



# Oral health–related quality of life among individuals with rheumatoid arthritis

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## Abstract

**Objective** To evaluate the oral health–related quality of life (OHRQoL) of individuals with rheumatoid arthritis (RA) in comparison with individuals with no RA.

**Method** A cross-sectional study was carried out with 112 individuals distributed into two groups. Group 1 (G1) consisted of 42 RA individuals and group 2 (G2) consisted of 70 individuals without RA. Participants' OHRQoL was assessed by means of the long form of the Oral Health Impact Profile (OHIP). The OHIP has 49 questions distributed across seven domains: functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability, and handicap. The overall score ranges between 0 and 196. A higher score denotes a greater negative impact on OHRQoL. All participants underwent oral examination for the evaluation of clinical variables. Sociodemographic and oral behavior variables were also collected. Data analysis included descriptive statistics, Mann-Whitney test, and regression analysis.

**Results** Individuals in G1 presented higher OHIP overall score ( $p = 0.006$ ) than G2 individuals. G1 individuals also presented higher scores in the functional limitation ( $p = 0.003$ ) and the physical disability ( $p = 0.005$ ) domains than G2 individuals. Individuals with RA ( $p = 0.044$ ), individuals who brushed their teeth less often ( $p = 0.019$ ), and those with a higher number of decayed, missing, and filled teeth (DMFT) ( $p = 0.038$ ) presented a significantly higher OHIP-49 overall score (more negative perception of their OHRQoL) than individuals without RA, individuals who brushed their teeth more often, and those with a lower DMFT.

**Conclusion** RA individuals had a more negative perception of their OHRQoL compared with individuals with no RA.

**Keywords** Oral health · Periodontitis · Quality of life · Rheumatoid arthritis

## Introduction

Rheumatoid arthritis (RA) is a systemic autoimmune inflammatory disease that in the long run, body organs, such as the heart, the lung, and the central nervous system, may be impaired [1]. Estimates of the prevalence have showed a figure between 0.5 and 1.0% worldwide [2]. The anticipated diagnosis enables the clinician to provide timely health care in order to attenuate functional limitations, which is an endpoint of the disease leading to inability to carry out everyday activities [3]. Those functional limitations may also undermine individual's hand performance, impairing his/her ability to accomplish self-care [4].

As regards oral health, recent systematic summaries of the literature have demonstrated an association between RA and oral outcomes [5, 6]. The most frequent issues are periodontal

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disease [5, 6] and tooth loss [5]. RA individuals are more affected by periodontal disease than the ones with no RA [7, 8]. A higher prevalence of clinical attachment loss also takes place more often among RA patients [9]. Moreover, RA individuals present an increased number of tooth losses in comparison with their counterparts without RA [8, 10], and the literature has demonstrated that xerostomia may be a complaint when RA individuals are visiting a health care facility [11].

Subjective information on individuals' physical and psychological aspects needs to be included in the portfolio of the provider during the assessment of patients' health status [12]. Indeed, information emerged from the clinical assessment of the health care deliverer along with the patients' perspective and perceptions give a more comprehensive understanding of the disease, which, in turn, may be helpful during the surveillance and treatment of the affected individual [13]. RA may deteriorate the health-related quality of life of affected individuals [14]. The adverse repercussions of RA are beyond the limits of symptoms and the associated functional limitations. The individuals' emotional and social well-being is negatively influenced as well [15]. Nonetheless, data on the oral health-related quality of life (OHRQoL) are still sparse in the literature [16]. Therefore, the aim of this study was to evaluate the OHRQoL of RA individuals in comparison with healthy individuals with no RA.

## Methods

### Setting, study design, participants, and eligibility criteria

The RA Outpatient Clinic of the Rheumatology Division of the Federal University of Minas Gerais (UFMG) in Belo Horizonte, Brazil, was the setting for this cross-sectional study. The study group (G1) consisted of 42 patients aged 18 years or more, who met the following inclusion criteria: diagnosis of RA based on the 2010 American College of Rheumatology and EULAR Classification Criteria [17], no other rheumatic disease (including Sjögren's syndrome), no treatment for periodontal disease within the last 6 months, no wearing of orthodontic appliances, no use of antibiotics within the last 90 days, no pregnancy or lactation, no neoplasia within the last 5 years, and the presence of at least eight teeth. Patients' medical history and medications were determined by review of medical charts.

