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**Perda Dentária como Preditor de Complicações e Prognósticos em Pacientes  
com Artrite Reumatoide**

Juiz de Fora

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Trabalho de Conclusão de Curso  
apresentado à Faculdade de  
Odontologia da Universidade Federal  
de Juiz de Fora, como requisito parcial  
à obtenção do título de Cirurgiã-  
Dentista.

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de Cirurgiã-Dentista.

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## RESUMO

A Artrite Reumatoide (AR) é uma doença autoimune crônica e sistêmica que se manifesta na cavidade oral principalmente através do desenvolvimento e da progressão da doença periodontal (DP), uma condição inflamatória na cavidade bucal que possui relação bidirecional com a doença reumatológica e com outras doenças sistêmicas, e que pode levar gradualmente à perda dentária (PD). Sabendo desta relação, o estudo objetivou avaliar e analisar as condições de saúde bucal e a perda dentária em pacientes com AR para determinar se o número de dentes ausentes poderia ser utilizado como um indicador adicional útil para a equipe médica, prevenindo exacerbações da doença sistêmica. Foi realizado um estudo transversal envolvendo pacientes com AR avaliados de acordo com protocolos e instrumentos específicos. Avaliou-se os prontuários médicos, que forneceram os dados demográficos, a história médica e da doença reumatológica, e os medicamentos utilizados por cada paciente. E foram realizadas a avaliação orofacial sistemática, a aplicação de questionários validados, e a coleta dos índices de atividade da doença reumatológica e da capacidade funcional (DAS-28 e HAQ). A partir da obtenção de todos os dados, eles foram analisados estatisticamente. A pesquisa incluiu 21 pacientes com idades entre 31 e 74 anos, dos quais 7 (33,4%) apresentavam remissão da AR e 14 (66,6%) exibiam algum nível de atividade da doença. Desses pacientes, 10 (47%) possuíam deficiência moderada a grave provocada pela AR. As análises estatísticas revelaram que os pacientes em polifarmácia (média dos ranks= 12,87) tendem a apresentar maior número de dentes perdidos quando comparados aos pacientes que fazem uso de menor número de medicamentos (média dos ranks = 6,33) ( $U = 17$ ,  $df = 1$ ,  $p = 0,029$ ), e que há um valor do Índice de Dentes Cariados Perdidos e Obturados (CPOD) maior em pacientes com algum grau de atividade de doença reumatológica. A análise de correspondência evidenciou que os pacientes em polifarmácia apresentaram maior prevalência de incapacidade moderada ou grave do HAQ, juntamente com pontuações moderadas a altas do CPOD. Conclui-se então que há uma relação entre o índice CPOD, a atividade da AR, o número de dentes perdidos e a necessidade de polifarmácia, tornando-os dados importantes para serem avaliados na rotina clínica médica dos pacientes com AR.

Palavras-chave: Artrite reumatoide. Perda dentária. Polifarmácia. Índice CPOD, Odontologia

## **ABSTRACT**

Rheumatoid Arthritis (RA) is a chronic, systemic autoimmune disease that manifests in the oral cavity primarily through the development and progression of periodontal disease (PD), an inflammatory condition in the oral cavity that has a bidirectional relationship with rheumatologic disease and other systemic conditions, and can gradually lead to tooth loss (TL). Given this relationship, the study aimed to evaluate and analyze oral health conditions and tooth loss in RA patients to determine whether the number of missing teeth could be used as an additional useful indicator for the medical team, predicting exacerbations of the systemic disease. A cross-sectional study was conducted involving RA patients assessed according to specific protocols and instruments. Medical records were reviewed, providing demographic data, medical and rheumatologic history, and medications used by each patient. A systematic orofacial assessment was carried out, validated questionnaires were administered, and indices of rheumatologic disease activity and functional capacity (DAS-28 and HAQ) were collected. After obtaining all the data, they were statistically analyzed. The study included 21 patients aged between 31 and 74 years, with 7 (33.4%) in remission of RA and 14 (66.6%) exhibiting some level of disease activity. Among these patients, 10 (47%) had moderate to severe disability caused by RA. Statistical analyses revealed that patients on polypharmacy (mean rank = 12.87) tended to have a greater number of missing teeth compared to those using fewer medications (mean rank = 6.33) ( $U = 17$ ,  $df = 1$ ,  $p = 0.029$ ), and there was a higher Carious, Missing, and Filled Teeth (DMF-T) index value in patients with some degree of rheumatologic disease activity. Correspondence analysis indicated that patients on polypharmacy had a higher prevalence of moderate to severe disability as assessed by HAQ, along with moderate to high DMF-T scores. It is concluded that there is a relationship between the DMF-T index, RA activity, the number of missing teeth, and the need for polypharmacy, making these data important to be assessed in the clinical routine of RA patients.

