

## ORIGINAL RESEARCH ARTICLE

# Benign and Malignant Neoplasms Affecting Periodontal Tissues: A Retrospective Study

Şivge Kurgan<sup>1</sup>, Canan Önder<sup>1,\*</sup>, Zeliha Güney<sup>2</sup>, Meral Günhan<sup>1</sup> and Ömer Günhan<sup>3</sup>

<sup>1</sup>Department of Periodontology, Faculty of Dentistry, Ankara University, Ankara, Turkey and <sup>2</sup>Department of Periodontology, Faculty of Dentistry, Yozgat Bozok University, Yozgat, Turkey and <sup>3</sup>Department of Pathology, Faculty of Medicine, TOBB University, Ankara, Turkey

\*Corresponding Author; gulec.canan@yahoo.com

## Abstract

**Purpose:** Oral neoplasms are the second most common oral lesions after reactive proliferative lesions. The aim of this study was to determine the distribution of the oral neoplasms by gender and age and to discuss clinical manifestations, diagnosis, and treatments of these lesions.

**Materials & Methods:** To collect the study material, a pathological retrospective archive analysis has been performed and 61 oral neoplasm cases were determined in a total of 423 samples. 61 biopsies and clinical data of patients were studied and classified based on their histopathologic diagnosis, age, gender and frequency.

**Results:** In our study, a total of 61 neoplastic lesions were examined, and the mean age was 45.5 ±18.2. The most common lesion in the oral neoplastic lesion was leukoplakia (n=15, 24.59%). This was followed by squamous cell carcinoma (SCC) (n =13, 21.31%) and squamous papilloma (n =11, 18.03%). The rest were gingival granular cell tumor, hemangioma, odontoma, lipoma, mucosal nevus, myxoma, ameloblastoma, leukemia, melanoma, lymphoma, and osteosarcoma.

**Conclusion:** This study provided important data on the frequency and histological distribution of oral benign and malign neoplasms. This study also highlights the diagnosis, and management of these oral neoplasms for the dentists.

**Key words:** leukoplakia; oral neoplasm; squamous cell carcinoma

## Introduction

A large variety of non-plaque periodontal lesions can develop in different oral tissues, from the oral mucosa to the fibrous connective tissue, cementum, and bone of the periodontium. Oral neoplasms (ON) are benign or malignant lesions that occur in the oral cavity. Among the malignant ones, squamous cell carcinomas (SCC) and salivary gland neoplasms such as mucoepidermoid carcinoma and adenoid cystic carcinoma are common. Oral malignant tumors have been reported as the 6th most common malignancy in Asia.<sup>1</sup> Gingival neoplasm (GN) is a rare disease that constitutes only a small subset of all oral neoplasms.<sup>2</sup> It represents less than 10% of all ON in Europe and the United States. However, it is the second most common malignancy in Japan, after tongue cancer.<sup>3</sup> GN is usually observed in the 6. and 7. decades, but it can be observed at much lower ages in developing countries.<sup>4,5</sup>

GN is often asymptomatic at onset; however, intraoral swelling or mass, ulceration, pain, prosthesis incompatibility, mobility, or

non-healing extraction wounds can be occurred.<sup>2-4</sup> These tumors often resemble inflammatory lesions that affect the periodontium, especially in their early stages, and this may lead to diagnostic delay.<sup>2,4</sup>

The etiology of these lesions may be genetic, traumatic, immunological.<sup>6</sup> Socio-economic status, smoking, alcohol addiction, malnutrition, viral infections, oral hygiene habits, presence of a family history of malignancy, and metal exposure are among the risk factors.<sup>7</sup>

The aim of this retrospective study was to give information about the clinical findings, etiologies, diagnostic processes, and treatment of neoplastic lesions in periodontal tissues and to determine the distribution of these lesions according to age, gender, and localization.