A total of 70 individuals with no RA or other rheumatic diseases randomly selected from a given population belonged to the control group (G2), and the same exclusion criteria were applied. These individuals were classified as having sociodemographic and schooling characteristics very much alike to those in G1. A structured interview made the access

to their medical history feasible. Figure 1 displays the flow-chart of the study.

### Ethical issues

The Committee on Ethics of the Federal University of Minas Gerais has approved this study (number of approval statement: CAAE 03128012.0.0000.5149/2012). Individuals were inquired regarding acceptance to participate in the study. Those who accepted to take part signed a form of informed consent. The study was performed in accordance with the Declaration of Helsinki.

### Sample size

The Power and Sample Size Calculation software (PS, version 3.0; Nashville, TN, USA) allowed us to accomplish sample size calculation. The following parameters of a previous study [16] were used for calculation: mean difference in the overall quality of life score between individuals with RA and individuals with no RA (control) of 6.1 and pooled standard deviation of 9.6. The ratio between individuals with no RA and individuals with RA is 1.66. For a study with sample power of 90%, 42 individuals in G1 and 70 individuals in G2 were necessary.

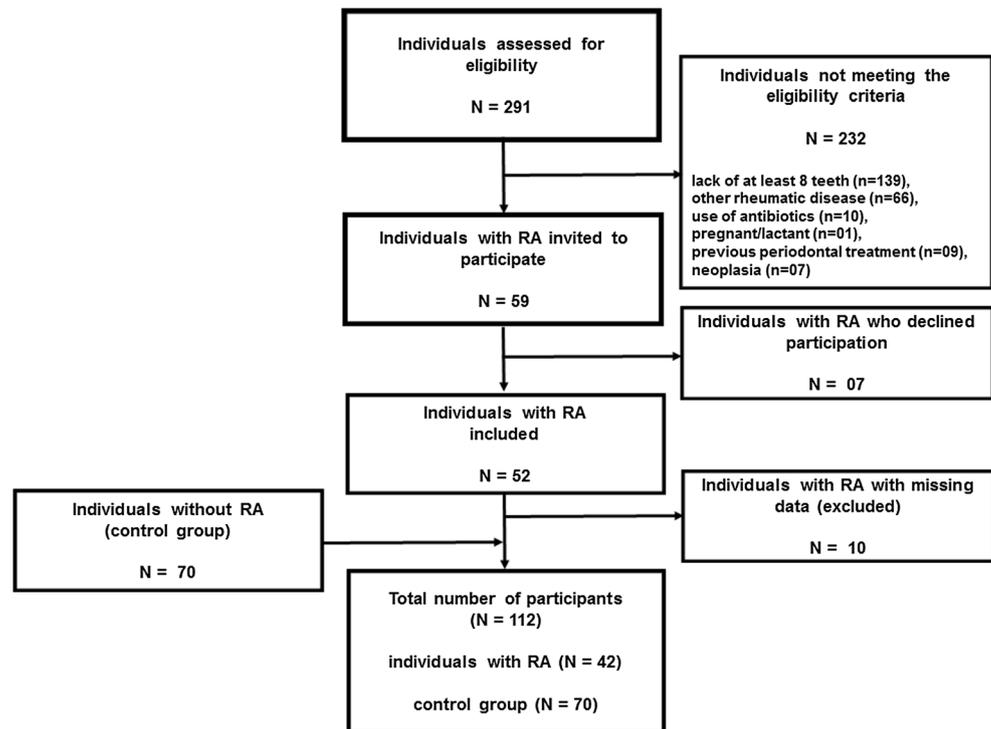
### Rheumatoid arthritis-related variables

One investigator (DCC) assessed disease activity among RA individuals using the erythrocyte sedimentation rate (ESR) Disease Activity Score in 28 joints (DAS28). Data on swollen and tender joint counts (on 28 joints), ESR, and patients' global health analogical scale were collected, and an overall score of disease activity was estimated for RA individuals [18]. The continuous variable disease duration (years), rheumatoid factor (IU/mL), ACPAs (anti-citrullinated protein antibodies in units/milliliter), and immunosuppressive therapy (cumulative dose of corticoids; milligram/prednisone) were also assessed. The variable bisphosphonates therapy (no current use/current use) was also evaluated.