**Keywords:** Rheumatoid arthritis. Tooth loss. Polypharmacy. DMF index, Dentistry.

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## LISTA DE ABREVIATURAS E SIGLAS

RA.....	Rheumatoid Arthritis
PD.....	Periodontal Disease
TL .....	Tooth Loss
DAS28 .....	Disease Activity Score
HAQ.....	Health Assessment Questionnaire
DMF-T.....	Decayed, Missing, and Filled Teeth
TMD .....	Temporomandibular Disorders
VLL DMFT .....	very low or low
MH DMFT .....	moderate or high
REM.....	DAS28 in remission
DA.....	DAS28 in disease activity
NOMD.....	HAQ no or mild disability
MOSD.....	HAQ moderate or severe disability
IP .....	In polypharmacy
NP.....	Not in polypharmacy

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Universidade Federal de Juiz de Fora (CEP – UFJF)

## 1 INTRODUÇÃO

A Artrite Reumatoide (AR) é uma doença crônica autoimune inflamatória que, apesar de ser sistêmica, afeta principalmente as articulações das mãos, pulsos, pés, tornozelos, joelhos, ombros e cotovelos. Cerca de 0,5% a 1% da população mundial é acometida pela doença, sendo mais prevalente no sexo feminino do que no masculino (3:1) e com maior incidência após os 55 anos (World Health Organization, 2023). No Brasil, a AR segue o mesmo padrão epidemiológico, afetando cerca de 1% da população brasileira, com maior prevalência em mulheres com idade entre 20 e 60 anos, sem distinção de grupos étnicos (Sociedade Brasileira de Reumatologia, 2022).

Caracterizada pela inflamação das membranas sinoviais presentes nas articulações, a AR é capaz de provocar a destruição tecidual dessas articulações gerando dor, deformidades e redução significativa na qualidade de vida. Embora menos comum, a AR ainda pode agir prejudicialmente nos sistemas cardiopulmonar, renal e nervoso, além de ser intimamente ligada a quadros de depressão e ansiedade (World Health Organization, 2023).

Na cavidade bucal, a AR pode se manifestar através de distúrbios da articulação temporomandibular (DTM), da síndrome de Sjögren secundária, provocando secura bucal, e, principalmente, do desenvolvimento ou da progressão da doença periodontal (DP), condição infecciosa e imuno-inflamatória crônica que destrói os tecidos de proteção e de suporte dos dentes, o que gradativamente, pode desencadear a perda dentária (PD) (Gualtierotti et al, 2018; González-Cháves et al, 2020).

A perda dos elementos dentários é capaz de prejudicar a função mastigatória, a fonética e ainda interferir negativamente na auto-estima e na saúde mental do paciente (Gerritsen et al, 2010; Batista et al, 2014), constituindo um problema de saúde pública global e refletindo em uma saúde bucal precária. A condição de saúde bucal pode ter um grande impacto sobre a saúde geral; desencadeando algumas doenças ou dificultando a resposta ao tratamento médico. (Savioli et al 2010; Fabri et al 2015, Pettersen et al, 2005). As perdas dos dentes estão relacionadas a dor na articulação temporomandibular, problemas com alimentação, mastigação, sorriso e têm um grande impacto sobre a vida diária, fazendo com que milhões de horas escolares e de trabalho sejam perdidas todos os anos (Silva et al., 2010; Bridges et al., 2014 ).

No contexto específico dos pacientes com AR, todos estes aspectos podem estar potencializados pela própria doença ou pelo seu tratamento. Estudos indicaram que mais de 9 dentes perdidos estão relacionados a acidentes cardiovasculares, diabetes e morte por qualquer causa, aumentando de 60% a 140% o risco de sua ocorrência (Liljestrand et al 2015).

Assim, conhecer e analisar a condição de saúde bucal e as perdas dentárias em AR é fundamental pois, quando os fatores de risco individuais são avaliados, o número de dentes perdidos pode ser um indicador adicional útil para a equipe médica, preditivo de agravos.

## **2 PROPOSIÇÃO**

O presente estudo teve como objetivo analisar a saúde bucal de pacientes diagnosticados com Artrite Reumatoide e verificar se o número de dentes perdidos pode ser usado como indicador preditivo de agravos da doença reumatológica, auxiliando na definição do prognóstico da doença.

### **3 ARTIGO CIENTÍFICO**

A redação deste manuscrito seguiu as orientações de preparo e submissão (Anexo A) de trabalhos da revista intitulada Journal of Applied Oral Science, ISSN 1679-7765, Qualis A2 na área de avaliação em Odontologia.

O projeto possui parecer consubstanciado emitido pelo Comitê de Ética em Pesquisa com Seres Humanos da Universidade Federal de Juiz de Fora (CEP – UFJF), CAAE 85435317.8.0000.5147 (Anexo B).

