

Oral Conditions of Elders and Middle-aged Individuals with Multiple Myeloma

Marina L Bezerra¹, Luiz CCM Alves², Renan AA Tabosa³, Sarah LO Dantas⁴, Thalita JF da Rocha⁵, Fátia MN Nigri⁶, Giovanna R Neri⁷, Danilo LF Lima⁸

ABSTRACT

Aim and objective: The aim and objective of the present study was to assess the oral conditions of middle-aged and elderly individuals with multiple myeloma.

Materials and methods: This cross-sectional, observational study was carried out in the city of Fortaleza, Ceará, in Northeastern Brazil. An oral examination was performed with 19 patients with multiple myeloma, and information on gender, age, diagnosis, diagnosis duration (months/years), and treatment duration (months/years) were collected. The gingival bleeding index (GBI) and probing depth (PD) were measured to check for periodontal disease, and the decayed, missing, and filled teeth (DMFT) index was used to assess dental conditions. Inferential statistics were also used, as well as the Mann–Whitney test to compare genders and continuous variables and the chi-square test for comparisons among the same groups with categorical variables. All statistical tests adopted a significance threshold of $p \leq 0.05$.

Results: Among the 19 patients analyzed, 10 (52.6%) were elderly, and 9 (47.4%), middle-aged. The mean age of the participants was 63.4 ± 11.7 years, ranging from 48 to 83 years old. Statistical significance was found regarding missing teeth in the elderly group ($p = 0.037$), restored teeth in the middle-aged group ($p = 0.029$), and gingival bleeding among women ($p = 0.050$). Hyposalivation was observed in 89.5% of the individuals, of which 68.4% were characterized as moderate to severe.

Conclusion: Better dental conditions were observed in the middle-aged group when compared to the elderly. Men presented the lowest GBI values. The salivary flow of patients with multiple myeloma was reduced, and most of them showed moderate to severe hyposalivation. It can be assumed that such a situation is caused by the action of drugs, chemotherapy, or even age. Improvements in the oral health of these patients are needed in order to promote a better quality of life.

Clinical significance: Knowledge of the oral manifestations of multiple myeloma patients is essential to assist in the early diagnosis of these alterations, as well as to propose an adequate treatment plan, aiming to improve these patients' quality of life.

Keywords: Multiple myeloma, Oral health, Periodontal diseases.

The Journal of Contemporary Dental Practice (2021): 10.5005/jp-journals-10024-3108

INTRODUCTION

Hematologic diseases have shown to be closely related to the oral cavity.¹ The presence of oral petechiae or ecchymosis, ulcers, spontaneous gingival bleeding without a local cause, and hyposalivation may constitute an oral manifestation of a hematologic problem.² Oral manifestations of patients with hematologic diseases can occur due to the disease itself or as a consequence of treatment.³ Therefore, oral health care is of fundamental importance for systemic balance and to prevent the progression of hematologic disorders, such as lymphomas, leukemias, and multiple myeloma.²

Multiple myeloma (MM) is an incurable B-cell neoplasm characterized by the uncontrolled proliferation of clonal plasma cells in the bone marrow, which can influence the production and secretion of immunoglobulin, with several consequences, including increased risk of infection and kidney failure, among others.³ MM accounts for 1% of all cancers and is the second leading hematologic malignancy after lymphoma. The disease is highly prevalent among middle-aged black individuals and people aged 50 to 60 years, and its age-standardized incidence rate is approximately five cases per 100,000 people in Western countries. The prognosis of MM varies according to age and is worse in patients over 65 when compared to younger individuals.^{3,4}

Autologous peripheral stem cell transplantation is usually the treatment of choice for patients under 65 years and whose

^{1–5}University of Fortaleza (UNIFOR), Fortaleza, Ceará, Brazil

⁶University Center Christus (Unichristus), Fortaleza, Ceará, Brazil

^{7–8}University Center Christus (Unichristus), Fortaleza, Ceará, Brazil; University of Fortaleza (Unifor), Fortaleza, Ceará, Brazil.

Corresponding Author: Giovanna R Neri, University Center Christus (Unichristus), Fortaleza, Ceará, Brazil, e-mail: gjovanne@hotmail.com

How to cite this article: Bezerra ML, Alves LCCM, Tabosa RAA, *et al.* Oral Conditions of Elders and Middle-aged Individuals with Multiple Myeloma. *J Contemp Dent Pract* 2021;22(6):610–614.