### OHRQoL assessment tool

Participants' OHRQoL was assessed by means of the long form of the Oral Health Impact Profile questionnaire (OHIP-49) [19]. This tool was conceived in Australia and a reliable Brazilian version has already been confirmed [20]. OHIP-49 is made up of 49 questions unequally apportioned among seven domains: functional limitation (9 questions), physical pain (9 questions), psychological discomfort (5 questions), physical disability (9 questions), psychological disability (6 questions), social disability (5 questions), and handicap (6 questions). Each question presents 5 answer alternatives as represented by an ordinal scale: 0 indicates "never," 1

Fig. 1 Flowchart of the study



indicates “hardly ever,” 2 indicates “sometimes,” 3 indicates “fairly often,” and 4 indicates “very often.” The overall score is achieved through the sum of the 49 questions’ scores and varies from 0 to 196. There is also the feasibility for scores for each of the seven domains. The higher the score, the greater the negative impact on participants’ OHRQoL.

### Assessment of oral conditions

The number of decayed, missing, and filled teeth (DMFT) was recorded as described elsewhere [21]. Two calibrated examiners (SMM and JDC) assessed periodontal status using a periodontal probe (PCP 15, Hu-Friedy, North Carolina, Chicago, IL, USA). The following parameters were recorded: plaque index, probing depth, clinical attachment level, and bleeding on probing. Two or more interproximal sites with probing depth  $\geq 4$  mm or one site with probing depth  $\geq 5$  mm were suggestive of periodontitis [22].

During assessment of sialometry, individuals were advised to have no eating or drinking for half an hour. During assessment of unstimulated sialometry, individuals were informed to spit the saliva that had been accumulated for 5 min. During assessment of stimulated sialometry, the strategy was very much alike and individuals were advised to chew a sialogogue for saliva collection. The variables’ unstimulated sialometry and stimulated sialometry were analyzed as continuous variables (milliliter/minute (mL/min)). Information on prosthesis wearing (no/yes) was also obtained.

### Sociodemographic and oral behavior variables

Information on sociodemographics was recorded as follows: sex (male/female), age (years), and schooling (years). Household income was assessed taking into account the Minimum Wage per month in Brazil (BZM), which was equal to US\$ 300 during data collection and was represented by the overall income of the members of each participant’s family, who were economically active. The number of BZMs earned by the family members of the participants was recorded.

Oral hygiene habits, such as frequency of tooth brushing (times/day) and use of dental floss (times/day), were recorded based on participants’ answers. Smoking was also assessed: number of years of smoking and number of packs/year.

### Statistical analysis

Data analysis was accomplished by means of the software Statistical Package for the Social Sciences—SPSS (IBM, 22.0; Armonk, NY, USA). The Mann-Whitney test was employed to draw comparisons between participants of G1 and G2 regarding the OHIP-49 overall score and domains’ scores. A  $p < 0.05$  indicated statistical significance for the overall score. For the domains, the Bonferroni correction was adopted and values of  $p < 0.007$  were considered a threshold of significance [23, 24]. The Pearson correlation was employed to test the correlation of the continuous variables disease duration, rheumatoid factor, ACPAs, and immunosuppressive therapy with the OHIP-49 overall score and domains’

scores among G1 individuals. The Mann-Whitney test was used to assess differences in the OHIP-49 overall score and domains' scores between G1 individuals not currently undergoing bisphosphonates therapy and G1 individuals currently undergoing bisphosphonates therapy. A  $p < 0.05$  was indicative of statistical significance.

