The frequency and distribution pattern of minor salivary gland tumors in a government dental teaching hospital, Chennai, India

Nandimandlam Venkata Vani, MDS, and Irulandy Ponniah, MDS, Chennai, India
DEPARTMENT OF ORAL AND MAXILLOFACIAL PATHOLOGY, TAMIL NADU GOVERNMENT DENTAL COLLEGE AND HOSPITAL

Objectives. Data are not available regarding distribution of minor salivary gland tumors from the specialist pathology setting in India. The purpose of this study was to determine the relative frequency and distribution of minor salivary gland tumors and to compare the data with pertinent studies.

Study design. The records and archival samples of the Department of Oral and Maxillofacial Pathology, Tamil Nadu Government Dental College and Hospital, Chennai, India, served as source material for this retrospective study. All cases with a diagnosis of minor salivary gland tumors recorded between 1971 and August 2008 were retrieved and reviewed.

Results. A total of 185 minor salivary gland tumors were identified with reference to the latest World Health Organization classification, representing a relative frequency of 1.52% over the study period of 37 years (1971-2008) from 12,147 biopsy samples. Malignant tumors (75%) predominated over benign tumors (25%). The age range was 12-82 years with a mean of 46 years. Mucoepidermoid carcinoma was the most frequent tumor (34%), followed by pleomorphic adenoma (22%), adenoid cystic carcinoma (15%), and polymorphous low-grade adenocarcinoma (10%). The overall gender distribution was almost equal. Palate was the most frequent involved site, followed by alveolar mucosa and floor of the mouth.

Conclusions. The present study shows a higher proportion of malignant tumors and a tendency toward male predilection during the past decades. The overall data are consistent with hospital-based studies from Asia and series from other geographic regions. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:e32-e39)

The global annual incidence for all salivary gland tumors as quoted by the World Health Organization (WHO), varied from 0.4 to 13.5 cases per 100,000 population. In India, the overall incidence of salivary gland tumors can be ascertained from cancer registries established under National Cancer Registry Programme (NCRP) by the Indian Council for Medical Research (ICMR). In general, the rate of incidence of salivary gland cancers are assessed based on the data (collected actively) provided by the cancer registries for health care planning. However, the geographic area and population covered by these registries are small compared with the larger area and total population in India. Furthermore, the possibility of repetition of cases is unlikely to be eliminated owing to the active nature of data collection by cancer registries from multiple hospital sources and others.

In the past 18 years, as retrieved from the PubMed database, there have been only a few recorded analysis of salivary gland tumors in the Indian population by institution-based studies. However, the reported numbers of minor salivary gland tumors were either negligible or showed wide differences in the relative frequency of distinct minor salivary gland tumors (MSGT) in a given population (Australoids/Dravidian). Furthermore, none of the earlier studies come from a specialist setting that diagnoses MSGT. Therefore, it would be prudent to obtain data on the distribution of MSGT from the oral pathology biopsy registry of an institution, the Tamil Nadu Government Dental College and Hospital under the Ministry of Health and Family Welfare, Government of Tamil Nadu, India, one of the oldest dental institutions that caters to the dental needs of a large population in one of the southern states in India (Tamil Nadu).

The purpose of the present study was to determine the relative frequency and distribution of MSGT between 1971 and 2008 and to compare the data with pertinent studies.

MATERIAL AND METHODS
This retrospective study was based on the files of histopathology reporting registry and archival samples of the Department of Oral and Maxillofacial Pathology, Tamil Nadu Government Dental College and Hospital, Chennai, India. The Indian population includes several...
major ethnic groups, such as Indocaucasoid, Mongoloid, and Australoid, and the linguistic family includes Austroasiatic, Tibeto-Burman, Indo-European, and Dravidian. The Australoid/Dravidian population is confined to southern India; their language family is further subdivided into Telugu, Kannada, Malayalam, and Tamil. The present study represents mainly the Australoid/Dravidian/Tamil population found in the southern Indian state of Tamil Nadu.