Source of support: Nil

Conflict of interest: None

chemotherapy has not been effective. For patients who cannot undergo transplantation, chemotherapy is used as palliative treatment to prevent the disease from progressing and decrease pain symptoms.^{5,6} However, some complications may arise from the treatments proposed for MM.⁷ Salivary flow rates are often reduced due to chemotherapy or complications resulting from *peripheral stem cell transplantation* and may cause many oral complications, such as gingivitis, periodontitis, and decay.⁸

Changes in demographic patterns have redesigned the age structure of the Brazilian population and increased the number of people over 50 years of age.⁹ Population aging introduces

challenges to public health policies in meeting the people's new demands.⁹ Attention to dental care in patients with MM, middle-aged and elderly, will help control these hematologic diseases and prevent dental health problems.³ However, adequate care for these patients in the Brazilian public health-care system is still quite limited.¹⁰ Additionally, there is a lack of data regarding MM patients' oral conditions in the country. Such information is essential for the development of specific public policies to better assist these patients. Therefore, the objective of the present study was to assess the oral conditions of elders and middle-aged individuals with multiple myeloma.

MATERIALS AND METHODS

A quantitative cross-sectional study was carried out at the Ceará Hematology and Hemotherapy Center (*Centro de Hematologia e Hemoterapia do Ceará—HEMOCE*), located in Fortaleza, Ceará, Brazil. It included men and women aged over 40 years who used chemotherapy drugs and that were authorized by a doctor to undergo an oral examination. Patients with diabetes and hypertension were also included. People who had undergone transplantation were excluded. The diagnostic criteria for multiple myeloma were in accordance with the consensus of the International Myeloma Working Group.¹¹ This study was approved by the Research Ethics Committee of the University of Fortaleza (Approval No. 1.699.991), and all participants signed an informed consent form. The study was conducted according to the 2008 revision of the Helsinki Declaration.

Nineteen patients aged 48–83 years were evaluated by an experienced examiner. They were also asked to answer a questionnaire with information on gender, age, treatment duration (months/years), oral hygiene conditions (frequency of tooth brushing, tongue brushing, flossing, and mouthwash use), self-perceived gingival bleeding, dry mouth, lesions in the oral mucosa, and use of at least one xerostomic medication.

The salivary flow was measured by asking the patient to chew a 2-cm silicone device attached to dental floss in order to stimulate salivary production. The saliva produced during a period of 5 minutes was collected in a container, and the total volume was divided by 5 and recorded in mL/minute.

The sialometric values were estimated according to the standards established by the Brazilian Association of Halitosis (*Associação Brasileira de Halitose – ABHA*): 0.00–0.049 mL/minute—*asialism*; 0.05–0.5 mL/minute—*severe hyposalivation*; 0.51–0.9 mL/minute—*moderate hyposalivation*; 0.91 to 1.19 mL/minute—*mild hyposalivation*; 1.2–2.5 mL/minute—*ideal salivation*; and >2.5 mL/minute—*sialorrhea*.¹²

The gingival bleeding index (GBI) and probing depth (PD) were used to check for periodontal disease and the decayed, missing, and filled teeth (DMFT) index to assess the patients' dental status.

The GBI was measured by probing the gingival margins on four dental surfaces (buccal, lingual or palatal, mesial, and distal) to analyze the number of bleeding surfaces. The result was given in percentage by calculating the ratio between the bleeding surfaces and all the surfaces. Patients were within the normal range when the index was less than 10%; localized gingivitis was suggested when the index was between 10% and 30%, and generalized gingivitis was suggested when the index was greater than 30%.¹³

PD was determined using a UNC 15 probe on six dental surfaces: mesiobuccal, vestibular, distal-vestibular, mesio-palatine, palatine, and distal-palatine. Subsequently, the stage, degree, severity, and

risk of disease progression of the periodontal condition were ranked according to the new classification of periodontal diseases.¹³

Dental conditions were assessed using the DMFT index, which identifies the total number of decayed (D), missing (M), or filled (F) teeth (**T**) in each patient. A score range of 0–32 was used to determine such conditions.¹⁴

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 23.0 (SPSS Inc., Chicago, USA). Descriptive statistics were used, and the data were presented as frequencies, means, and standard deviations. Inferential statistics were also used. The Mann–Whitney test was conducted to compare genders and continuous variables, and the chi-squared test to compare the same groups with the categorical variables, both with a significance threshold set at $p \leq 0.05$.