## Materials and Methods

Gingival localized biopsy results of 61 patients who were histopathologically diagnosed with oral neoplasia were included in this retrospective study. This study was approved by the Ankara University Faculty of Dentistry Clinical Research Ethics Committee (Ethics no: 10/02) in accordance with the Declaration of Helsinki (1964). Biopsy samples were obtained by examining the biopsy materials of the patients who applied to Ankara University Faculty of Dentistry Department of Periodontology, and the archives of Gülhane Medical School Department of Pathology and Private Gören Pathology Laboratory between 2010–2015.

ONs were classified into 14 groups: squamous papilloma, pigmented neoplasia, hemangioma, gingival granular tumor, odontoma, lipoma as benign tumors, and SCC, leukoplakia, lymphoma, leukemia, ameloblastoma, osteosarcoma as malignant tumors. Records with missing data and without histopathological section slides were excluded. The cases were grouped according to the characteristics such as demographic findings of the patient, regions, and number of the lesions, and histopathological diagnosis. Microscopic sections were examined by an experienced pathologist (ÖG). Age, sex, and anatomical location of lesions were obtained from medical records and analyzed for each lesion. In the evaluation of the data, descriptive statistical methods were used with SPSS 28.0.1.0 Software (SPSS for Windows v.28, IBM SPSS Inc., New York, NY, USA).

## Results

In our study, a total of 61 neoplastic lesions were examined, and the mean age was  $45.5 \pm 18.2$ . The most common lesion among ONs was leukoplakia ( $n=15$ , 24.59%). This was followed by SCC ( $n=13$ , 21.31%) and squamous papilloma ( $n=11$ , 18.03%). The rest were gingival granular tumor (GGT) ( $n=4$ , 6.55%), ameloblastoma, hemangioma and leukemia ( $n=3$ , 4.91%), melanoma and odontoma ( $n=2$ , 3.27%), lipoma, lymphoma, myxoma, nevus and osteosarcoma ( $n=1$ , 1.63%) (Figure 1).

### Gender

Table 1 shows the distribution of neoplastic lesions by gender. 26 of the 61 neoplastic lesions were found in women (42.62%), and 35 were in men (57.38%). The female/male ratio is 0.74:1. While leukoplakia and SCC were observed more frequently in males (respectively;  $F/M=4/11$ ,  $F/M=6/7$ ); the granular gingival tumor was observed more frequently in women ( $F/M=3/1$ ).

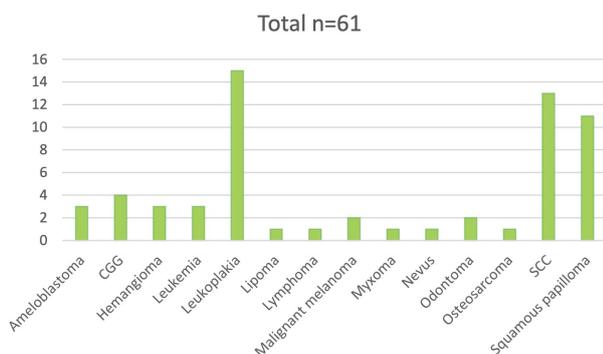


Figure 1. Distribution of neoplastic lesions between the groups

Table 1. Distribution of neoplastic lesions by gender

Lesion	Gender		Total n (%)
	Female n (%)	Male n (%)	
Ameloblastoma	1 (33.33%)	2 (66.67%)	3
GGT	3 (75%)	1 (25%)	4
Hemangioma	2 (66.67%)	1 (33.33%)	3
Leukemia	2 (66.67%)	1 (33.33%)	3
Leukoplakia	4 (26.67%)	11 (73.33%)	15
Lipoma	0 (0%)	1 (100%)	1
Lymphoma	1 (100%)	0 (0%)	1
Malignant melanoma	0 (0%)	2 (100%)	2
Myxoma	1 (100%)	0 (0%)	1
Nevus	0 (0%)	1 (100%)	1
Odontoma	1 (50%)	1 (50%)	2
Osteosarcoma	0 (0%)	1 (100%)	1
SCC	6 (36.15%)	7 (53.85%)	13
Squamous papilloma	5 (45.45%)	6 (54.55%)	11
Total	26 (41.54%)	35 (58.46%)	61

