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JSM Dental Surgery

Research Article

# The Impact of Oral Pathology Diseases in Dental Clinical Practice: A 5-Year Retrospective Study

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Submitted: 14 February 2017

Accepted: 07 March 2017

Published: 09 March 2017



Keywords

- Oral pathology
- Prevalence
- Retrospective study
- General practice
- Dental

**Abstract**

**Objectives:** Oral and maxillofacial lesions are frequently reported among the pathologies affecting oral cavity. The aim of our study was to investigate the frequency and spectrum of oral and maxillofacial lesions biopsied in a hospital population in Italy, in order to provide insight into the prevalence of head and neck pathologies.

**Materials and Methods:** A retrospective study of 2731 specimen analyses recorded between 2010 and 2015 was conducted. The histopathological reports were retrieved from the Stomatology and Oral Surgery Department at the University Hospital in Pisa and were divided into categories considering several variables (type of lesion, anatomical localization, gender and age of the affected patient). A statistical analysis was conducted in order to evaluate the prevalence for each cluster of pathology and its relationship with the other identified variables.

**Results:** In our sample, the most common lesions were periapical inflammatory diseases (30.25%) and non-neoplastic proliferative diseases (30.17%). The most common location of the lesions was bone, followed by cheek lining and gingiva. Precancerous lesions represented 9.01% of the sample, followed by benign tumours and malignant tumours. Males represented 46.2% of the sample, while females were 53.8%. The most affected age range was from 60 to 69 years of age, while patients of extreme age (under 10 years old and over 90 years old) were less affected.

**Conclusion:** Many of our findings are consistent with those reported in literature, suggesting that the study of demographic characteristics and their association with occurrence of lesions should be considered in performing differential diagnoses.

## ABBREVIATIONS

NNPD: Non-Neoplastic Proliferative Diseases; MRONJ: Medication-Related Osteonecrosis of the Jaw

## INTRODUCTION

An oral and maxillofacial pathology lesion comprehends a wide variety of mucosal diseases, which recognize different aetiological factors and include autoimmune, inflammatory, proliferative, precancerous and cancerous lesions.

The possibility of identifying the frequency of each lesion is fundamental in order to understand disease patterns within populations and support differential diagnosis.

At present time, the most reliable diagnostic tool is represented by histopathological analysis, which is essential in terms of morphological characterization of the lesion and still remains the gold standard for obtaining a definitive diagnosis.

Although the incidence for each pathologic condition has been investigated, only few studies analyze the impact of oral pathology disease in the general population, and data on the frequency of histological confirmed lesions are particularly scarce in Italy.

The aim of our study is to describe the occurrence of oral lesions diagnosed in patients who attended the Stomatology and Oral Surgery Department at the University Hospital in Pisa

between 2010 and 2015 and to analyse the existence of factors relating to the development of oral soft tissue lesions, defining clinical characteristics for each different type.

## MATERIALS AND METHODS

A retrospective study was carried out at the Stomatology and Oral Surgery Department at the University Hospital in Pisa. The histological examination reports from January 2010 to December 2015 were collected and analysed, and their number was correlated to the total number of surgical interventions carried out in the same period of time.

Lesions were classified into nine diagnostic categories, as detailed in Table (1).

The histological examination reports recorded several information about the patient, such as gender, age at the moment of diagnosis, the observed type of lesion and its anatomical localization. Considering all the data obtained when collecting the reports, we proceeded to classification of the sample according to the identified variables.

In order to determine whether there was a correlation between pathology and gender, reports were stratified by sex and age at diagnosis. For the latter stratification, 6 groups were identified: less than 40, 40-49, 50-59, 60-69, 70-80, more than 80.

All results were analysed using the SPSS 12.0 Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY), evaluating aspects of descriptive statistics and also using the Student's t test to determine significant differences between the means of two groups. In the case of more than two groups, a one-way variance analysis was employed. To evaluate association or independence between qualitative variables, the $\chi 2$ test was used.

Significance was considered for values of $p<0.05$.

## RESULTS

The reviewed records referred to a total of 2731 patients (mean age 54.21 years, standard deviation - SD + 38.48, ranging from 0 to 94 years), out of 15727 patients who underwent surgical interventions. Males represented 46.2% (1262 cases, mean age 53.35 years, SD + 34.09, ranging from 0 to 92 years) while females were 53.8% (1469 cases, mean age 55.06 years, SD + 34.71, ranging from 0 to 94 years) (Figure 1). The difference between the mean age of males and females was statistically significant ($p<0.05$), with a lower value for females comparing to males.