RESULTS

Among the 19 patients analyzed, 10 (52.6%) were male and 9 (47.4%) were female, and 10 (52.6%) were elderly and 9 (47.4%) were middle-aged. Brazilian parameters were used for categorization into middle-aged (40–59 years) and elderly (60 years or more).¹⁵ The mean age of the participants was 63.4 ± 11.7 years, ranging from 48 to 83 years old. The mean age of the male patients was 63.40 ± 11.75 years, while that of the female patients was 60.11 ± 8.32 years. Treatment duration ranged from 7 months to 5 years, with a mean duration of 1.72 ± 1.29 years. There was no dietary restriction during treatment.

All participants reported brushing their teeth 1 to 5 times daily (mean of 2.26 ± 0.99 times). Only three (15.8%) participants reported flossing, and four (21.1%) stated using some type of mouthwash. However, most of the participants (78.9%) said they brushed their tongues daily. Self-perceived gingival bleeding was described by three (15.8%) participants, and eight (42.1%) reported feeling dry mouth. No lesions in the oral mucosa were observed. Also, there were no significant associations between genders, nor between middle-aged individuals and elders (Table 1).

The calculation of the DMFT index showed a mean of 21.53 ± 6.90 teeth (mean of 0.85 ± 2.01 for decayed teeth; 18.78 ± 8.81 for missing teeth, and 2.10 ± 3.24 for restored teeth). The middle-aged group had a mean of 18.4 ± 6.34 teeth and the elderly of 23.3 ± 6.86 teeth. Male individuals presented a mean of 18.80 ± 7.09 teeth, while the women had a mean of 23.44 ± 6.14 teeth. Regarding missing teeth, the elders had a mean of 22.7 ± 6.25 missing teeth and the middle-aged individuals, 14.4 ± 9.5 ; the men had a mean of 16.0 ± 9.38 missing teeth, and the women, 21.8 ± 7.42 . No statistical significance was observed in the mean DMFT values between genders. However, the elderly group showed to have significantly more missing teeth ($p = 0.05$) than the middle-aged group (Fig. 1), while the latter had significantly more restored teeth than the elders ($p = 0.036$) (Table 2).

Table 1: Oral hygiene habits of all groups

Oral hygiene habits	Yes	No
Tongue brushing	15 (78.9%)	4 (21.1%)
Flossing	3 (15.8%)	16 (84.2%)
Mouthwashing	4 (21.1%)	15 (78.9%)
Gingival bleeding	3 (15.8%)	16 (84.2%)
Dry mouth	8 (42.1%)	11 (57.9%)
Oral lesions	0 (0%)	19 (100%)



Fig. 1: An elderly patient with multiple myeloma, with missing and decayed teeth



Fig. 2: Patient, of the middle-aged group, with multiple myeloma, presenting gingival inflammation characteristic of gingivitis

Table 2: Decayed, missing, and filled teeth (DMFT) and gingival bleeding index (GBI): Comparison between age-groups

Variables	Middle age		Elders		p value
	Median	First-third quartiles	Median	First-third quartiles	
Decayed	0, 0	0-0	0, 0	0-0	0.292
Missing	12, 0	7-24	24, 5	19-26	0.050*
Filled	2, 0	0-8	0, 0	0-0	0.036*
DMFT	20, 0	12-24	24, 5	19-29	0.152
GBI	12, 5	8.7-15	15, 0	7.5-25	0.653

*Mann-Whitney test

Table 3: Decayed, missing, and filled teeth (DMFT) and gingival bleeding index (GBI): Comparison between male and female groups

Variables	Men		Women		p value
	Median	First-third quartiles	Median	First-third quartiles	
Decayed	0.0	0.0-0.0	0.0	0.0-0.0	0.292
Missing	20.0	7.0-24.0	25.0	19.0-26.0	0.110
Filled	1.0	0.0-5.0	0.0	0.0-1.0	0.339
DMFT	20.5	12.0-24.0	25.0	20.0-26.0	0.164
GBI	11.4	7.5-15.0	16.6	8.7-25.0	0.253

*Mann-Whitney test

GBI analysis revealed that seven participants (36.8%) did not have gingivitis, nine (47.4%) had localized gingivitis (Fig. 2), and three (15.8%) presented generalized gingivitis. In relation to age, the elderly had a mean GBI of $19.75 \pm 19.15\%$, while the middle-aged group's mean GBI was $14.42 \pm 11.98\%$, thus lacking statistical significance. Although the male group presented a mean GBI of $12.61 \pm 9.27\%$, and the female group, a mean GBI of $22.35 \pm 20.5\%$, no statistically significant difference was observed (Table 3).