Bivariate analyses were conducted. The chi-square test was used to compare G1 and G2 with respect to sex and the clinical variables periodontitis and prosthesis wearing. Student's  $t$  test was used to compare G1 and G2 with respect to sociodemographic variables (age, schooling, and income), oral behavior variables (tooth brushing, flossing, number of years smoking, and number of packs/year), and clinical variables (unstimulated sialometry, stimulated sialometry, number of missing teeth, and DMFT). A  $p < 0.25$  in the bivariate analyses endorsed the inclusion of the variables in the regression model. In this conclusive model, values of  $p < 0.05$  were acknowledged as statistically significant.

## Results

In G1 (RA), five individuals were male (11.9%) and 37 were female (88.1%). RA individuals' mean age was 52.04 years ( $\pm 11.08$ ). In G2 (control), 16 individuals were male (22.9%) and 54 were female (77.1%). Control individuals' mean age was 41.34 years ( $\pm 13.87$ ).

Table 1 displays the results of the analysis with which the comparison of OHRQoL between G1 and G2 was carried out. Individuals in G1 presented higher OHIP-49 overall score ( $p = 0.006$ ) than G2 individuals. G1 individuals also presented higher scores in the functional limitation ( $p = 0.003$ ) and the physical disability ( $p = 0.005$ ) domains than G2 individuals.

Table 2 shows that, in G1, the correlation between disease activity (DAS28), disease duration, rheumatoid factor, ACPAs, and immunosuppressive therapy with OHIP-49 overall score and domains' scores was weak. Moreover, no

difference between individuals not currently undergoing bisphosphonates therapy and individuals currently undergoing bisphosphonates therapy was observed ( $p > 0.05$ ).

Table 3 shows the results of the comparisons between G1 and G2 with respect to sociodemographic and oral behavior variables. Individuals in G1 were significantly older than individuals in G2. Individuals in G2 presented a significantly higher schooling than individuals in G1. The variables age ( $p < 0.001$ ), schooling ( $p < 0.001$ ), income ( $p = 0.062$ ), tooth brushing ( $p = 0.084$ ), and flossing ( $p = 0.178$ ) were incorporated into the regression model.

Table 4 presents the results of the comparisons between G1 and G2 with respect to clinical variables. The number of individuals wearing prosthesis in G1 was significantly higher than that in G2. The number of missing teeth and DMFT among individuals in G1 was significantly higher than among individuals in G2. Stimulated sialometry in G2 was significantly higher than that in G1. The variables prosthesis wearing ( $p = 0.040$ ), unstimulated sialometry ( $p = 0.072$ ), stimulated sialometry ( $p = 0.016$ ), number of missing teeth ( $p = 0.003$ ), and DMFT ( $p = 0.001$ ) were included in the regression model.

Table 5 displays the results of regression model. RA, tooth brushing, and DMFT were predictors of a significant impact on OHRQoL. Individuals with RA ( $p = 0.044$ ), individuals who brushed their teeth less often ( $p = 0.019$ ), and those with a higher DMFT ( $p = 0.038$ ) presented a significantly higher OHIP-49 overall score (more negative perception of their OHRQoL) than individuals without RA, individuals who brushed their teeth more often, and those with a lower DMFT.

## Discussion

This study showed that individuals with RA had a more negative perception of their OHRQoL compared with individuals without RA. The main negative repercussions were observed in the functional limitation and physical disability domains.

**Table 1** Comparison of oral health-related quality of life between rheumatoid arthritis and control individuals

	G1 (rheumatoid arthritis) Median (min-max)	G2 (control) Median (min-max)	$p$ value
Functional limitation	15.0 (3–30)	10.0 (0–28)	0.003*
Physical pain	10.5 (2–28)	09.5 (0–26)	0.094*
Psychological discomfort	06.5 (0–20)	05.5 (0–20)	0.030*
Physical disability	06.0 (0–25)	01.0 (0–28)	0.005*
Psychological disability	03.0 (0–23)	00.5 (0–17)	0.075*
Social disability	00.0 (0–16)	00.0 (0–16)	0.042*
Handicap	00.0 (0–12)	00.0 (0–12)	0.070*
Overall score	49.5 (9–132)	23.0 (0–116)	0.006**