Most of the reports referred to periapical inflammatory lesions, accounting for 30.25% of diagnoses (826 cases, 409 males, 417 females) and non-neoplastic proliferative diseases (NNPD) with 30.17% of the sample (823 cases, 336 males, 487 females), being the two most common pathologies affecting oral cavity. Nonetheless, the third most represented group was represented by precancerous lesions, with a 9.01% of the sample (246 cases, 112 males, 134 females), followed by benign tumours (8.24%, 225 cases, 115 males, 110 females), malignant tumours (6.11%, 167 cases, 87 males, 80 females), medication-related osteonecrosis of the jaw (MRONJ) (5.20%, 142 cases, 52 males, 90 females), cysts of various aetiology (4.50%, 123 cases, 73 males, 50 females), oral mucocele (3.37%, 92 cases, 51 males, 41 females), immunomediated lesions (3.19%, 87 cases, 34 males, 53 females) (Table 2).

**Table 1:** Classification of oral lesions and description of the pathologies included in each category.

| Category | Pathologies |
|---|---|
| Immunologically mediated lesions | Lichen planus, pemphigus vulgaris, Sjögren's syndrome |
| Non-Neoplastic Proliferative Diseases | Reactional lesions induced by traumatic, chemical or biological agents, such as inflammatory fibrous hyperplasia, pyogenic granuloma, and peripheral giant cell granuloma |
| Periapical inflammatory lesions | Periapical granuloma and radicular cysts |
| Oral mucocele | Mucous extravasation cyst and mucous retention cyst |
| Cysts of various aetiology | Odontogenic, non-odontogenic, unspecifiedcysts |
| Medication-related osteonecrosis of the jaw | Related to therapy with bisphosphonates, antiresorptives (denosumab) and antiangiogenic drugs |
| Benigntumours | Odontogenic tumours, papilloma, soft tissue tumours (lymphangioma, hemangioma, neurofibroma,granular cell tumour, lipoma) |
| Precancerous lesions | Epithelial morphologic changes (clinical appearance of leukoplakia) and actinic cheilitis |
| Malignanttumours | Non-Hodgkin lymphoma, adenoid carcinoma, oralsquamouscell carcinoma |

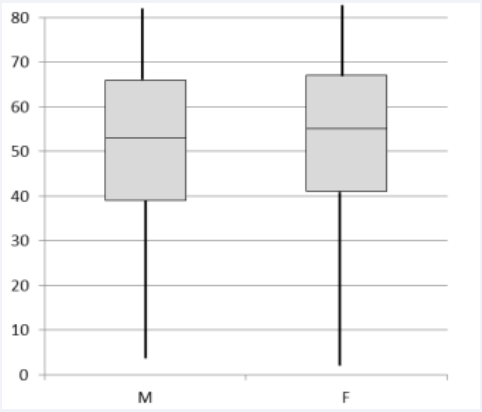


**Figure 1** Boxplot representing sample distribution per gender and age. Pathology was mainly distributed among pateints between 40 and 70 years of age, with a higher mean age for females.

Considering the development of disease in females, the most frequent pathology was represented by NNPD (33.15%), followed by periapical inflammatory lesions (28.39%), while in males periapical pathology was more common than NNPD (32.41% and 26.62% respectively). MRONJ were 6.13% in females, which presented a statistically significant difference comparing to incidence in males (4.12%); this data could be related to the use of anti-resorptive drugs due to the higher incidence of breast neoplasms in females and to the administration of drugs

**Table 2:** Distribution of pathology on the total sample, per gender and males/ females ratio.

| DIAGNOSTIC CATEGORY | M | F | M: F RATIO | TOT | PERCENTAGE OF TOTAL |
|---|---|---|---|---|---|
| Immunomediated | 34 | 53 | 0.64 | 87 | 3.19 |
| NNPD | 336 | 487 | 0.69 | 823 | 30.14 |
| Oral mucocele | 51 | 41 | 1.24 | 92 | 3.37 |
| Cysts of various aetiology | 73 | 50 | 1.46 | 123 | 4.5 |
| Periapical inflammatory lesions | 409 | 417 | 0.98 | 826 | 30.25 |
| MRONJ | 52 | 90 | 0.58 | 142 | 5.2 |
| Precancerous lesions | 112 | 134 | 0.84 | 246 | 9.01 |
| Benigntumours | 115 | 110 | 1.05 | 225 | 8.24 |
| Malignanttu-mours | 87 | 80 | 1.09 | 167 | 6.11 |
| TOTALE | 1262 | 1469 | 0.86 | 2731 | 100 |

Abbreviations: NNPD: Non-Neoplastic Proliferative Diseases; MRONJ: Medication-Related Osteonecrosis of the Jaw

acting on bone metabolism in post-menopausal osteoporosis. Precancerous lesions were 9.12% in females, while malignant tumours accounted for the 5.45% in females; this data could be justified by the spread of alcohol consumption and tobacco use also among females, with an increased risk of developing malignant lesions. Males showed a prevalence of precancerous lesions (8.87%) and malignancies (6.89%). Our results show a higher percentage of malignancies among males, even if the number of males in the sample was lower.