A total of 12,147 cases of oral and maxillofacial lesions were recorded between 1971 and August 2008. After necessary permissions were obtained from the authorities concerned, a manual search of the registries was undertaken to identify 209 cases as MSGT and another 8 cases identified from a review of odontogenic tumors. Information regarding outpatient/hospital number, age, gender, location, clinical provisional, and histopathologic diagnosis, and availability of glass slides and tissue blocks were double-checked for reliability and appropriateness.

Twenty-two cases, including 3 from review of odontogenic tumors, were excluded for lack of tissue blocks or other information, and 10 cases that failed to meet the criteria for salivary gland tumors were also omitted. Primary and recurrent tumors were compared and were considered as single entries. The final 185 cases were reassessed for their distribution characteristics and reclassified with reference to the recent WHO classification. Where necessary, sections were prepared for routine and special stains. On morphologic evaluation, consensus was reached for 177 cases, and immunohistochemistry (pancytokeratin, S100, glial fibrillary acidic protein (GFAP), vimentin, smooth muscle actin, and c-Kit) was used in 8 cases; 1 case of adenoid cystic carcinoma (ACC) was changed to salivary duct carcinoma (SDC). 2 cases of ACC were altered to pleomorphic adenoma (PA), 1 case each of adenocarcinoma not specified (NOS) and mucoepidermoid carcinoma (MEC) was altered to PA, and in 2 cases of PA and 1 case of basal cell adenocarcinoma (BCAC) immunohistochemistry supported the morphologic diagnosis. It may be noted that of the 185 cases, 44 cases comprising 11 benign MSGT (25%), 28 malignant MSGT (63%), and 5 odontogenic tumors (11%) were reclassified to yield 11 cases of benign and 33 cases of malignant MSGT. The data were entered into Microsoft Excel 2007 for analysis and graph formation.

**RESULTS**

Of the revised 185 MSGT (Table I), benign and malignant tumors comprised 25.4% and 74.6%, respectively. PA (87%) was the most frequently encountered benign tumor, and MEC (45.6%), ACC (19.5%), polymorphous low-grade adenocarcinoma (PLGA) (13%), NOS (10%), and BCAC (6.5%) were the most frequently encountered malignant tumors. Overall, MEC (34%) and PA (22%) were the most frequently encountered MSGT.