GGT: gingival granular tumor, SCC: squamous cell carcinoma

Table 2. Distribution of neoplastic lesions by age

Lesion	Age (year)	
	Mean $\pm$ SD	Median (1st quartile–3rd quartile)
Ameloblastoma	$45.7 \pm 16.3$	49 (31.5–58.2)
GGT	$27.5 \pm 28.5$	26 (2.8–52.7)
Hemangioma	$40.7 \pm 25.8$	48 (18–59.7)
Leukemia	$55.7 \pm 2.5$	56 (53.5–57.7)
Leukoplakia	$49.5 \pm 13$	50 (44.3–55.5)
Lipoma	39	39
Lymphoma	69	69
Malignant melanoma	$40.5 \pm 0.7$	40.5 (40–41)
Myxoma	19	19
Nevus	54	54
Odontoma	$24 \pm 0.0$	24 (24–24)
Osteosarcoma	33	33
SCC	$61.3 \pm 13.9$	63 (55.3–72)
Squamous papilloma	$34.8 \pm 15.1$	6 (54.55)
Total	$45.5 \pm 18.2$	37 (22.8–46.3)

Data shown as mean  $\pm$  SD, median–interquartile range. Student–t test

GGT: gingival granular tumor, SCC: squamous cell carcinoma

### Age

The mean age in neoplastic lesions was  $45.5 \pm 18.2$  (Table II). Leukemia was frequently observed in the 5th decade ( $55.7 \pm 2.5$ ); other lesions were distributed over a wide age range (Table 2).

### Anatomical Localizations of Lesions

Table 3 shows the distribution of oral cavity neoplasms according to different anatomical localizations. The gingiva was the most common area of neoplasia with 34 cases (55.73%). The gingiva is followed by the oral mucosa with 18 cases (29.50%). The floor of the mouth, the tongue, and maxillo–mandibular alveolar process distributions of the lesions were found very low (Respectively, floor of the mouth:  $n=5$  (7.81%), mandibular alveolar process:  $n=2$  (3.12%), tongue and maxillary alveolar process:  $n=1$  (1.56%).

## Discussion

The goal of this study was to determine the frequency and distribution of oral neoplastic lesions in biopsy materials. In our study,

**Table 3.** Distribution of neoplastic lesions by localization

Lesion	Localization					
	Oral mucosa	Gingiva	Floor of mouth	Mandibular molar alveolar process	Tongue	Maxillary molar alveolar process
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Ameloblastoma	0 (0%)	2 (66.67%)	0 (0%)	0 (0%)	0 (0%)	1 (33.33%)
GGT	1 (25%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	0 (0%)
Hemangioma	1 (33.33%)	2 (66.67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leukemia	0 (0%)	3 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Leukoplakia	5 (33.33%)	9 (60%)	0 (0%)	0 (0%)	1 (6.67%)	0 (0%)
Lipoma	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lymphoma	1 (100%)	0 (23.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Malignant melanoma	0 (0%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Myxoma	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nevus	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Odontoma	0 (0%)	0 (0%)	0 (0%)	2 (100%)	0 (0%)	0 (0%)
Osteosarcoma	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
SCC	4 (13.77%)	6 (36.15%)	3 (23.08%)	0 (0%)	0 (0%)	0 (0%)
Squamous papilloma	5 (45.45%)	6 (54.55%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	18 (29.50%)	34 (55.73%)	5 (8.20%)	2 (3.27%)	1 (1.63%)	1 (1.63%)

GGT: gingival granular tumor, SCC: squamous cell carcinoma

a total of 423 biopsy materials were examined, and 61 (14.42%) biopsy materials diagnosed as neoplastic lesions were included. In a study conducted in Kuwait in 2012, the incidence of neoplastic lesions in the oral soft tissues was reported as 31%.<sup>8</sup> In a multi-center study conducted in 2016, this rate was reported as 34.4%,<sup>9</sup> while this rate was 23.5% in another retrospective study.<sup>10</sup> All three studies<sup>8–10</sup> revealed the incidence of neoplastic lesions in all oral soft tissues, whereas the biopsy materials included in our study are lesions observed only in periodontal tissues. The difference between the rates may be due to the difference between the evaluated regions. Also, these differences between the study results; may be related to geographic region, age group, race, and duration of data collection.