Table (3) shows the distribution of the sample among decades: we used these data to compose 6 age groups that were used for subsequent evaluation.

The first group identified was composed by patients less than 40 years old, who were mostly affected by periapical inflammatory lesions (39.63% in females, 42.87% in males), while malignant lesions, immunomediated lesions and MRONJ were more common in elderly patients. In the group ranging from 40 to 49, we observed a higher incidence of immunomediated pathology in males and of MRONJ in females, together with a statistically significant increase in precancerous lesions and malignant tumours comparing to the first group ($p<0.05$).

The group where immune mediated lesions were more common was between 50 and 69 years of age. Neoplasms and precancerous lesions presented an increasing rate, with a peak of incidence in the eighth decade for malignant tumours and in the seventh decade for precancerous lesions. The results are reported in (Table 4).

Finally, considering the location of the lesion, we identified twelve different sites, and evaluated where it was more common to find disease. Site distribution showed that the most common location of the lesions was bone; this result was consistent with the outcome of the reports, being periapical inflammatory lesions the most represented lesions among the samples, and also considering that also MRONJ were pathologies affecting the bone. The most common mucous membranes presenting disease were cheek lining and gingiva (12.20% and 11.97% respectively) (Table 5).

The most common localization for malignant lesions was tongue (29%), followed by cheek lining (23%) and gingiva (21%); the remaining 34% was represented by mouth floor, palate and retromolarregion.

## DISCUSSION

The aim of our study was to describe the prevalence of oral and maxillofacial pathology among a population represented by the patients referred to the University Hospital in Pisa, in order to provide an insight on the impact of oral affections on everyday surgical practice and to compare the results to global reports.

Women represented the majority of the sample as reported by other authors [1]. However, men showed a higher number of cases of malignant pathology, with a statistically significant difference between the two groups ($p<0.05$).

Our sample did not exclude any group of age. This may have influenced the results, as other studies in literature focus on younger or elderly patients, such as Jones and Franklin who only took into account patients over 17 (1), Das and Das who included patients up to 20 [2], or Shulman et al. [3], and Corrêa et al. [4], who mainly focused on patients over 60 years of age. More than 80% of the patients (83.78%) were diagnosed between their thirties to seventies, with a peak in the seventh decade.

The results showed a high proportion of inflammatory lesions, affecting both the bone and oral soft tissues, consistently with global reports [1,5-8]. Malignancies and precancerous affections were less common, though we found a higher percentage of these pathologies among our sample comparing to literature, with a percentage of 9.01% for precancerous lesions and of 6.11% for malignant pathology for the total sample [1,9].

Non-neoplastic proliferative pathology and periapical inflammatory lesions were the most common diagnostic categories, representing together more than 60% of all submitted specimens, according to previous literature (10). Franklin et al.

**Table 3:** Number of patients for each group of age and percentage on total. The data show a peak of incidence in the age range from 60 to 69. Patients of extreme age (under 10 years old and over 90 years old) were the less affected.

| AGE RANGE | N PATIENTS | PERCENTAGE |
|---|---|---|
| 0-9 | 20 | 0.73 |
| 19-Oct | 94 | 3.44 |
| 20-29 | 178 | 6.52 |
| 30-39 | 339 | 12.41 |
| 40-49 | 454 | 16.62 |
| 50-59 | 526 | 19.26 |
| 60-69 | 598 | 21.9 |
| 70-79 | 371 | 13.58 |
| 80-89 | 134 | 4.91 |
| >90 | 17 | 0.62 |
| TOT | 2731 | 100% |

**Table 4:** Classification of the reports per age, gender and pathology. The results are shown in terms of percentage per group of age.