### Table I. Frequency of 185 minor salivary gland tumors and gender distribution

<table>
<thead>
<tr>
<th>Histologic type</th>
<th>Abbreviation</th>
<th>n</th>
<th>% within group</th>
<th>% overall</th>
<th>Male, n</th>
<th>Female, n</th>
<th>NS, n</th>
<th>M:F ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleomorphic adenoma</td>
<td>PA</td>
<td>41</td>
<td>87.23</td>
<td>22.16</td>
<td>18</td>
<td>23</td>
<td>0</td>
<td>1:1.27</td>
</tr>
<tr>
<td>Basal cell adenoma</td>
<td>BCA</td>
<td>2</td>
<td>4.25</td>
<td>0.18</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1:1</td>
</tr>
<tr>
<td>Cystadenoma</td>
<td>CYA</td>
<td>1</td>
<td>2.13</td>
<td>0.54</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Myoepithelioma</td>
<td>MYO</td>
<td>1</td>
<td>2.13</td>
<td>0.54</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Oncocytoma</td>
<td>ONC</td>
<td>1</td>
<td>2.13</td>
<td>0.54</td>
<td>0</td>
<td>0</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Sialadenoma papilliferum*</td>
<td>SP</td>
<td>1</td>
<td>2.13</td>
<td>0.54</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>47</td>
<td>100</td>
<td>25.4</td>
<td>22</td>
<td>25</td>
<td>0</td>
<td>1:1.1</td>
</tr>
<tr>
<td>Malignant</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>MEC</td>
<td>63</td>
<td>45.65</td>
<td>34.05</td>
<td>35</td>
<td>28</td>
<td>1</td>
<td>1.25:1</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>ACC</td>
<td>27</td>
<td>19.56</td>
<td>14.59</td>
<td>14</td>
<td>11</td>
<td>2</td>
<td>1:1.27</td>
</tr>
<tr>
<td>Polymorphous low-grade adenocarcinoma</td>
<td>PLGA</td>
<td>18</td>
<td>13.04</td>
<td>9.73</td>
<td>5</td>
<td>12</td>
<td>1</td>
<td>1:2:4</td>
</tr>
<tr>
<td>Adenocarcinoma not specified</td>
<td>NOS</td>
<td>14</td>
<td>10.14</td>
<td>7.57</td>
<td>10</td>
<td>4</td>
<td>0</td>
<td>2:5:1</td>
</tr>
<tr>
<td>Basal cell adenocarcinoma</td>
<td>BCAC</td>
<td>9</td>
<td>6.52</td>
<td>4.86</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>1:2:5:1</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
<td>CCC</td>
<td>2</td>
<td>1.45</td>
<td>0.89</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Salivary duct carcinoma</td>
<td>SDC</td>
<td>2</td>
<td>1.45</td>
<td>0.89</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1:1</td>
</tr>
<tr>
<td>Carcinoma ex pleomorphic adenoma</td>
<td>CXPA</td>
<td>1</td>
<td>0.72</td>
<td>0.54</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Mucinous adenocarcinoma</td>
<td>MAC</td>
<td>1</td>
<td>0.72</td>
<td>0.54</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Sebaceous carcinoma</td>
<td>SC</td>
<td>1</td>
<td>0.72</td>
<td>0.54</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>138</td>
<td>74.6</td>
<td>73</td>
<td>62</td>
<td>3</td>
<td>1:2:1</td>
<td></td>
</tr>
<tr>
<td>Benign + malignant</td>
<td></td>
<td>185</td>
<td>100</td>
<td>95</td>
<td>87</td>
<td>3</td>
<td>1:1:1</td>
<td></td>
</tr>
</tbody>
</table>

NS, Not specified.
* Dysplasia and carcinoma-in-situ in the exophytic component.
The 185 MSGT out of 12,147 oral biopsies represented a relative frequency of 1.52% over the study period (1971 to August 2008). Assessment over decades revealed a gradual increase in the number of MSGT, with a higher proportion of malignant MSGT in the past 2 decades and predilection toward male gender during the past decade (Table II).

As shown in Table III, the age of the patients ranged from 12 to 82 years, the average age was 46 years, and benign tumors occurred at a lower mean age than malignant tumors. Except for PLGA (men 55 years, women 46 years) and BCAC (men 63 years, women 45 years), no gender difference in the mean age was noted with other MSGT. PA (67%) and MEC (33%) were the MSGT that occurred in patients under 20 years of age, and SDC was the only MSGT that occurred at a significantly lower mean age, 25.5 years. The third to seventh decades accounted for most MSGT, with peaks for benign tumors in the fourth and fifth decades and for malignant tumors in the fifth and sixth decades. No gender significance was noted.

Table IV shows the palate (50.5%) to be the single most frequent site for both benign and malignant tumors, followed by alveolar mucosa (14.4%), oral floor (12.2%), buccal mucosa (7.7%), and intraosseous sites (5.5%). Palate was the most frequent site for PA and MEC, followed by ACC and PLGA. MSGT in the alveolar mucosa, floor of the mouth, buccal mucosa, and retromolar and intraosseous locations were invariably found to be malignant. Upper lip was the second most frequent site for PA (71%), whereas PLGA (29%) was the only malignant tumor that occurred in this location. MEC (60%) and PLGA (30%) were the most frequent intraosseous tumors.

DISCUSSION

In this study, the data obtained were compared with 43 institution-based studies representing different geographic regions. Review of the literature revealed that the relative frequency of MSGT from institutional studies ranges from 0.03% to 1.9% (Fig. 1). Minor salivary gland tumors in our study represented 1.52% of all oral biopsies.