\*Mann-Whitney test with Bonferroni correction. Significance level  $< 0.007$

\*\*Mann-Whitney test. Significance level  $< 0.05$

**Table 2** Relationship between clinical-related variables with OHIP-14 overall score and domains' scores among rheumatoid arthritis individuals

	Functional limitation	Physical pain	Psychological discomfort	Physical disability	Psychological disability	Social disability	Handicap	Overall score
<b>Disease activity (DAS28)</b>								
Coefficient	0.20	0.32	0.13	0.19	0.13	0.26	0.04	0.23
<i>p</i> value*	0.203	0.035	0.391	0.212	0.387	0.088	0.766	0.136
<b>Disease duration (years)</b>								
Coefficient	-0.09	-0.10	0.07	-0.13	0.03	-0.15	-0.01	-0.06
<i>p</i> value*	0.565	0.535	0.629	0.389	0.854	0.337	0.965	0.697
<b>Rheumatoid factor (UI/mL)</b>								
Coefficient	-0.21	-0.16	-0.07	-0.06	-0.11	-0.06	-0.02	-0.14
<i>p</i> value*	0.177	0.297	0.633	0.674	0.492	0.702	0.869	0.382
<b>ACPs (units/mL)</b>								
Coefficient	0.10	-0.11	0.15	0.19	-0.01	-0.06	0.24	0.08
<i>p</i> value*	0.597	0.585	0.430	0.321	0.959	0.759	0.227	0.689
<b>Immunosuppressive therapy#</b>								
Coefficient	-0.07	0.04	0.05	-0.01	0.06	-0.01	0.08	0.02
<i>p</i> value*	0.645	0.767	0.731	0.929	0.687	0.961	0.612	0.894
<b>Bisphosphonates therapy</b>								
No current use								
Median (min–max)	15.0 (3.0–30.0)	10.0 (2.0–28.0)	6.0 (0.0–20.0)	5.0 (0.0–25.0)	4.0 (0.0–23.0)	0.0 (0.0–16.0)	0.0 (0.0–12.0)	43.0 (9.0–132.0)
Current use								
Median (min–max)	15.0 (4.0–29.0)	13.0 (2.0–22.0)	7.0 (0.0–20.0)	8.0 (0.0–20.0)	0.0 (0.0–12.0)	0.0 (0.0–15.)	0.0 (0.0–8.0)	58.0 (9.0–101.0)
<i>p</i> value**	0.898	0.934	0.676	0.721	0.158	0.671	0.347	0.769

DAS disease activity score, ACPs anti-citrullinated protein antibodies

\*Spearman correlation. Significance level < 0.05

\*\*Mann-Whitney test. Significance level < 0.05

#Cumulative dose of corticoids; mg/prednisone

**Table 3** Comparison of sociodemographic characteristics and oral behaviors between rheumatoid arthritis and control individuals

	G1 (rheumatoid arthritis)	G2 (control)	<i>p</i> value
Sex			
Male	05 (11.9)*	16 (22.9)*	= 0.272***
Female	37 (88.1)*	54 (77.1)*	
Age (years)	52.04 (11.08)**	41.34 (13.87)**	< 0.001****
Schooling (years)	8.00 (3.56)**	10.88 (3.73)**	< 0.001****
Income (BZW)	2.83 (2.26)**	3.72 (2.50)**	= 0.062****
Tooth brushing (times/day)	2.95 (0.69)**	2.68 (0.90)**	= 0.084****
Flossing (times/day)	1.23 (1.28)**	0.92 (0.94)**	= 0.178****
Smoking (number of years)	3.93 (11.83)**	2.34 (7.79)**	= 0.394****
Smoking (number of packs/year)	34.76 (114.56)**	19.55 (71.01)**	= 0.387****

BZW Brazilian minimum wage/month

\*Number (%)

\*\*Mean (standard deviation)

\*\*\*Chi-square test

\*\*\*\*Student's *t* test

The oral determinants for the negative impact on the OHRQoL of RA individuals were to brush the teeth less often and a higher DMFT (number of decayed, missing, and filled teeth).