| | <40 | | 40-49 | | 50-59 | | 60-69 | | 70-79 | | >80 | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F | M | F |
| Immunomediated | 0.62 | 0.31 | 1.76 | 0.66 | 1.15 | 2.87 | 2.08 | 2.6 | 0.75 | 4 | 0.74 | 1.48 |
| NNPD | 11.49 | 16.15 | 13 | 15.64 | 11.49 | 19.35 | 13.02 | 21.35 | 13.5 | 17 | 10.37 | 14.81 |
| Oral mucocele | 5.59 | 3.88 | 1.32 | 1.76 | 0.38 | 0.77 | 1.04 | 0.35 | 0 | 0.25 | 0.74 | 0.74 |
| Cysts | 3.42 | 2.95 | 1.76 | 1.76 | 3.07 | 1.72 | 2.78 | 1.56 | 1.75 | 1.25 | 2.96 | 0 |
| Periapical lesions | 20.81 | 19.88 | 19.82 | 20.26 | 13.22 | 18.2 | 11.11 | 10.94 | 10.25 | 8.25 | 8.15 | 4.44 |
| MRONJ | 0.31 | 0.16 | 0.22 | 0.88 | 1.34 | 2.68 | 2.43 | 4.34 | 6.25 | 7.5 | 2.22 | 11.85 |
| Precancerous | 2.17 | 1.71 | 4.19 | 4.63 | 4.41 | 6.51 | 5.9 | 6.77 | 4 | 5.75 | 4.44 | 4.44 |
| Benign tumours | 4.35 | 4.5 | 4.63 | 3.08 | 4.21 | 3.26 | 4.17 | 3.99 | 2.75 | 5.5 | 6.67 | 3.7 |
| Malignant tumours | 1.09 | 0.62 | 2.42 | 2.2 | 3.07 | 2.3 | 3.3 | 2.26 | 4.25 | 7 | 7.41 | 14.81 |
| Total | 49.84 | 50.16 | 49.12 | 50.88 | 42.34 | 57.66 | 45.83 | 54.17 | 43.5 | 56.5 | 43.7 | 56.3 |

Abbreviations: NNPD: Non-Neoplastic Proliferative Diseases; MRONJ: Medication-Related Osteonecrosis of the Jaw

**Table 5**: Site distribution of lesions, total data and partition per gender.

| SITE | N Males | Mean age M | N Females | Mean age F | N Tot | Mean age Tot |
|---|---|---|---|---|---|---|
| Gingiva | 126 | 49.95 | 201 | 58.87 | 327 | 56.59 |
| Cheek lining | 128 | 56.52 | 205 | 56.28 | 333 | 56.37 |
| Lip | 106 | 45.87 | 114 | 44.35 | 220 | 47.15 |
| Bone | 575 | 50.39 | 582 | 50.73 | 1157 | 50.52 |
| Maxillary sinus | 85 | 53.56 | 83 | 51.39 | 168 | 52.49 |
| Tongue | 125 | 57.66 | 121 | 55.63 | 246 | 57.17 |
| Salivary glands | 3 | 67.56 | 4 | 51.75 | 7 | 59.86 |
| Alveolar mucosa | 29 | 61.45 | 62 | 62.48 | 91 | 62.15 |

[1], and Rich et al. [8], found that mucosal pathology represented 36% and 45% of all cases respectively, a percentage reported also by Bhaskar [6], a result which is consistent with our data. Wan and Savage [11], though, report that connective tissue pathology was the predominant diagnostic category, while Weir et al. [5], described a lower occurence. However, the inclusion of different classes of pathology in each category could represent a factor which makes the comparison with literature more difficult.

Periapical inflammatory lesions presented a higher prevalence than the one recorded by other authors (1,12), probably due to inclusion of both periapical granuloma and periapical radicular cysts in our classification. We decided to include periapical radicular cysts in the group of periapical inflammatory lesions because of the common aetiology with periapical granuloma; our results agree with other studies, with periapiacal radicular cyst being the most common odontogenic cyst [7,13].

Precancerous lesions presented a percentage of 9.01%, and were mostly represented by abnormalities of oral soft tissue with clinical appearance of leukoplakia [14], with all cases being found over 20 years of age. Sixto-Requeijo et al. [9], report 15.5% of diagnosis, but the data could be difficult to compare due to the great difference in sample size. Leukoplakia is most frequently reported in middle-aged males, with an increasing prevalence with age [15-17]. While males below the age of 40 presented a percentage of pathology of 2.17%, the prevalence almost doubled in the 40-49 year-old group, reaching a 5.90% in the category between 60 and 69. Also in females the most affected group of age was the one between 60 and 69, with a 6.77%, which is a higher percentage than the one reported in males. Our result may be related to the spreading of alcohol consumption and tobacco use in females, which has decreased the difference in prevalence of precancerous lesions.

This data is also consistent with the different male-female ratio reported in case of oral squamous cell carcinoma, which recognizes the same risk factors of precancerous lesions [15].