## **Tooth loss as a predictor of complications and prognosis in Rheumatoid Arthritis**

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## Tooth loss as a predictor of complications and prognosis in Rheumatoid Arthritis

### ABSTRACT

**Introduction:** Rheumatoid Arthritis (RA) is a chronic, systemic autoimmune disease that manifests in the oral cavity mainly through the development or progression of periodontal disease (PD), an inflammatory condition in the oral cavity that has a bidirectional relationship with rheumatologic disease and other systemic conditions, which can gradually lead to tooth loss (TL). **Objective:** To evaluate whether the number missing teeth could serve as an additional useful indicator for the medical team, predicting systemic disease exacerbations. **Methods:** This was a cross-sectional study involving RA patients evaluated according to specific protocols and instruments. Included the analysis of medical records and a systematic orofacial which yielded the Decayed, Missing, and Filled Teeth (DMFT) index. Validated questionnaires were administered, and disease activity and functional capacity indices (DAS-28 and HAQ) were collected. **Results:** Were included 21 patients, with a mean DAS28 of 3,12 and a mean HAQ of 1,077. Analysis of the DAS28 revealed that 7 (33.4%) patients were in remission from RA, while 14 (66.6%) exhibited some level of disease activity. Among these patients, 10 (47%) had moderate to severe disability caused by RA. Statistical analyses revealed that patients on polypharmacy (mean=12.87) tended to have a greater number of missing teeth compared to those using fewer medications (mean=6.33) ( $p = 0.029$ ). Additionally, a higher DMF-T value was observed in patients with some degree of disease activity ( $p=$ ). Correspondence analysis indicated that patients on polypharmacy had a higher prevalence of moderate to severe disability as assessed by HAQ, along with moderate to high DMF-T scores. **Conclusion:** It is concluded that there is a relationship between the DMF-T index, RA activity, the number of missing teeth, and the need for polypharmacy, making these data important to be assessed in the clinical routine of RA patients.

**Keywords:** Rheumatoid arthritis, tooth loss, polypharmacy, DMF index, Detistry.

## INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune inflammatory chronic disease that, despite being systemic, mainly affects the joints of the hands, wrists, feet, ankles, knees, shoulders, and elbows. Approximately 0.5 to 1% of the world's population is affected by this disease, which is more prevalent among females (3:1 ratio) and has a higher incidence after the age of 55.<sup>1</sup> In Brazil, RA follows a similar epidemiological pattern, affecting 1% of the Brazilian population, with a higher prevalence among women between 20 and 60 years old, without distinction among ethnic groups.<sup>2</sup>

It is characterized by inflammation of synovial membranes present in the joints. RA can cause tissue destruction in these joints, resulting in pain, deformities, and a significant reduction in quality of life. RA can also damage the cardiopulmonary, renal, and nervous systems, although these are not common findings, and it may also be closely related to depression and anxiety<sup>1</sup>.

In the oral cavity, rheumatoid arthritis (RA) can manifest as temporomandibular disorders (TMD), Sjögren's syndrome, which causes oral dryness, and, notably, in the development and progression of periodontal disease (PD). Periodontal disease is an infectious and immune-inflammatory condition that destroys the supporting and protective tissues of the teeth, which, if left untreated, can gradually lead to tooth loss<sup>3,4</sup>.

Tooth loss can impair mastication and phonetics, and negatively affect self-esteem and mental health<sup>5,6</sup>, making it a significant global health issue. Oral health conditions can substantially impact overall medical health by either contributing to the onset of certain diseases or interfering with the effectiveness of treatments<sup>7,8,9</sup>. Additionally, tooth loss is associated with temporomandibular joint pain, nutritional challenges, and esthetic concerns, which can profoundly impact daily life, leading to missed school and work days throughout the year<sup>10,11</sup>.

In the context of rheumatoid arthritis (RA), these issues can be exacerbated by both the disease and its treatments. Studies have shown that losing more than nine teeth is associated with an increased risk of cardiovascular events and diabetes, elevating the risk of mortality from any cause by 60% to 140%<sup>12</sup>.

Therefore, assessing and analyzing oral health conditions and tooth loss is crucial in RA patients. Evaluating individual factors, including the number of missing teeth, can provide the medical team with additional indicators that may predict potential complications.

## METHODS

A cross-sectional study was conducted with rheumatoid arthritis (RA) patients diagnosed according to the American College of Rheumatology criteria, at a university hospital. Patients were excluded if they had a history of smoking, alcohol or drug addiction, cognitive impairment, metastasis, cancer, diabetes, or if they had received any dental treatment within the six months prior to the evaluation.

The patients were attended by the team and the following evaluation tools were used:

- 1- Demographic data, medical history, and information regarding the treatments patients were receiving were obtained from clinical files and notes<sup>13</sup>.
- 2- The Disease Activity Score based on 28 joints (DAS 28) was used to assess the activity of rheumatoid arthritis (RA)<sup>14</sup>.
- 3- The Health Assessment Questionnaire (HAQ) was employed to evaluate the functional capacity of RA patients<sup>15</sup>.
- 4- The DMF-T (Decayed, Missing, and Filled Teeth) index was utilized to assess oral health status and identify missing teeth<sup>13</sup>.

### Statistical Analysis:

The Mann-Whitney U test was used to compare DMF-T scores, DAS28, HAQ scores, and the number of decayed, filled, and missing teeth between groups of patients with and without polypharmacy. Additionally, the Kruskal-Wallis test was performed to explore potential variations among all patient groups concerning DAS28 (remission, low activity, and moderate activity) and HAQ (mild, moderate, and severe disability). Subsequently, a post hoc test was conducted when the number of groups exceeded two.