Dental caries has a negative impact on the quality of life of individuals. The higher the number of decayed teeth or the DMFT, the more negative is the perception of the individuals regarding their OHRQoL [25, 26]. However, scientific evidence on the impact of oral conditions on OHRQoL among RA subjects is still limited, and only two articles, one conducted in Germany [16] and one in Finland [27], compared the OHRQoL of RA patients with a control group of individuals without such condition. Both studies used, in the methods, the short form of the OHIP questionnaire [28]. In the present

study, no difference between groups was observed regarding the impact of oral conditions on OHIP domains that assess psychological and social outcomes. These findings contrast with the results of the Finnish study [27], in which individuals with RA had a greater deterioration in the overall score and in all quality of life domains, including those that measure psychosocial aspects when compared with individuals without RA. According to these authors, the individual with RA cares and, sometimes, feels embarrassed due to his/her oral condition, and the related distress may hamper his/her ability to socialize, leading to social isolation [16, 27].

Concurring with previous studies [16, 27], individuals with RA evaluated in the present study had a more negative impact of oral conditions on the OHRQoL in the domains of

**Table 4** Comparison of clinical variables between rheumatoid arthritis and control individuals

	G1 (rheumatoid arthritis)	G2 (control)	<i>p</i> value
Periodontitis			
No	23 (54.8)*	33 (47.1)*	0.558***
Yes	19 (45.2)*	37 (52.9)*	
Prosthesis wearing			
No	23 (54.8)*	52 (74.3)*	0.040***
Yes	19 (45.2)*	18 (25.7)*	
Sialometry unstimulated (mL/min)	0.72 (0.49)**	0.88 (0.43)**	0.072****
Sialometry stimulated (mL/min)	1.68 (0.78)**	2.11 (0.96)**	0.016****
Missing teeth	7.21 (5.50)**	4.28 (4.71)**	0.003****
DMFT	18.85 (5.62)**	14.78 (7.16)**	0.001****

BZW Brazilian minimum wage

\*Number (%)

\*\*Mean (standard deviation)

\*\*\*Chi-square test

\*\*\*\*Student's *t* test

**Table 5** Regression model evaluating the association between independent variables and the OHIP-49 overall score

	Coefficient	Standard error	<i>p</i> value*
Rheumatoid arthritis; yes (G1), no (G2)	−0.339	0.168	0.044
Age (years)	0.001	0.005	0.821
Schooling (years)	−0.009	0.020	0.671
Income (BZW)	−0.031	0.043	0.471
Tooth brushing (times/day)	−0.214	0.091	0.019
Flossing (times/day)	0.059	0.068	0.388
Prosthesis wearing; no, yes	0.236	0.176	0.181
Sialometry unstimulated (mL/min)	−0.345	0.212	0.105
Sialometry stimulated (mL/min)	0.133	0.103	0.201
Missing teeth	0.008	0.018	0.679
DMFT	0.030	0.014	0.038

\*Significant at  $p < 0.05$ *BZM* minimum wage per month in Brazil, *DMFT* decayed, missing, and filled teeth

functional limitation and physical disability [19, 20]. Difficulties in oral functioning such as chewing, speaking, and smiling may be related to tooth loss or the presence of decayed teeth [29]. In the present study, the number of decayed, missing, and filled teeth (DMFT) and the number of missing teeth were greater in the RA group. DMFT index was one of the main determinants for the negative impact on the OHRQoL of individuals in this group. These data contrast with the findings of a previous study [16], in which no impact of oral outcomes (such as DMFT, missing teeth, and periodontal outcomes) on the quality of life was observed in RA individuals. The variable tooth brushing was also a determinant for the impairment of OHRQoL. Individuals who brushed their teeth less often were more likely to present a more negative perception of their OHRQoL. RA individuals may present restrictions of hand and finger movement [30], which in turn may impair the capacity of the affected individuals to carry out tooth brushing [31]. Individuals who are unable to accomplish adequate oral hygiene are more likely to present oral diseases, such as dental caries. The findings presented herein underscore the importance of the oral health care provider in the surveillance and guidance of patients with RA with respect to their oral hygiene practices [32].