According to our study results, the most common lesion was leukoplakia (n=15, 24.59%). Although oral leukoplakia is not a neoplastic lesion; histopathologically, epithelial atrophy, hyperplasia with or without hyperkeratosis, and mild-to-severe epithelial dysplasia can be observed in Leukoplakia. There is a wide range of varying data regarding the possibility of malignant transformation of leukoplakia that makes it a premalignant lesion. However, the lowest risk of malignant transformation reported in the literature was increased by five times compared to control<sup>11</sup>. Anderson and Ishak reported in their review (2015) that the incidence of leukoplakia was widely distributed according to population and gender (0.2%–4.9%).<sup>12</sup> They mentioned that these results may be associated with the fact that the included studies were conducted in different countries and the effect of daily habits on lesion development. Discrepancies with our results may be due to environmental and genetic factors.

According the results of our study, the female/male ratio in neoplastic lesions was 0.72:1. Consistent with our results, this ratio was expressed as 0.93:1 for Canada, 0.67:1 for Iran, 0.97:1 for Japan and 0.85:1 for South Korea in a multicenter study.<sup>10</sup>

The mean age of all examined biopsy specimens was 41.5 ± 17.3, and the mean age of those diagnosed with neoplastic lesions was 45.5 ± 18.2. Feng et al. reported in their study that the mean age of individuals diagnosed with neoplasia was 56.9 ± 18.9.<sup>13</sup> These differences, among other reasons, may be explained by the different inclusion criteria used in each study and the frequency of biopsy.

### Squamous papilloma

Oral squamous papilloma (SP) are common benign human papillomavirus-related lesions of the oral mucosa presenting as a papillary or verrucous exophytic mass.<sup>14</sup> It often occurs in the tongue and soft palate; however, periodontal tissues may be affected.<sup>14</sup> It occurs with higher incidence in adults, especially in the third and seventh decades.<sup>15</sup> In our study, 11 patients were diagnosed with squamous papilloma. The mean age was 34.8 ± 15.1, and it was frequently observed in the gingiva of male patients, consistent with the literature.

### Gingival granular cell tumor (GGT)

Gingival granular cell tumor (GGT) is a rare benign lesion and occurs at birth on the alveolar median ridge of the maxilla.<sup>16</sup> It more frequently affects females.<sup>17,18</sup> Etiology is unclear.<sup>19</sup> The therapeutic approach of the lesion is surgical excision, because spontaneous regression of the lesion is not possible.<sup>20</sup> In our study, three of the four cases were female, and it occurred in the maxillary gingiva, consistent with the literature.

### Hemangioma

Hemangiomas are the common benign vasoformative tumors of infancy and childhood<sup>21,22</sup> and characterized microscopically by the proliferation of blood vessels.<sup>23</sup> It does not show tendency to malignant transformation.<sup>24</sup> The incidence is higher in females (65%) than males (35%).<sup>25</sup> These lesions often appear to originate from the interdental gingival papilla and to spread laterally to involve adjacent teeth.<sup>26</sup> Consistent with the literature, in our study, it was observed more frequently in women, the female/male ratio was found to be 2:1, and most of the lesions were observed in the gingiva.

### Odontoma

Odontoma is defined to be one the most common odontogenic tumor of the oral cavity and is composed of dental tissues of the jawbones.<sup>27</sup> Odontogenic tumors are rare with a incidence of 0.002% to 0.1%.<sup>28</sup> Odontoma is usually observed in the second and third decades (3–71 years of age).<sup>29–31</sup> There is no observed tendency

over sex. Both two cases included in our study were 24 years old and the female: male ratio was 1:1. Both lesions were in the mandibular alveolar process in accordance with the literature.