## RESULTS

### I. Demographic and clinical data:

The study included 21 patients, comprising 3 males (14.3%) and 18 females (85.7%), with ages ranging from 31 to 74 years. Medical comorbidities were observed, with the most prevalent being hypertension (n=8, 35%), sinusitis (n=5, 25%), osteoporosis (n=4, 20%), and chronic kidney disease (n=3, 15%). The evaluation of medical files revealed that 15 patients (71.4%) were receiving polypharmacy, defined as the concurrent use of five or more medications.

The DAS28 assessment revealed a mean DAS28 score of 3.12, with 7 patients (33.3%) in disease remission and 14 patients (66.7%) experiencing active rheumatoid arthritis. The HAQ assessment indicated a mean HAQ score of 1.077, with 10 patients (47.6%) exhibiting moderate to severe disability due to RA.

### II. Evaluation of Medical and Dental Parameters Between Patients on and not on Polypharmacy:

The Mann-Whitney U test demonstrated a significant statistical difference in the number of missing teeth between the group of patients on polypharmacy (mean rank = 12.87) and the group not on polypharmacy (mean rank = 6.33) ( $U = 17$ ,  $df = 1$ ,  $p = 0.029$ ). This indicates that patients on polypharmacy tend to have a higher number of missing teeth compared to those using fewer medications. No significant statistical differences were observed in the other variables studied (Table 01).

**Table 01-** Evaluation of DMF-T index in relation to DAS28 and HAQ between patients on and not on polypharmacy.

		Mean Ranks	U	Z	p
<b>DMF-T</b>	<b>Not on Polypharmacy</b>	8.50	60	1.183	0.237 <sup>ns</sup>
	<b>on Polypharmacy</b>	12.00			
<b>DAS28</b>	<b>Not on Polypharmacy</b>	13.00	33	-0.934	0.381 <sup>ns</sup>
	<b>on Polypharmacy</b>	10.20			
<b>HAQ</b>	<b>Not on Polypharmacy</b>	7.75	25.5	-1.524	0.132 <sup>ns</sup>
	<b>on Polypharmacy</b>	12.30			

<b>Decayed</b>	<b>Not on Polypharmacy</b>	11.00	45	0.000	1.000 <sup>ns</sup>
	<b>on Polypharmacy</b>	11.00			
<b>Filled</b>	<b>Not on Polypharmacy</b>	12.92	27.5	-1.474	0.239 <sup>ns</sup>
	<b>on Polypharmacy</b>	9.46			
<b>Missing</b>	<b>Not on Polypharmacy</b>	6.33	17	-2.209	<b>0.029*</b>
	<b>on Polypharmacy</b>	12.87			

<sup>ns</sup> – Not significant; \* – Significant at 5% level.

### III. Evaluation of the Decayed, Missing, and Filled Teeth (DMF-T) Index and Medical Parameters:

The Kruskal-Wallis test indicated a significant effect on DMF-T scores with respect to DAS28 activity levels ( $H(2) = 7.178$ ,  $df = 2$ ,  $p = 0.028$ ). Post-hoc analysis using Dunn's test with Bonferroni correction revealed significant differences in DMF-T values between patients on remission and those with low disease activity ( $p = 0.022$ ). However, no significant differences were observed between patients on remission and those with moderate disease activity ( $p = 0.551$ ), or between patients with low and moderate disease activity ( $p = 0.551$ ). These results suggest that a higher DMF-T value is associated with some degree of disease activity (Table 02). Patients with low or moderate disease activity had mean DMF-T scores of 15.92 and 11.00, respectively, whereas patients on remission had a mean DMF-T score of 6.79. Although no statistically significant difference was found in the number of missing teeth relative to disease activity, a trend towards a higher average number of missing teeth was observed in patients with some level of disease activity. Patients with low or moderate activity had mean numbers of missing teeth of 15.92 and 9.56, respectively, compared to 8.43 in patients in remission. No statistically significant difference was found in the total DMF-T index across different HAQ levels.

**Table 02-** DMF-T and rheumatologic parameters evaluation.

				Mean Ranks	H	df	p*
DMF-T	DAS28:	remission		6.79	7.178	2	<b>0.028*</b>
		Low activity		15.92			
		Moderate activity		11.00			
		Intense activity		0			

DMF-T	HAQ:	Low disability	11.68	2.514	2	0.284 <sup>ns</sup>
		Moderate disability	8.36			
		Severe disability	14.67			
<b>Missing teeth</b>	HAQ:	Low disability	11.50	3.264	2	0.196 <sup>ns</sup>
		Moderate disability	8.21			
		Severe Disability	15.67			
<b>Missing teeth</b>	DAS28:	remission	8.43	5.543	2	0.063 <sup>ns</sup>
		Low activity	15.92			
		Moderate activity	9.56			

<sup>ns</sup> – Not significant; \* – Significant at 5% level.

#### IV. Evaluation of Oral Health Condition Using the DMF-T Index in Relation to Rheumatological Parameters:

For this analysis, variables were categorized as follows: DMF-T was classified into "very low to low" (< 8.9) and "moderate to high" (> 9), based on World Health Organization criteria (2013)<sup>7</sup>; DAS28 was categorized into "active disease" or "remission"; and HAQ was categorized into "no to mild disability" and "moderate to severe disability." These categorizations were evaluated using the Chi-squared ( $\chi^2$ ) test. It was considered that a higher DMF-T score indicates worse oral health condition.