The present study showed higher frequency of malignant tumors (75%) than benign tumors (25%) and a
steady increase in the frequency of malignant MSGT with more upward trend in the past 2 decades (Tables I and II). The relative proportion of malignant salivary gland tumors (both minor and major) according to the consolidated report by the NCRP for Chennai cancer registry was 0.49% in 1984-1993, 0.39% in 1990-2000, and 0.41% in 2001-2003 per 100,000 persons.\(^2\)\(^-\)\(^7\) This indicates that the incidence of salivary gland cancers shows a downward trend. Although our institution-based study revealed a steady increase in the frequency of malignant MSGT, this should not be construed as actual increase; rather it could be more likely attributed to case referral from government medical institutions.

The literature shows that the frequencies of benign and malignant tumors are consistent with different stud-
ies across geographic regions,\textsuperscript{11,28,33-38,40-46,48-50} which range from 50\% to 70\%; in only 2 studies was a higher frequency (benign 94\%\textsuperscript{26} and malignant 76\%\textsuperscript{16}) outside this range observed.

In the regional context, the frequency of malignant MSGT found in the present study (75\%) is considerably more than the range found in countries such as Japan (33\%-38\%),\textsuperscript{51,52} China (54\%-65\%),\textsuperscript{48-50} Thailand (53\%-69\%),\textsuperscript{46,47} Iran (56\%),\textsuperscript{41} and Jordan (45\%-46\%),\textsuperscript{42,43} and it is also more than the reported frequency of 57\% in the Sri Lankan population,\textsuperscript{44} which is geographically and genetically closer.\textsuperscript{53} Within India and especially in the state of Tamil Nadu and adjoining region, the study by Subashraj et al.\textsuperscript{12} (Pondicherry, near Chennai) found a lower frequency of 39\% malignant MSGT, whereas it was 70\% according to Durairajan et al.\textsuperscript{11} (Chennai). Those 2 studies and ours represent the same population groups (Dravidian/Tamil linguistics) and come from similar institutional settings.

The above observations indicate that the frequency of malignant MSGT might differ from region to region where geographic or ethnic factors have an affect. This seems to be the reason for the variations noted between neighboring countries, such as Japan, Thailand, Iran, and China, compared with our findings. However, when it comes to Sri Lanka and India or within the state of Tamil Nadu in India, it is difficult to attribute either ethnic or geographic factors. If ethnic affect can be attributed, it can explain the close figures between our findings (Chennai, benign 25\%, malignant 75\%) and those of Durairajan et al.\textsuperscript{11} (Chennai, benign 30\%, malignant 70\%) but needs further evidence to explain the difference from Subashraj et al.\textsuperscript{12} (Pondicherry [near Chennai], benign 61\%, malignant 39\%) for the same population group as ours and the similar frequency shown by Jansisyonant et al.\textsuperscript{16} (USA, benign 24\%, malignant 76\%) for an ethnically distinct population located in a Western geographic region.

In the present study, the age of patients ranged from 12 to 82 years (mean 46.11\textpm14.07 years), with peak incidence in the fifth and sixth decades of life for both genders (Table III). The higher mean age for malignant tumors, with rare exception,\textsuperscript{16} is similar to other reports.\textsuperscript{13,17-19,47,50,51} Analysis of gender predilection showed a female predominance in the present study (75\%) in all decades except the most recent; however, the overall distribution was not significant (male-female ratio 1.1:1). Female predilection has been reported by most studies,\textsuperscript{13-18,23,26,28,40,46,47,51,52} and only a few studies have reported equal distribution.\textsuperscript{19,22,27,36,37,50} The trend was different with malignant tumors, where male predilection was noted, similar to the observation by 2 other studies.\textsuperscript{19,50} The situation is also similar to the consolidated report published by the NCRP for the Madras metropolitan tumor registry, based in Chennai, India (Fig. 2).\textsuperscript{2,7} However, the data from the cancer registry show variable peaks compared with the gradual increase in the present study, except during 1981-90.