### Lipoma

Lipomas are benign, soft tissue neoplasms of mature adipocytes. The incidence of oral lipoma (OL) is 1–4% of all benign oral lesions.<sup>32</sup> OL has been reported in salivary glands, lip, tongue, buccal mucosa, gingiva, and floor of the mouth. The incidence of the lesion was reported to be female/male=0.33:1 and the age range was 9–92.<sup>33</sup> There was only one case in our study, and it constituted 1.56% of all oral neoplasms evaluated in accordance with the current literature findings. It was seen in a male patient, and the age range is also compatible with the literature data.

### Nevus

Melanocytic nevi are benign proliferation of melanocytes<sup>34</sup>, and their incidence are 4.35 cases per 10 million individuals.<sup>35</sup> They are lesions that should be differentiated from melanoma and often involve periodontal tissues as it does. Oral melanotic nevi (OMN) are observed mainly in the hard palate and buccal mucosa. They are seen in female more frequently especially with the age of 35 years.<sup>36</sup> The only case in our study was a 54-year-old male patient, and the lesion was observed in the gingiva.

### Odontogenic myxoma

Odontogenic myxoma (OM) are odontogenic tumors that can involve periodontal tissues by showing peripheral localization together with ameloblastoma and odontogenic fibroma. OM is a benign odontogenic tumor of mesenchymal cells.<sup>37</sup> The incidence of OM is 0.5–17% in odontogenic tumors for Asia, Europe, and America populations<sup>38,39</sup> and 1–19% for Africa<sup>40,41</sup>. The lesion is frequently observed in the third decade in female patients with mandibular localization.<sup>40,41</sup> The case diagnosed with myxoma in our study was a 19-year-old female patient, and the lesion was observed in the mucosa.

### Ameloblastoma

Ameloblastoma is a locally aggressive, benign, odontogenic neoplasm and constitutes 10% of all tumors that is seen in the mandible molars and ramus.<sup>42–44</sup> The etiology is unknown.<sup>45,46</sup> It is more common in young adults; seen equally at both gender.<sup>43,44</sup> Reichart et al. reported that the mean age was 35 years and female/male ratio was 1.0:1.14 for 3677 ameloblastoma cases.<sup>44</sup> The mean age was 45.7 ±16.3 years, and the female/male ratio was 0.5:1 in our study. Lesions were observed two times more frequently in the mandible than in the maxilla.

### Leukoplakia

Leukoplakia is the potentially malignant precursor white lesion of the oral mucosa that cannot be characterized as any other definable lesion.<sup>47</sup> Lesions cannot be rubbed off and are generally asymptomatic. Dysplasia or carcinoma can be seen in 20% of leukoplakic lesions.<sup>12</sup> Lesions occur most frequently on the mandibular gingiva, tongue, buccal mucosa and floor of the mouth. It usually takes place after the age of 30 years, and peak incidence occurs after the age of 50 years.<sup>48</sup> It is more common in female India and almost 1:1 in the Western world. In our study, it was observed more frequently in males (F/M=0.36:1), and the mean age was 49.5 ±13 years, consistent with the literature.

### Squamous cell carcinoma (SCC)

Oral SCCs account for approximately 90% of oral and oropharyngeal malignancies.<sup>49</sup> These tumors can arise from the floor of the mouth, alveolar surface, oral tongue, buccal surface, and hard palate.<sup>50,51</sup> SCC is observed in male patients dominantly<sup>52</sup>, and the global SCC M:F ratio is about 5.5:2.5<sup>53</sup>, ranging from 1.2:1<sup>54</sup> to 3.02:1<sup>55</sup>. The mean age is 46.93 years.<sup>56</sup> In our study, the mean age was 61.3 ±13.9 years, and it was most frequently observed in the gingiva of male patients. Although our results are consistent with the literature findings, the differences in rates may be related to genetic and environmental factors.