A strong and statistically significant association was observed between the DMF-T index and DAS28 ( $\chi^2 = 9.450$ ,  $p = 0.002$ ,  $\Phi = 0.671$ ). Specifically, 86% of patients with active disease had a DMF-T score categorized as "moderate to high," compared to 28.6% of patients on remission (Table 03).

**Tabela 03-** Categorized DMF-T and rheumatologic parameters

		$\chi^2$	df	p	Phi
DMF-T	DAS28: Remission   Disease Activity	9.450	1	0.002**	0.671
DMF-T	HAQ: no to mild disability   moderate to severe disability	0.687	1	0.635 <sup>ns</sup>	

<sup>ns</sup> – Not significant; \*\* – Significant at 5% level.

Among patients with active disease, 7.14% had a DMF-T score categorized as "very low to low," while 92.86% had a DMF-T score categorized as "moderate to high" ( $Z = -8.81$ ,  $p = 0.000$ ) (Table 04). No significant relationship was observed between DMF-T and HAQ ( $\chi^2(1) = 0.687$ ,  $p = 0.635$ ) or between DMF-T and polypharmacy ( $\chi^2(1) = 0.093$ ,  $p = 0.576$ ) (Table 05).

**Table 04-** Comparison of DAS -28 and severity of DMF-T :

		DMF-T		
		Very low to low	Moderate to high	
<b>DAS28</b>	Remission	5 <sub>a</sub> (71.4%)	2 <sub>b</sub> (28.6%)	7
	Disease activity	1 <sub>a</sub> (7.1%)	13 <sub>b</sub> (92.9%)	14
<b>Total</b>		6 (28.6%)	15 (71.4%)	21

*Each subscript letter (a or b) denotes a subset of DMF-T (Very low to low: < 8.9; moderate to high: 9 – 13.9) categories whose column proportions do not differ significantly from each other at the .05 level.*

**Table 05-** Evaluation of HAQ and Severity of DMF-T

		DMF-T		
		Very low to low	Moderate to high	
<b>HAQ</b>	No disability to mild disability	4 <sub>a</sub> (36.4%)	7 <sub>a</sub> (63.6%)	11
	Moderada to high disability	2 <sub>a</sub> (20.0%)	8 <sub>a</sub> (80.0%)	10
<b>Total</b>		6 (28.6%)	15 (71.4%)	21

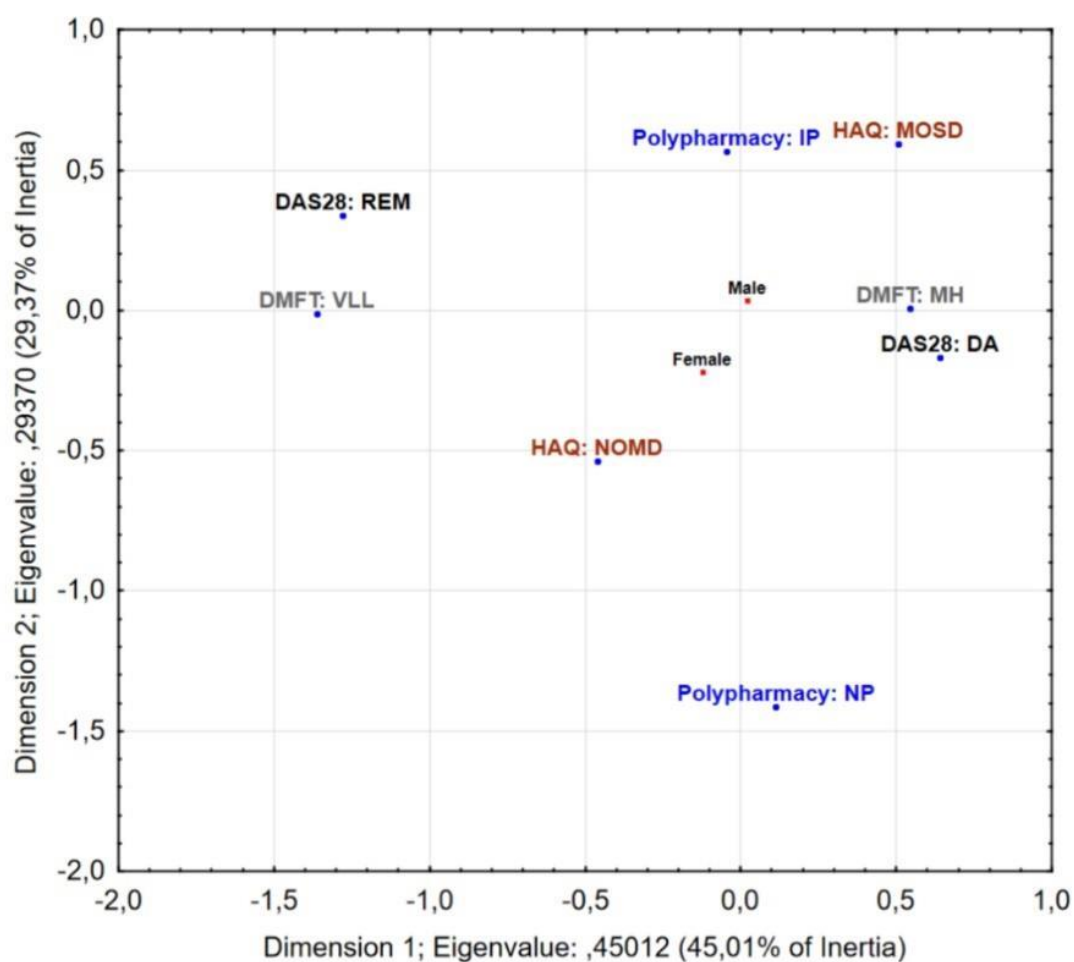
*Each subscript letter denotes a subset of DMF-T (very low to low: < 8.9; moderate to high: 9 – 13.9) categories whose column proportions do not differ significantly from each other at the .05 level.*