As for PD, three patients presented stage 4, grade B periodontitis, thus indicating a loss of interproximal insertion of 5 mm or more in the worst site or radiographic bone loss extending to half or to the apical third of the root, with direct evidence of insertion loss progression equal to or greater than 2 mm in 5 years and commensurate destruction with biofilm deposits.¹³

A total of 7 (36.8%) patients used xerostomic medications in addition to chemotherapy, while 12 (63.2%) did not. The group that used these medications differed significantly from those who did not ($p = 0.031$), thus suggesting a possible effect of such drugs on the salivary flow and/or in xerostomia. Some of the xerostomic

medications used were antihypertensives, anticoagulants, gastric protectors, antibiotics, anti-inflammatory agents, analgesics, antidiabetics, antivirals, vitamin B and bisphosphonates, antidepressants, uricosuric agents, and chemotherapy drugs.

With regard to salivary flow, 89.5% of the individuals presented hyposalivation, of which seven (36.8%) were characterized as severe, six (31.6%) as moderate, four (21.1%) as mild, and only two (10.5%) patients had an ideal salivary flow: one elder and one middle-aged. No statistical significance was observed among genders and age-groups (Table 4).

DISCUSSION

Despite its utmost importance, oral health is usually neglected by most people, a situation that is even worse in patients with systemic diseases who do not often seek help from dental surgeons due to some type of restriction. Dental surgeons should always be aware of changes in the oral cavity since many systemic manifestations may affect the oral mucosa, especially gingival tissues. These tissues

Table 4: Salivary flow measurement

<i>Classification salivary flow</i>	<i>Frequency</i>	<i>Percentage</i>
Asialia	0	0
Severe hyposalivation	7	36.8
Moderate hyposalivation	6	31.6
Mild hyposalivation	4	21.1
Ideal salivation	2	10.5
Sialorrhea	0	0
Total	19	100

can reflect various systemic alterations, and cause-and-effect relationships between periodontal diseases and several conditions, such as ischemic cardiovascular diseases,¹⁶ pneumonia,¹⁷ birth of premature and low-weight babies,¹⁸ and hematologic diseases,¹⁹ have been described since the 1990s. Therefore, the periodontal status of patients with hematologic alterations is of paramount importance.

MM is currently the second most prevalent hematologic neoplasm, accounting for approximately 1% of all malignant neoplasms. Its occurrence in patients under 40 years of age is rare; people aged over 60 years are more likely to develop the disease, with a median age at diagnosis of 65 years.⁴ The mean age found herein was 63.4 ± 11.7 years, which is in line with the disease's epidemiology.

Although the present study sample was not that large, two aspects must be taken into account: The disease's incidence in Brazil is four people for every 100 thousand inhabitants, and some patients were not able to undergo more invasive oral exams, such as PD.

According to the latest regional oral health survey, released by the Brazilian Ministry of Health in 2010, entitled "SB Brazil," older adults aged 65 to 74 years in Fortaleza had a DMFT index of 27.2 teeth.²⁰ The elderly individuals investigated in this study presented a DMFT index of 23.3 ± 6.86 teeth. Such discrepancy may be explained by the population's access to dental health in the past 10 years.

Meanwhile, according to Guimarães et al.,²¹ women seek dental care more often than men and are hence subjected to nonconservative and/or iatrogenic procedures throughout life, resulting in fewer missing teeth. Some authors found that the oral hygiene habits of women are more effective when compared to men, thus rendering their oral health care better.^{22,23} However, the results found in our study are contradictory since the male patients presented a lower mean DMFT (18.80 ± 7.09 teeth) than the female patients (23.44 ± 6.14 teeth) and a lower mean of missing teeth (16.0 ± 9.38 vs 21.88 ± 7.42 missing teeth among women).

