-	-	1(1.4)
Metastatic	1	-	-	-	-	-	1(1.4)
Total	49(70)	6(8.58)	8(11.45)	1(1.42)	2(2.85)	4(5.7)	70(100)

**Table 4.The different malignant salivary gland tumors: distribution by sex, diagnosis, Mean age, M/F ratio, and Age range.**

Diagnosis	Mean age	Age range	Male	Female	M/F ratio	Total (%)
Mucoepidermoid carcinoma	47.6	10-75	14	7	2	21(30)
Adenocarcinoma	54.17	38-86	12	6	2	18(25.7)
Adenoid cystic carcinoma	47.33	32-75	6	9	0.66	15(21.5)
SCC lymphoma	61.6	50-73	4	1	4	5(7.15)
Undifferentiated carcinoma	52.4	16-70	3	2	1.5	4(5.7)
Acinic carcinoma	40	22-65	4	-	-	1(1.4)
Metastatic	40	40	-	1	-	1(1.4)
Total	50.18	10-86	43	27	1.6	70(100)

It is reported in some studies that the incidence of MSGTs in females is more than in males<sup>16,18,28</sup>. This inconsistency in different reports can be due to this fact that in some regions, females are confined to their homes and don't come for treatment. As another reason, one can mention to this reality that the number of males and females in a society population is different that can affect the incidence of MSGTs in men and women.

The average age was 50.18 years of old for malignant tumors with an age range of 10-86 and most cases were in the fourth, fifth, and seventh decades of life. This result is compatible with some studies in which MSGTs were observed in all ages but the highest incidence was in 4<sup>th</sup>, 5<sup>th</sup>, and 7<sup>th</sup> decades<sup>16,18,29</sup>.

Also in this study, mucoepidermoid carcinoma (21cases) was the commonest malignancy. Mucoepidermoid carcinoma is the commonest salivary gland malignancy and makes up 4.2 - 12% of all salivary gland neoplasms<sup>17</sup>. It develops most commonly in the major salivary glands, most often in the parotid (45-70%)<sup>30</sup>. In several studies, mucoepidermoid carcinoma was found as the commonest cancer of salivary glands which is in consistency with the result of the present study<sup>8,26,25,29,31</sup>, although in some researches, adenoid cystic carcinoma is reported as the commonest cancer<sup>32,27,33</sup>.

Other malignant tumors of the salivary glands are found less often. Their incidence is reported to range from 0.1 to 5%<sup>17</sup>. The range for these tumors is 1.4 to 25.7% in our study. The tumors including adenoid cystic carcinoma, adenocarcinoma, SCC, undifferentiated carcinoma, metastatic melanoma, acinic cell carcinoma and lymphoma.

Also in the study of Berjis and Sonbolestan<sup>31</sup> which was done in Isfahan, the commoner types of MSGTs were mucoepidermoid carcinoma (25.8%), lymphoma (19.35%), SCC (14.51%), adenocarcinoma (14.51%), metastatic tumors(9.67%), malignant mixed tumor(8/06%), acinic cell carcinoma (4.83%), and monomorphic carcinoma (3.22%).

Cancer location is a factor that may be important for its typing. It seems that each salivary gland is consistent with a special type of cancer. For example, in the study by Kolude et al, which was done in the Ibadan of Nigeria, adenoid cystic carcinoma has a predilection for the submandibular gland<sup>26</sup>.

The commonest site for MSGTs in Kerman population was the parotid (70%) which is in agreement with the results obtained in several studies<sup>4,17,22,29,24,26,32</sup>. Although, it is seen in some researches that palate is reported as the commonest site of malignancies<sup>33,34</sup>.

It seems that the differences in the results of many studies in reporting the location of MSGTs are due to the differences in the ratio of major to minor salivary gland cancers. Because, based on many researches, the commonest site in major salivary glands is parotid and in minor salivary glands is palate<sup>29,36,35</sup>.

Despite a considerable volume of literature written about MSGTs in many countries, the incidence of these cancers hasn't yet been thoroughly documented or analyzed in Iran. However, comparison between the findings of this study with the results obtained by other investigators shows a relation consistency.

## References

1. Harrison IB, Session RB, Ki Hong W. Head and Neck Cancer. Lippincott Williams Wilkins; Philadelphia, 1999: p. 309, 721-24.
2. Daley T, Tarling M. Nonsquamous cell malignant tumors of the oral cavity: An over review. J. Canada Dent Assoc 2003;69(9):577-582.
3. Prabhu SR, Wilson DF, Daftary DK, Johnson NW. Oral diseases in the Tropics. Oxford Medical Publication; United States, 1992: p.478-79.
4. Kasangaki A, Kamulegeya A. Neoplasms of the salivary glands: A descriptive retrospective study of 142 cases-Mulago Hospital Uganda. J Contemp Dent Prac 2004;5(3):1-11.