## V. Correspondence Analysis Between Evaluated Parameters

Multivariate correspondence analysis was employed, in which the Decayed, Missing, and Filled Teeth (DMF-T) scores were dichotomized based on established cutoffs (<8.9: very low or low; >9: moderate or high) (World Health Organization, 2013). Disease activity was categorized using DAS28 as "remission" or "disease activity." The Health Assessment Questionnaire (HAQ) levels of disability were classified as "no or mild disability" and "moderate or severe disability." Polypharmacy was categorized as "in polypharmacy" or "not in polypharmacy."

The analysis, which accounted for 74.38% of the data variance, revealed that patients categorized with DAS28 as “remission” tended to have DMF-T scores classified as “very low or low.” Conversely, patients in polypharmacy exhibited a higher prevalence of moderate to severe disability according to HAQ, along with moderate to high DMF-T scores (Figure 01). These findings suggest potential associations between the variables.

**Figure 01-** Analysis of DMF-T, DAS28, and HAQ Scores in the Context of Polypharmacy in RA.



*DMFT very low or low - VLL; DMFT moderate or high - MH; DAS28 in remission - REM; DAS28 in disease activity - DA; HAQ no or mild disability - NOMD; HAQ moderate or severe disability - MOSD; In polypharmacy - IP; Not in polypharmacy - NP*



## DISCUSSION

To the best of our knowledge, this study is the first to investigate the association between missing teeth and rheumatoid arthritis (RA). This approach is particularly significant as it may serve as an important prognostic indicator. The potential link between tooth loss and worsening RA can be explained by the main cause of tooth loss: periodontal disease<sup>17</sup>. Periodontal disease is known to induce chronic low-level inflammation and recurrent bacteremia, which can have systemic adverse effects. Immunoinflammatory mediators, including activation of antibodies, lipopolysaccharides, and cytokines, are closely associated with poorer responses to medical therapy, exacerbation of chronic conditions, and the development of cardiometabolic disorders<sup>8,9,18</sup>. These factors reinforce the role of immune responses and bacterial infections on the pathophysiology of chronic diseases, such as RA.

It is important to note that the data indicate that patients with RA who are on polypharmacy tend to have a greater number of missing teeth compared to those using fewer medications. This finding highlights a bidirectional impact pathway. As discussed, tooth loss is associated with the initiation and exacerbation of chronic conditions that often require pharmacological management. Periodontitis, which leads to tooth loss, has been implicated as a potential risk factor for various chronic diseases, including Alzheimer's disease, cardiovascular diseases, diabetes mellitus, osteoporosis, chronic orofacial pain, and pulmonary diseases<sup>19-23</sup>. Conversely, polypharmacy can lead to oral complications that increase the prevalence of tooth loss<sup>24</sup>. Therefore, the combined effects of polypharmacy and tooth loss can significantly influence the progression of RA and its treatment.

It is important to note that the data demonstrated that patients with RA on polypharmacy tend to have a greater number of missing teeth compared to patients who use fewer medications. This finding demonstrates a bidirectional impact pathway. Tooth loss is associated, as discussed above, with the triggering and worsening of chronic processes that require a drug therapeutic approach. Periodontitis leading to tooth loss has been implicated as a potential risk factor for chronic diseases, including Alzheimer's disease, cardiovascular diseases, diabetes mellitus, osteoporosis, chronic orofacial pain and pulmonary diseases<sup>19-23</sup>. On the other hand, polypharmacy can generate oral complications that increase the prevalence of tooth loss<sup>24</sup>. Together, polypharmacy and tooth loss can, therefore, impact the evolution of RA and its treatment.

Furthermore, regarding the association between the DMFT index and DAS28, a significant and strong relationship was observed. Specifically, 86% of patients with active rheumatic disease exhibited DMFT scores categorized as "moderate to high," compared to only 28.6% of patients with no activity. These findings reinforce existing scientific evidence on the long-term impact of oral diseases. It can be suggested that higher DMFT scores reflect the

severe damage caused by oral diseases over a lifetime, attributable to cumulative infectious and inflammatory processes. The association of worse DMFT values with greater disease activity as measured by DAS28 confirms that worsening oral health exacerbates RA and complicates its treatment, thereby deteriorating the overall prognosis.