Benign tumours accounted for the 8.24% of the sample, similar to the results of other Authors, such as Mendez et al. [10], who reported a 7.66% of incidence on a 10- year period. We included in this category odontogenictumours, which by definition are benign affections because of the absence of metastatic lesions; this fact may have, though, influenced our results, not having classified odontogenictumours in a different category. Some Authors focused their study on benign tumours [18], finding a greater prevalence in females comparing to males; in our study, though, the majority of diagnosis of benign tumours referred to males for the overall sample, while in two groups of age (under 40 and between 70 and 79) females were mostly affected. The majority of authors did not find a relationship between gender and prevalence of benign tumours, except in the case of pyogenic granuloma, which is more common in females [19, 20].

Malignant tumours represented the 6.15% of the sample. Oral squamous cell carcinoma was the 92% of the reports of

malignancy, with 29% of lesions affecting the tongue. The eighth decade was the most affected in females, while in males the peak was registered in the seventh decade; however, males presented a rising pathology prevalence from the sixth decade, suggesting an earlier onset for this affection in men. Although literature reports that males are more likely to develop squamous cell carcinoma than females, the male-female ratio disparity has decreased over the past years, probably due to a change in women's behaviour in relation to smoking and alcohol consumption [15,21]. Our results are slightly higher than those reported in literature: Skinner and Weir [22] report the most similar results in terms of percentage, while Mujica et al. [23], and Satorres et al. [12], report lower percentage of pathology. This may be due to the number of patients included in the study, as Skinner and Weir evaluated a sample of 2675 patients, a number which is more similar to the one of our report. Considering the most affected site, Sixto-Requeijo et al. [9], report the tongue as the most common location of malignancies, therefore our result is consistent with literature, though their data show a lower percentage, probably related to the difference of sample size.

MRONJ was the sixth pathology per incidence, with a 5.20%. We defined this category according to the AAOMS Position paper [24], therefore we included osteonecrotic lesions caused not only by bisphosphonates, but also by antiresorptive (denosumab) and antiangiogenic therapies. Our result is not easily comparable, since similar studies refer to BRONJ (Bisphosphonate-related Osteonecrosis of the Jaw) and most of them consider clinical aspects instead of biopsy data [25,26], therefore further studies are needed for the evaluation of the prevalence of this affection

Cysts of various aetiology accounted for the 4.50% of the sample. Other authors [7,9]. Report higher rates for this pathology comparing to our results, though this data could be related to the inclusion in this category of periapical cysts, which we decided to classify as periapical inflammatory pathology.

Oral mucocele was the most common affection of salivary glands, and represented 3.37% of the sample, with patients under 30 years of age being the most affected group. Kelloway et al. [27], report a percentage of 2% of all submitted histopathology for mucous extravasation cyst and mucous retention cyst, while other Authors [2,9,13,28], found higher percentages for this affection. This result is probably due to the difficulty in collecting tissue samples. The most affected area was represented by lower lip, consistently with literature and association with traumatic factors.

Immunomediated lesions were the less common in our sample, with 3.19%. Considering the results obtained by other authors [9,27], we found a low percentage of immunomediated mucosal pathology, even if we included in this category a wide variety of lesions. Other studies, in fact, mostly evaluate the incidence of oral lichen planus, which in our case was classified together with several immunomediated affection. This makes our data more difficult to compare to current literature.

The aim of our study was to describe the occurrence of the most common pathologies affecting oral cavity, both in terms of bone and soft tissue lesions, in order to give a perspective on the distribution of disease in Italy and to compare the results obtained to international literature. The classification we provided may help clinicians by clustering different pathologies and giving their relative prevalence. This is of particular importance considering that 9 patients out of 100 could develop precancerous lesions and 6 out of 100 a malignant lesion.

## CONCLUSION

In our study, the most commonly encountered oral and maxillofacial pathology disease was relating to periapical inflammatory lesions, followed by non-neoplastic proliferative diseases. The third affection per frequency was represented by precancerous lesions, a result which outlines the importance of biopsy and histopathological examination in order to identify lesions at risk of malignancy. This is the first comprehensive study to report on the prevalence of oral and maxillofacial pathology in the Italian population, and provides insight into lesions which are most commonly biopsied, together with highlighting the need for more consistent diagnostic criteria between studies.

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**Cite this article**

*Izzetti R, Gabriele M, Caramella D (2017) The Impact of Oral Pathology Diseases in Dental Clinical Practice: A 5-Year Retrospective Study. JSM Dent Surg 2(1): 1013.*