In the present study, a difference was observed between missing and restored teeth among the elderly and middle-aged patients with myeloma. The middle-aged group had more restored teeth, while the elderly, more missing teeth (Table 2 and Fig. 1). These results can be explained by the improvements in primary dental care over the past years in Brazil, which contributed to better oral health care in the general population.²⁴

The gingival bleeding measured by the GBI was within the standards and currently suggests localized gingivitis.^{13,25} The mean GBI of the male patients ($12.61 \pm 9.27\%$) was much lower than the women's mean GBI (22.35 ± 20.5). Although gingival bleeding is strongly related to inadequate dental plaque control, hormonal

changes throughout life in women, especially middle-aged (Fig. 2) and older women, may explain the higher GBI values.²⁶

It is also noteworthy that some patients with MM may present progressive tissue deposition of light-chain proteins that become amyloid fibrils and that, if the oral cavity is affected, it may lead to gingival bleeding.²⁷ Hematologic conditions and their association with non-plaque-induced gingival disease continue to appear in the new classification of periodontal diseases.¹³ This is because gingivitis, which is characterized by gingival bleeding, is the most common oral manifestation of hematologic disorders, depending on the etiology.²⁸

According to the literature, several conditions can influence salivary production. Hematologic diseases, notably leukemia, can affect the oral cavity, but there are not many studies showing a direct relationship between multiple myeloma and decreased salivary flow, as observed in the present study. Also, chemotherapy and some drugs used in the treatment of patients with multiple myeloma can cause xerostomia or oral dryness.²⁹ It should be noted that decreased salivary flow or hyposalivation is not listed as side effects in most drug labels. In fact, the side effects are almost always described as an oral dryness sensation or xerostomia and less as hyposalivation. It is important to highlight that the association between hyposalivation and xerostomia is not always present, as observed herein.^{30,31}

Several classes of drugs and chemotherapy compromise salivary flow and reduce salivary amylase and IgA levels, thus increasing salivary viscosity and plaque accumulation and, hence, leading to dental caries.³² Dehydration, specific medications, head and neck radiation therapy, advanced age, and diabetes mellitus are also described as the most common causes of hyposalivation. Moreover, decreased salivary flow is associated with the presence of dental caries and erosion, gingivitis, halitosis, and mucosal changes.³³

Some of the drugs used by the participants in the present study were opioids and antihypertensive and chemotherapeutic agents, which are closely related to the decrease in salivary flow and, consequently, to the most severe levels of hyposalivation.³⁴ Our findings demonstrate such an effect, as only two (10.5%) participants exhibited ideal salivary flow. The age of the patients should also be considered since the aging process itself leads to a decrease in salivary production.

According to Trentin and Oppermann,³⁵ the nonuse of dental floss may be due to several factors, such as age, gender, and socioeconomic factors. Thus, individuals with low levels of income and education often have more difficulty performing oral hygiene, which leads to greater gingival bleeding.³⁶ Considering the present study's mean GBI, the low frequency of dental flossing and the poor use of mouthwash among the participants may have increased the final values. However, the adequate frequency of tooth brushing might explain why just a few participants had a GBI above 30%.

Infection is the leading cause of mortality among patients with MM. Immunodeficiency associated with the underlying disease, in addition to accumulated immunosuppression due to the various types of treatments received over the course of the disease, is the cause of increased susceptibility to infection.³ Oral infections, such as periodontal diseases, should be controlled to decrease the risk of mortality. In addition, the accumulation of plaque-retentive factors may be associated with inflammation and infection, thus demonstrating the need to improve oral hygiene among the analyzed population.

CONCLUSION

It can be concluded that patients with multiple myeloma are predominantly of advanced age. Better dental conditions were observed in the middle-aged group compared to the elders. Men retained the lowest GBI values. The salivary flow of patients with multiple myeloma was reduced, and most of them exhibited moderate to severe hyposalivation. It can be assumed that such a situation is caused by the action of drugs, chemotherapy, or even age. The oral health of these patients requires improvement in order for a better quality of life.