It is intriguing to note that HAQ scores were not associated with oral health status in this study. Despite the fact that disability, particularly affecting the upper limbs, could potentially make oral hygiene more challenging and exacerbate oral health problems<sup>25</sup>, this association was not observed. This lack of correlation may be attributed to the fact that the Health Assessment Questionnaire (HAQ) primarily focuses on self-reported outcomes rather than direct process measures. Therefore, while HAQ assesses functional limitations, it may not fully capture the impact of physical disability on oral hygiene practices and oral health.

Oral health is directly linked to systemic health. A study conducted with 300 patients at the Division of Rheumatology, Clinical Medicine, North Jutland Region Hospital, Hjørring, Denmark, concluded that there is a significant relationship between the signs and symptoms of periodontal disease and rheumatological disease activity, adversely affecting disease management<sup>26</sup>. Consistent with this study, the analyses in the present research also suggested associations between oral health status (measured by DMF-T), disease activity (assessed by DAS28), functional disability (evaluated by HAQ), and polypharmacy (defined as the use of five or more concomitant medications) in patients with rheumatoid arthritis (RA). Nevertheless, this study has some limitations, including the relatively small sample size and the cross-sectional design. These factors make it challenging to evaluate the direct causal relationship between exposure and outcome.

A previous prospective cohort study demonstrated that the number of missing teeth, a marker of prior periodontal disease, is associated with an increased risk of diabetes mellitus (DM), cardiovascular disease (CVD), and mortality<sup>12</sup>. Similarly, the present study indicates a relationship between the DMF-T index and RA disease activity, as well as between the number of missing teeth and the need for polypharmacy. Based on these findings, the number of missing teeth and the DMF-T index—both of which are readily measurable—may serve as important prognostic markers and warrant additional follow-up in patients with RA.

## **CONCLUSION**

The analyzed data indicate a significant relationship between the DMF-T index and RA disease activity, as well as between the number of missing teeth and the need for polypharmacy. Therefore, these indicators are important parameters for assessing the prognosis of patients with RA.

## **ACKNOWLEDGMENTS**

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## **4 CONCLUSÃO**

Os dados analisados no trabalho indicam uma importante relação entre o índice CPOD e a atividade da AR e o número de dentes perdidos e a necessidade de polifarmácia. Assim, estes indicadores são medidas importantes para alertar quanto ao prognóstico de pacientes com AR e devem ser avaliados na rotina clínica médica dos pacientes com AR.

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# ANEXO A

## Manuscript Preparation

### Article Submission Format

#### Title page

It must be submitted in a separate file from the main file and contain:

- a) The title of the manuscript in English.
- b) The names of the authors in direct order followed by their institutional affiliation. For Brazilian authors, the affiliations must be in Portuguese, in Spanish for Latin Americans and in English for other nationalities.

Authorship should be attributed following the recommendations of the [ICMJE](#): substantial contributions to the conception or design of the study; or collection, analysis, or interpretation of the study data; writing or critical review with important intellectual contribution; final approval of the version to be published; and agreement to take responsibility for all aspects of the work, ensuring that issues related to the accuracy and integrity of any part of the study have been properly investigated and resolved.

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#### Main file

The manuscript must have been previously translated or revised into English by a company, freelance professional or authors who are native English speakers.

- a) Title of the work in English.
- b) A structured abstract of no more than 300 words in a single paragraph, containing the following subsections: brief introduction, objective, methodology, results and conclusions.
- c) Keywords: These are the words or expressions that identify the content of the article. To determine the keywords, authors should consult the [MeSH](#) and [DeCS](#) subject lists. Three to 5 keywords should be added, separated from each other by periods and the first letter of the first word should be capitalized. Ex: Dental implants. Fixed prosthesis. Photoelasticity. Passive fit.
- d) Introduction: Summarize the reasoning and proposal of the study, citing only relevant references. Establish the hypothesis of the study.
- e) Methodology: The material and methods are presented in sufficient detail to allow the observations to be confirmed. Include the city, state and country of all manufacturers after the first mention of products, instruments, software, equipment, etc. Published methods should be referenced and discussed briefly, unless modifications have been made. Indicate the statistical methods used, if applicable. See the section on ethical principles and registration of clinical trials.
- f) Results: Should be presented in a logical sequence in the text, with tables and illustrations. Do not repeat all the data from the tables and illustrations in the text, emphasizing only the important observations.
- g) Discussion: Emphasize the new and important aspects of the study in context with observations from previous research. Do not repeat in detail data or information cited in the introduction or results. Point out the implications of your findings and their limitations.
- h) Conclusion: Briefly list the conclusions that can be drawn from the research. Do not just restate the results, but establish conclusions that are relevant to the objectives and justified by the data. In most situations, the conclusions are true only for the population of the experiment.
- i) Acknowledgments (where appropriate): Thank those who have made a significant contribution to the study.

implications of your findings and their limitations.

h) Conclusion: Briefly list the conclusions that can be drawn from the research. Do not just restate the results, but establish conclusions that are relevant to the objectives and justified by the data. In most situations, the conclusions are true only for the population of the experiment.

i) Acknowledgments (where appropriate): Thank those who have made a significant contribution to the study (people, laboratories, sectors, etc.).

j) Funding: Specify sponsors, financial aid, scholarships and/or programs, citing the name of the funding organization and the file number.

k) Declarations: Add, after the acknowledgments, if any, declarations of conflict of interest and availability of research data.

l) References (see References section).