As in the present study, review of the literature revealed the palate as being the most commonly affected site.\textsuperscript{12,19,22,23,26,28,33-38,40,42,44,46,47,49-51} However, the anatomic distribution of MSGT found in the present study differs from other reported studies. Unlike most other reported series,\textsuperscript{12,19,22,23,26,28,33-36,40,42,44,46,49-51} where either the buccal or labial mucosa was identified as the second most common site, the present study found the alveolar mucosa (14.6\%) to be instead, which agrees with reports from Thailand.\textsuperscript{47} Alveolar mucosa was the third most common site in Sri
Lanka (12%) and in Philadelphia, USA (13%). The present study also found statistically significant correlation for malignant MSGT occurring at specific sites (Table IV), where tumors occurring in sites such as alveolar mucosa, floor of the mouth, retromolar, and intraosseous were invariably found to be malignant, whereas 66% of MSGT in the palate were malignant. The latter finding agrees with Jansisyonant et al.

The frequency of intraosseous MSGT (5.5%) found in the present study is within the global range of 0.2%-11%. Like us, Pires et al. and Buchner et al. reported the floor of the mouth, alveolar (15%), and buccal mucosa, was the most frequently affected site. The literature shows that the frequency of PA ranges from 42% to 100% of benign MSGT and 17% to 66% of all MSGT. As shown in Table I, PA, representing 87% of benign and 22% of all MSGT, was the most frequent among benign MSGT. However, the frequency of PA as a proportion of all MSGT is lower and agrees with other studies (<40% of MSGT) from different geographic regions but is at variance with the other study (58%) representing the same population group as the present study.

Another Indian study and that from Sri Lanka also reported lower figures, of 30% and 37%, respectively. This pattern of variability within similar population groups and geographic regions was also noted in studies from North America (21%-44%), South America (17%-53%), Europe (33%-56%), Africa (26%-51%), and Jordan (41%-51%).

The rest of the benign MSGT in this series, as in others, were negligible compared with studies from North America and Europe, especially regarding the frequency of canalicular adenoma (CA). In those series, a higher range of 3%-12% of MSGT was noted compared with the virtual absence of CA in others. In contrast, myoepithelioma (MYO) with a frequency of >6% of MSGT was noted in only a few series, from Uganda (9%), Nigeria (32%), Jordan (14%), and China (7%). The case is similar with BCA, with only 2 studies with figures of 3% and 8%. Interestingly, regardless of geographic, ethnic, or institutional setting, oncocytomas are almost nonexistent.

The above observations mainly emphasize 2 points: First, there is no racial or geographic relationship to the frequency of PA, because variations are found between both intra- and intergroup studies; and second, there is complete absence or negligible presence of MYO and CA in most series, notably the former in American and the latter in Asian subjects. In the latter context, although others might consider them to be due to differences in diagnostic interpretations, mere differences in interpretation alone would be unlikely to account for the consistent findings in Asian populations regarding CA, especially from large series, such as Tilakaratne et al., Tian et al., and Wang et al. Whether the variable frequencies of MYO and CA are linked to genetic or other factors needs to be addressed beyond speculation.

Of the malignant tumors, MEC, ACC, and PLGA were the most frequently encountered, followed by NOS and BCAC. MEC represented 34% of all MSGT and 46% of malignant MSGT. The literature shows that the proportion of MEC ranges from 7% to 46% of all MSGT and from 17% to 68% of malignant MSGT. In the present study, similarly to other reports, no significant gender predilection was noted, whereas many other studies showed female predilection. The mean age was 48 years (range 12-82 years) with peaks in the fifth and sixth decades of life. MEC was the only malignant tumor that occurred in the second decade of life in our series. The palate, followed by the alveolar mucosa, floor of the mouth, intraosseous, and buccal mucosa, was the most frequently affected site. The literature shows that the lower lip was the second most frequent site for MEC, but the present study found that to be the alveolar mucosa, which is similar to 2 other studies.