Sjögren's syndrome is a chronic inflammatory autoimmune disease characterized by the infiltration of autoreactive lymphocytes into the exocrine glands resulting in glandular dysfunction [33]. Sjögren's syndrome (SS) occurs as a primary disease or secondary manifestation of autoimmune diseases, such as rheumatoid arthritis (20–32%) [34]. The main clinical manifestations observed in individuals with SS are the symptoms of sicca that corresponds to dryness of the mouth and eyes due to decreased saliva and tears [34]. When compared with the general population, individuals with the syndrome have a higher prevalence of dental caries and tooth loss [35]. These patients also present a significant

deterioration of OHRQoL [35]. In our population, no patient had diagnosis of Sjögren's syndrome. Our results showed that stimulated salivary flow in patients of the control group was significantly higher than that in the group of patients with RA, but all patients exhibited stimulated and unstimulated salivary flow at normal range as described elsewhere [36]. The possible influence of reduced stimulated salivary flow on the development of caries and tooth loss observed among RA patients in this study deserves further investigation.

The information presented herein may be useful for the clinical practice of health care providers during the management of RA individuals. Knowledge on the impact of RA on these dimensions provides the clinician with the capacity to tailor, for that affected individual, specific treatment for the disease. Awareness on OHRQoL outcomes will also allow clinicians to list therapeutic benefits to be achieved by the patient if he/she strictly adheres to the proposed treatment regimen [37]. Maintenance of physical functions represents a fundamental long-term goal for patients with RA [38]. In this regard, alertness on the aspects that may have interference in the quality of life of an affected individual is quite important to outline effective therapeutic approaches, as well as to adapt the reality of that affected person to the recommended treatment [39]. This subjective and multidimensional pool of information may prove useful for a more assertive counseling and guidance of the RA patient regarding his/her oral health [16].

The following statements are limitations of this study. The first regards sample size. However, it is necessary to be aware that the study was carried out in a reference center for rheumatic diseases' treatment, where acquisition of accurate and reliable indicators for the evaluation of a given health condition is feasible [40]. Moreover, the sample size power has been calculated. A sample power higher than 80% provides

validity to our results [41]. The second limitation regards study design. Case-control or longitudinal studies would have allowed us to obtain more robust findings. However, the cross-sectional design with a control group ensured a high descriptive power of the variables of interest and the comparison of RA individuals with non-affected individuals. Celerity during data collection and representativeness of a specific population have also been characteristics of the study presented herein [42].

Future studies should evaluate the impact of the treatment for RA on the OHRQoL of affected individuals. Chronic diseases are conditions characterized by the continuous presence of symptoms and, therefore, require unending medical care [43]. Although no cure for RA exists, treatment for this disease may help in the reduction of inflammatory parameters, slowing down joint damage, and mitigating adverse effects on the affected individual's physical ability [44]. Treatment for RA involves a combination of anti-rheumatic drugs that may have systemic side effects [45]. Information on how such drugs affect oral health may be useful for improving therapeutic modalities for RA patients. In addition to the knowledge on the clinical aspects of the disease and its treatment, it is highly recommended for the health care provider to be familiar with the perceptions of the affected individual regarding the consequences of these outcomes both in his/her social life and in the accomplishment of his/her basic activities [16, 27].

## Conclusion

Individuals with RA presented a more negative perception of their OHRQoL compared with individuals with no RA. The main impact regards the functional limitation and physical disability domains. The oral determinants for the negative impact on the OHRQoL of RA individuals were to brush the teeth less often and a higher DMFT (number of decayed, missing, and filled teeth).

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## Compliance with ethical standards

**Ethical approval of research involving human participants/informed consent** The Committee on Ethics of the Federal University of Minas Gerais has approved this study (number of approval statement: CAAE 03128012.0.0000.5149/2012). Individuals who agreed to participate signed an informed consent form. The study was performed in accordance with the Declaration of Helsinki.

**Disclosures** None.

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