REFERENCES

- Gaddey HL. Oral manifestations of systemic disease. *Gen Dent* 2017;65(6):23–29. PMID: 29099362.
- Gomes AOF, Silva JA, Noce CW, et al. The frequency of oral conditions detected in hematologic inpatients. *Hematol Transfus Cell Ther* 2018;40(3):240–244. DOI: 10.1016/j.htct.2018.02.006.
- Rajkumar SV. Multiple myeloma: 2020 update on diagnosis, risk-stratification and management. *Am J Hematol* 2020;95(5):548–567. DOI: 10.1002/ajh.25791.
- Palumbo A, Anderson K. Multiple myeloma. *N Engl J Med* 2011;364(11):1046–1060. DOI: 10.1056/NEJMra1011442.
- Gertz MA, Dingli D. How we manage autologous stem cell transplantation for patients with multiple myeloma. *Blood* 2014;124(6):882–890. DOI: 10.1182/blood-2014-03-544759.
- Almeida TMX, Cavalcanti ÉFF, Freitas ADS, et al. Can dentists detect multiple myeloma through oral manifestations? *Rev Bras Hematol Hemoter* 2018;40(1):43–49. DOI: 10.1016/j.bjhh.2017.08.006.
- Khosla J, Yeh AC, Spitzer TR, et al. Hematopoietic stem cell transplant-associated thrombotic microangiopathy: current paradigm and novel therapies. *Bone Marrow Transplant* 2018;53(2):129–137. DOI: 10.1038/bmt.2017.207.
- Torres SR. Oral features of graft-versus-host disease. *Rev Bras Hematol Hemoter* 2014;36(1):9–11. DOI: 10.5581/1516-8484.201400005.
- Cruz PKR, Vieira MA, Carneiro JÁ, et al. Difficulties of access to health services among non-institutionalized older adults: prevalence and associated factors. *Rev Bras Geriatr Gerontol* 2020;23(6):e190113. DOI: 10.1590/1981-22562020023.190113.
- Peres KG, Peres MA, Boing AF, et al. Reduction of social inequalities in utilization of dental care in Brazil from 1998 to 2008. *Rev Saúde Pública* 2012;46(2):1–8. DOI: 10.1590/s0034-89102012000200007.
- Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* 2014;15(12):e538–e548. DOI: 10.1016/S1470-2045(14)70442-5.
- Lima DLF, Carneiro SDRM, Barbosa FTS, et al. Salivary flow and xerostomia in older patients with type 2 diabetes mellitus. *PLoS One* 2017;12(8):e0180891. DOI: 10.1371/journal.pone.0180891. eCollection 2017.
- Adam R, Goyal CR, Qaqish J, et al. Evaluation of an oscillating-rotating toothbrush with micro-vibrations versus a sonic toothbrush for the reduction of plaque and gingivitis: results from a randomized controlled trial. *Int Dent J* 2020;70(Suppl. 1):S16–S21. DOI: 10.1111/ijdj.12569.
- Pontigo-Loyola AP, Márquez-Corona ML, Minaya-Sánchez M, et al. Correlation between the caries status of the first permanent molars and the overall DMFT index: a cross-sectional study. *Medicine (Baltimore)* 2020;99(5):e19061. DOI: 10.1097/MD.00000000000019061.
- IBGE. Pesquisa Nacional por Amostra de Domicílios Contínua Quarto Trimestre de 2019. Available from: https://biblioteca.ibge.gov.br/visualizacao/periodicos/2421/pnact_2019_4tri.pdf.
- Orlandi M, Suvan J, Petrie A, et al. Association between periodontal disease and its treatment, flow-mediated dilatation and carotid intima-media thickness: a systematic review and meta-analysis. *Atherosclerosis* 2014;236(1):39–46. DOI: 10.1016/j.atherosclerosis.2014.06.002.
- Souto R, Silva-Boghossian CM, Colombo AP. Prevalence of *Pseudomonas aeruginosa* and *Acinetobacter* spp. in subgingival biofilm and saliva of subjects with chronic periodontal infection. *Braz J Microbiol* 2014;45(2):495–501. DOI: 10.1590/s1517-83822014000200017.
- Basha S, Swamy HS, Mohamed RN. Maternal periodontitis as a possible risk factor for preterm birth and low birth weight – a prospective study. *Oral Health Prev Dent* 2015;13(6):537–544. DOI: 10.1590/s1517-83822014000200017.