The second most common malignant MSGT is ACC, which accounted for 19.5% of malignant and 14.5% of all MSGT. The palate (37%), followed by the floor of the mouth (22%), alveolar (15%), and buccal mucosa (11%), was the most frequently involved site in our series. Like us, Pires et al. and Buchner et al. reported the floor of the mouth to be the second most frequent, whereas others have found it to be the third most frequent site.

The second most common malignant MSGT is ACC, which accounted for 19.5% of malignant and 14.5% of all MSGT. The palate (37%), followed by the floor of the mouth (22%), alveolar (15%), and buccal mucosa (11%), was the most frequently involved site in our series. Like us, Pires et al. and Buchner et al. reported the floor of the mouth to be the second most frequent, whereas others have found it to be the third most frequent site.

In the present study, like others, found no gender predilection, although a tendency toward female predilection has been reported. The mean age at diagnosis was 46 years (range 21-63 years) with peaks in the fifth and sixth decades of life. The mean age at diagnosis is 10 years lower than reported by others.

PLGA was the third most common malignant tumor, accounting for 13% of malignant MSGT and 10% of all MSGT. In agreement with other series, we found higher predilection for both site and gender distributions: 44% in the palate and 70% in women. It was
observed that PLGA show a lower frequency in Asian people, but our finding is at variance.

NOS is a heterogeneous group of tumors that could not be classified into a well defined specific category. It accounted for 10% of malignant and 7.5% of all MSGT in our study. The palate (33.3%) and alveolus (33.3%) were the most frequently involved sites, which is in accordance with Wang et al. Men (71%) were found to be affected more frequently than women, a finding in agreement with others.

BCAC occur mostly in the parotid gland and are considered to be rare in minor salivary glands. Nine cases accounted for 6.5% of malignant and 5% of all MSGT. The literature shows that BCAC occur at a frequency of 0.3%-3.7% of malignant tumors from some series (1-3 cases).12,14,19,28,30,34,51 whereas it was absent in other studies.10,11,13,15-18,20-24,26,27,29,31-36,38-47,49,50,52 The other malignant tumors found in this study were negligible to draw any comparison.

The order of the frequency of MEC, ACC, and PLGA in this study is also shared by others.13,15,16,18,22,28,29,32,33,36,44 A review of 41 series (present study included) reveals that MEC and ACC both occurred with almost equal frequency either as a first (51% and 49%, respectively) or second (41% and 46%, respectively) most frequent tumor, and the third most common tumor was either NOS (42%) or PLGA (34%).13,15,16,18,22,27-29,32,33,36,44 However, the patterns of frequency of common malignant MSGT differ between populations. As one moves from North American to Asian populations, a higher peak for MEC is evident in Americans, Africans, and southeast Asians, whereas Europeans and west Asians show a higher proportion of ACC,27-32,41-47 In contrast, PLGA is uncommon in South Americans, Africans, and west Asians, and southeast and east Asians, and NOS shows a higher proportion in these populations. Of the less frequent malignant MSGT, acinic cell carcinoma (AcCell) was infrequently found among Asians,10,12-14,51 carcinoma ex pleomorphic adenoma in Americans, and BCAC in all populations, with exceptions, in Europeans and south Asians.10,12,25,32,44,45

In conclusion, the present study found higher frequency of malignant tumors and predilection for male gender. Although the present study shows subtle differences both within India and in the neighboring regions, the overall data are consistent in some respects with hospital-based studies from Asia and other geographic regions.

The authors thank the Head of the Institution for granting permission to publish this work. They also thank all of the faculty, postgraduate students, and laboratory technicians who have served in the department for their invaluable efforts toward the diagnosis and preservation of vital sources of information and materials to accomplish this work more easily.

REFERENCES