5. Waldron CA, Mofty SK, Gnepp DR. *Tumors of intraoral minor salivary glands: A demographic and histologic study of 426 cases.* Oral Surg Oral Med Oral Pathol 1988;66(3):323-333.
- 6- Vargas PA, Gerhard R, Araujo Filho VJF, de Castro IV. *Salivary gland tumors in Brazilian population: A retrospective study of 124 cases.* Rev Hosp Clin 2002; 57(6):271-276.
7. Neville BW, Damm DD, Allen CM, Bouquot JE. *Oral and Maxillofacial Pathology.* 2<sup>nd</sup> ed. W.B Saunders; Philadelphia, 2002: p.406-7.
8. Loyola AM, de Araujo VC, de Sousa SO, de Araujo NS. *Minor salivary gland tumors. A retrospective study of 164 cases in a Brazilian population.* Oral Oncol. 1995;31(3):197-201.
9. Shah JP. *Cancer of head and neck.* BC Decker Inc; London, 2001: p.240,242-45.
10. Yu GY, Li ZL, Ma DQ, Zhang Y. *Diagnosis and treatment of epithelial salivary gland tumors in children and adolescents.* Br J Oral Maxillofac Surg 2002;40:389-92.
11. Jansisyanont P, Blanckaert R, Robert A. *Intraoral minor salivary gland neoplasm: A single institution experience of 80 cases.* Inter J Oral Maxillofac Surg 2002;31(3):257-61.
12. Licitra L, Grandi C, Prott FJ, et al. *Major and minor salivary glands tumors.* Crit Review Oncol Hematol 2003;45(2):215-22.
13. Koivunen P, Suutala L, Schorsch I, Jokinen K, Alho OP. *Malignant epithelial salivary gland tumors in Nourth Finland: Incidence and clinical characteristics.* Eur Arch Otorhinolaryngol 2002;259:146-49.
14. Greenburg M, Glick M. *Burket's Oral Medicine.* 10<sup>th</sup> ed. BC Decker Inc; Hamilton, 2003: p. 235.
15. Spohn M. *Support for people with oral and head and neck cancer.* <http://www.spohn.org>.
16. Shafkat A, Mohainmad L, Pouf A. *Clinicopathological study of primary salivary gland tumors in Kashmir.* JK-Prac 2002;9(4):231-33.
17. Ma'aita J K., Al-Kaisi N, Al- Tamimi S, Wraikat A. *Salivary gland tumors in Jordan: A Retrospective Study of 221 Patients.* Clin sci 1999;40(3):539-42.
- 18-Rahimi M. *Salivary gland tumors: A retrospective study of 104 cases.* J Mashhad Dent School 2000;1-2(24):80-4.
19. Hicks J, Flait ZC. *Mucoepidermoid carcinoma of salivary gland in children and adolescents: Assessment of proliferation markers.* Oral Oncol 2000;36:454-60.
20. Denis BP. *Salivary gland neoplasia in childhood.* Intern J Pedia Otorhinolaryngol 1999;49(1):235-38.
21. Saki N, Nik Akhlagh S. *Overview of a 15-year experience with benign and malignant tumors of submandibular gland.* Iran J Otorhinol 2004;36(16): 39-43.
22. Sousa J, DeSa O. *Salivary gland tumours: an analysis of 62 cases.* Indian J Cancer 2001;38(1):38-45.
23. Norman JE, Mc Gurk M. *Color atlas and text of the salivary glands.* Barcelona, Mosby; Spain, 1995: p. 173,175, 176,179, 199
24. Ostman J, Anneroth G, Gustafsson H, Tavelin B. *Malignant salivary gland tumors in Sweden 1960-1989-an epidemiological study.* Oral Oncol 1997;33(3):169-76.
25. Abiose BO, Oyejide O, Ogunniyi J. *Salivary gland tumors in Ibadan, Nigeria: a study of 295 cases.* Afr J Med Med Sci. 1990;19(3):195-9.
26. Kolude B, Lawoyin JO, Akang EE. *Salivary gland neoplasms: a 21year review of cases seen at University College Hospital, Ibadan.* Afr J Med Med Sci. 2001;30(1-2):95-8.
27. Luukkaa H, Klemi P, Leivo I, Koivunen P, Laranne J, Makitie A, et al. *Salivary gland cancer in Finland 1991-96: an evaluation of 237 cases.* Acta Otolaryngol. 2005;125(2):207-14.
28. Bell RB, Dierks EJ, Homer L, Potter BE. *Management and outcome of patients with malignant salivary gland tumors.* J Oral Maxillofac Surg. 2005;63(7):917-28.
29. Toida M, Shimokawa K, Makita H, Kato K, Kobayashi A, Kusunoki Y, et al. *Intraoral minor salivary gland tumors: a clinicopathological study of 82 cases.* Int J Oral Maxillofac Surg 2005;34(5):528-32.
30. Rice DH. *Malignant Salivary Gland Neoplasms.* Otolaryngol Clin North America 1999;35(5):875-86.
- 31- Berjis N, Sonbolestan SM. *Research of salivary gland tumors in medical science university hospitals of Isfahan.* J Isfahan Med School 1999;56(17):8-10.
32. Kayembe MK, Kalengayi MM. *Salivary gland tumors in Congo (Zaire).* Odontostomatol Trop. 2002;25(99):19-22.
33. Ledesma-Montes C, Garces-Ortiz M. *Salivary gland tumors in a Mexican sample. A retrospective study.* Med Oral 2002;7(5):324-30.
34. Poonsawat S, Punyasingh J, Weerapradist W. *A retrospective study of 60 cases of salivary gland tumors in a Thai population.* Quintessence Int. 2004 Jul-Aug;35(7):577-81.
35. Kusama K, Iwanari S, Aisaki K, Wada M, Ohtani J, Itoi K, et al. *Intraoral minor salivary gland tumors :A retrospective study of 129*

- cases. *J Nihon Univ Sch Dent.* 1997;39(3):128-32.
36. Waldron CA, Mofty SK, Gnepp DR. Tumors of intraoral minor salivary glands: A demographic and histologic study of 426 cases. *Oral Surg Oral Med Oral Pathol* 1988;66(3):323-33.