#### Graphic abstract

A graphic abstract is a visual format of the manuscript to summarize the essential findings of the study. It helps to disseminate easy and concise information, which can be quickly incorporated by readers and helps it to be shared, including on social media. JAOS therefore encourages this submission. An original figure that clearly indicates the sequence described in the manuscript needs to be designed (JPEG, minimum 300 dpi and 1080 x 1080 pixels - width x height) and sent as a separate file.

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#### Digital Assets

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Illustration captions and table titles should be clear, concise and located at the end of the main file in the form of a separate list and preceded by the corresponding numbering.

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Authors can be cited in the text in one of two ways:

1) Numerical only - References should be cited in ascending order in the paragraph.

E.g. ... and interfere with the bacterial system and tissue system.<sup>3,4,7-10</sup>

2) or alphanumeric:

*One author:* Gatewood<sup>31</sup> (2012)

*Two authors:* Cotti and Mercuro<sup>19</sup> (2016)

*Three authors:* Azar, Safi, Nikaein<sup>27</sup> (2012)

Three authors: Azar, Safi, Nikaein<sup>27</sup> (2012)

More than three authors: Gealh, et al.<sup>28</sup> (2014)

## References

References must comply with the "Uniform requirements for manuscripts submitted to Biomedical Journals - Vancouver."

All references must be cited in the text. They should be ordered according to their presentation in the text and numbered sequentially in ascending order. The abbreviations of the titles of the journals cited should be in accordance with the MEDLINE standard.

Do not include personal communications and bibliographic material without a publication date in the list of references.

Theses, dissertations, monographs and abstracts will not be accepted as references, even if they have a DOI.

Minimize references to publications in languages other than English. The title translated into English should be cited in square brackets and the original language inserted at the end of the reference.

List the names of the first 6 authors of the work; if this number is exceeded, the first 6 authors of the work should be cited, followed by the expression "et al." not written in italics and accompanied by a period.

Ex: Cintra LT, Samuel RO, Azuma MM, Ribeiro CP, Narciso LG, Lima VM, et al.

Do not exceed 40 references.

## Examples of References

### Book

Preedy VR, organizer. Fluorine: chemistry, analysis, function and effects. London: Royal Society of Chemistry;

## Examples of References

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Schubert O, Le V, Probst F. Chancen und Risiken von Zahnimplantaten [Dental implants - opportunities and risks]. MMW Fortschr Med. 2022;164(9):50-2. German. doi: [10.1007/s15006-022-0970-4](https://doi.org/10.1007/s15006-022-0970-4)

### Journal article exclusively on the Internet (with electronic identifier)

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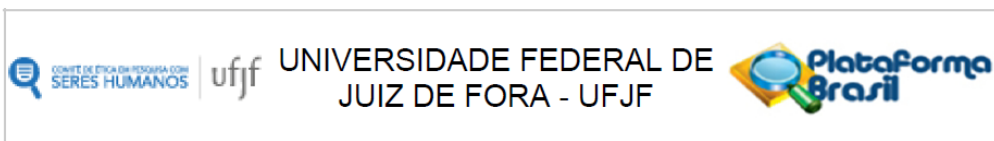
### Journal article with DOI

Francese MM, Gonçalves IV, Vertuan M, Souza BM, Magalhães AC. The protective effect of the experimental TIF4 and chitosan toothpaste on erosive tooth wear in vitro. Sci Rep. 2022;12(1):7088. doi: [10.1038/s41598-022-11261-1](https://doi.org/10.1038/s41598-022-11261-1)

### Journal article Epub ahead of print/In press/Forthcoming



## ANEXO B



### PARECER CONSUBSTANCIADO DO CEP

#### DADOS DA EMENDA

**Título da Pesquisa:** Marcadores salivares e clínicos bucais em Artrite Reumatóide: resultados antes e após a terapia com Anti-TNF

**Pesquisador:** Gisele Maria Campos Fabri

**Área Temática:**

**Versão:** 6

**CAAE:** 85435317.8.0000.5147

**Instituição Proponente:** FACULDADE DE ODONTOLOGIA

**Patrocinador Principal:** Universidade Federal de Juiz de Fora UFJF

#### DADOS DO PARECER

**Número do Parecer:** 6.336.408

#### Apresentação do Projeto:

Trata-se de emenda a projeto já aprovado neste CEP em que se solicita a prorrogação de prazo com a seguinte justificativa, depois de removida uma interpolação sem relação direta com a emenda:

"Justificativa da Emenda:

Solicitamos a extensão da data final do projeto visto que, estamos com um Número (n) reduzido de participantes devido as dificuldades impostas durante a pandemia e pelos critérios de inclusão que restringem muito a participação, mas, que são fundamentais para evitar viés metodológico...O projeto foi aprovado como Iniciação Científica com incremento de recursos humanos para viabilizar todos os procedimentos. Esclarecemos que o projeto está mantido conforme descrito inicialmente, com alteração