- Kolte RA, Kolte AP, Deshpande NM. Assessment and comparison of anemia of chronic disease in healthy subjects and chronic periodontitis patients: a clinical and hematological study. *J Indian Soc Periodontol* 2014;18(2):183–186. DOI: 10.4103/0972-124X.131321.
- Ministério da Saúde. Projeto SB Brasil 2010: Pesquisa Nacional de Saúde Bucal – Resultados Principais. Brasília (DF): Secretaria de Políticas de Saúde; 2011.
- Guimarães KB, Meireles SS, Marques MS, et al. Periodontal conditions in carriers of diabetes mellitus type 2 assisted in the Federal University of Paraíba. *Rev Odontol Ciênc* 2007;22:124–130.
- Lisbôa IC, Abegg C. Oral hygiene habits and use of dental Services by adolescents and adults in the municipality of Canoas, Rio Grande do Sul state, Brazil. *Epidemiologia e Serviços de Saúde* 2006;15:29–39. DOI: 10.5123/S1679-49742006000400004.
- Abegg C. Oral hygiene habits among Brazilian adults in a urban área of Southern Brazil. *Rev Saúde Pública* 1997;31(6):586–593. DOI: 10.1590/S0034-89101997000700007.
- Sousa Queiroz RC, Ribeiro AGA, Tonello AS, et al. Is there a fair distribution of the structure of dental services in the capitals of the Brazilian Federative Units? *Int J Equity Health* 2019;18(5):1. DOI: 10.1186/s12939-018-0899-5.
- Trombelli L, Farina R, Silva CO, et al. Plaque-induced gingivitis: case definition and diagnostic considerations. *J Clin Periodontol* 2018;45:S44–S67. DOI: 10.1002/JPER.17-0576.
- Zuza EP, Pires JR, Martins AT, et al. Evaluation of the gingival condition in response to the hormonal peaks of the women's reproductive cycle: controlled clinical trial. *Rev Periodontia* 2010;20:60–66.
- Oliveira KKV, Dias IO, Martins ICV, et al. Manifestações orais nas doenças hematológicas: revisão de literatura. *Revista da Universidade Vale do Rio Verde, Três Corações* 2015;13(2):216–235. DOI: 10.5892/ruvrd.v13i1.2275.
- Porter SR, Mercadante V, Fedele S. Oral manifestations of systemic disease. *Br Dent J* 2017;223(9):683–691. DOI: 10.1038/sj.bdj.2017.884.
- Gonnelli FAS, Palma LF, Giordani AJ, et al. Low-level laser therapy for the prevention of low salivary flow rate after radiotherapy and chemotherapy in patients with head and neck cancer. *Radiol Bras* 2016;49(2):86–91. DOI: 10.1590/0100-3984.2014.0144.
- Villa A, Wolff A, Narayana N, et al. World Workshop on Oral Medicine VI: a systematic review of medication-induced salivary gland dysfunction. *Oral Dis* 2016;22(5):365–382. DOI: 10.1111/odi.12402.
- Pedersen A, Sorensen C, Proctor G, et al. Salivary secretion in health and disease. *J Oral Rehabil* 2018;45(9):730–746. DOI: 10.1111/joor.12664.
- Sweeney MP, Bagg J, Baxter WT, et al. Oral disease in terminally ill cancer patients with xerostomia. *Oral Oncol* 1998;34(2):123–126. DOI: 10.1016/S1368-8375(97)00076-6.
- Moore PA, Guggenheimer J, Etzel KR, et al. Type I diabetes mellitus, xerostomia, and salivary flow rates. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2001;92(3):281–291. DOI: 10.1067/moe.2001.117815.
- Montenegro FLB, Pereira CMM, Marchini L, et al. Reported oral side-effects of medications in the elderly: a very important point for discussion by interdisciplinary health care staff. *Anal do Meeting de Função Oral do Idoso* 2004;22:480.
- Trentin MS, Oppermann RV. Prevalence of interproximal oral hygiene habits and its influence on dental plaque presence and gingival bleeding in a group of students. *Rev Fac Odontol* 2001;6(2):15–22.
- Gesser HC, Peres MA, Marcenes W. Gingival and periodontal conditions associated with socioeconomic factors. *Rev Saúde Pública São Paulo* 2001;35(3):289–293. DOI: 10.1590/S0034-89102001000300012.