### Leukemia

Leukemia is the malignant disease of the white blood cells, and its incidence is 9 cases per 100,000 general population.<sup>57</sup> The oral manifestations of leukemia are oral ulcerations, mucosal pallor, petechia, gingival enlargement and bleeding.<sup>58,59</sup> Gingival involvement is common as the first sign of leukemic involvement.<sup>60</sup> Hou et al. (1997) reported the female/male ratio as 0.66/1.<sup>58</sup> In the same study, acute leukemias were frequently observed in individuals under the age of 20, and chronic leukemias were observed in individuals under the age of 30. In our study, all individuals diagnosed with leukemia were under the age of 30, and all lesions were observed in the gingiva in accordance with the literature.

### Melanoma

Oral mucosal melanoma is a rare tumor that is associated with the malign transformation of melanocytes. Periodontal tissues are the areas where oral melanomas are frequently involved.<sup>60</sup> It constitutes approximately 25% of all mucosal melanomas of the head and neck region<sup>58,60</sup> and about 0.5% of all oral malignancies<sup>61,62</sup>. It is more prevalent in afro Americans than in Whites<sup>62,63</sup>, slightly more prevalent in men<sup>64</sup>, and it is observed between the ages of 24–85 and in the alveolar ridge and hard palate.<sup>65</sup> In our study, lesions were observed in the mucosa and gingiva in male patients at the third decade.

### Lymphoma

Among malignant lesions, lymphoma is the second most common lesion in the head and neck neoplasms after SCC.<sup>66</sup> There are 2 subtypes as Hodgkin's and non-Hodgkin's lymphoma (NHL). Hodgkin's lymphoma often presents as nodal disease, while non-Hodgkin's lymphoma is presenting up to 40% at an extra nodal site which are oral cavity and jaws with an incidence of 2% to 3%.<sup>67–69</sup> The mean age is 71 years (35–89), and the female/male ratio is 53:47. It occurs in the upper jaw (maxilla, palatal bone) with 28% incidence and followed by the palatal soft tissue (20%), a mandible (20%) and vestibule and gingivae (maxillary or mandibular soft tissue involvement only) (17%).<sup>70</sup> In our study, only one of the 64 cases was Non-Hodgkin's Lymphoma, and the patient was a 69-year-old female.

### Osteosarcoma

Osteosarcoma is originated from bone-forming mesenchymal cells and it's the most common primary bone malignancy. 77% of all osteosarcomas are diagnosed in persons aged 55 years and above. It is observed more frequently in men (1:0.8).<sup>71</sup> The only case included in our study belonged to a 33-year-old male patient and was observed in the mandible.

## Conclusion

This study provided important data on the frequency and histological distribution of oral benign and malign neoplasms. In this multicenter study, the limited number of cases may not be sufficient to reach a general interpretation for the Turkish population. Additionally, these results emphasize that dentists who examine the oral tissues most frequently play an important role in the diagnosis and the treatment of these lesions.

## Acknowledgements

A retrospective study conducted by the same authors and evaluating the distribution and histological features of reactive lesions affecting periodontal tissues was published in the journal *J Dent Fac Atatürk Uni* in 2021. The results of this and our previous studies were presented as an oral presentation at the 46th Turkish Society of Periodontology International Symposium and Congress in 2016, and the abstract was included in the proceedings book.

## Author Contributions

S.K.: Formal analysis, Methodology, Project administration, Writing - original draft, review & editing. C.O.: Conceptualization, Formal analysis, Methodology, Project administration, Supervision, Writing - original draft, review & editing. Z.G.: Writing - original draft, review & editing. M.G.: Methodology, Project administration, Supervision, Writing - review & editing. O.G.: Data curation, Formal analysis, Methodology, Project administration, Supervision, Writing - review & editing.

## Conflict of Interest

Authors declare that they have no conflict of interest.

## Authors' ORCID(s)

S.K. 0000-0002-7868-4217  
 C.O. 0000-0002-8995-6361  
 Z.G. 0000-0001-6897-0773  
 M.G. 0000-0002-3848-6195  
 O.G. 0000-0002-3712-1469

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