ORAL HEALTH AND RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

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SUMMARY

Objectives: Patients suffering from rheumatoid arthritis (RA) are repeatedly affected by oral diseases or problems, including dental caries and periodontal diseases (PDs). Periodontitis and rheumatoid arthritis are chronic inflammatory destructive diseases that share many similarities. The objective of this study was to assess oral health status including examination of hard dental tissues and periodontium in patients with rheumatoid arthritis and compare the results with healthy controls. We hypothesize some interlink between oral diseases and RA.

Methods: The epidemiological case-control study involved a total of 64 subjects divided into an experimental group (14 rheumatoid arthritis cases) and a control group (50 healthy individuals). Disease activity in the subjects with RA was assessed by the Disease Activity Score (DAS28). The number of Decayed, Missing and Filled Teeth (DMFT) and Community Periodontal Index of Treatment Need (CPITN) as a basic epidemiological oral health indexes were recorded. Finally, the data were analysed statistically.

Results: The RA patients (19.21, SD = 6.95) showed a higher caries index level measured by DMFT than the control group (17.72, SD = 6.19); the difference was not statistically significant (U = 387.5, p = 0.547). In terms of a mean number of teeth decayed (p = 0.078), teeth filled due to caries (p = 0.397), and missing teeth (p = 0.126), the two groups were not significantly different. In terms of periodontal health, a significant difference was observed between the two groups concerning the CPI maximum score (p = 0.003). The RA patients showed higher prevalence of periodontitis than the controls.

Conclusions: A complete basic oral examination, along with an oral health instruction including adequate oral and dental hygiene, is crucial to prevent dental caries and periodontal diseases and associated complications in RA patients, since they appear to be more vulnerable than the non-RA population.

Key words: rheumatoid arthritis, oral health, tooth decay, DMFT, periodontitis

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INTRODUCTION

Oral health is an integral part of the overall health of the human body. Dental caries and periodontal diseases are the most common chronic infectious oral diseases. Oral diseases are a major global public health problem, having both high prevalence and major negative impact on individuals, communities and society. Rheumatoid arthritis (RA) and periodontal diseases (PDs) are chronic, inflammatory, destructive and progressive diseases, that may have similar pathophysiological mechanisms and risk factors (1). Chronic diseases are currently considered as a major public health problem.

Rheumatoid arthritis is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder of unknown aetiology that primarily involves synovial joints (2). The worldwide prevalence of RA is about 0.24% (3). The annual incidence of RA in the United States and other western nations of northern Europe is about 40 per 100,000 persons (4, 5). According to epidemiologic data, RA is more prevalent in women compared to men, with a lifetime RA risk of 3.6% in women compared to 1.7% in men (6). Among modifiable risk factors, cigarette smoking has the strongest association with RA, while diet and nutrition have been shown to play a significant role as environmental triggers (7, 8). The disease is treated by suppressing symptoms using non-steroid anti-inflammatory drugs (NSAIDs) and glucocorticoids, as well as drugs that act long-term and improve the overall prognosis of the disease, such as classical DMARDs (e.g., methotrexate, sulfasalazine), biological DMARDs (e.g., anti-TNF alfa, anti-IL-6) and targeted synthetic DMARDs (JAK inhibitors). These immunosuppressive drugs may have various side effects (9). Oral manifestations can be a consequence of the disease itself (e.g. xerostomia) or a consequence of the treatment (10–12).

The exact cause of RA is not well known. A significant role is believed to be played by genetics and environmental factors. It is also evident that various cytokines, growth factors, immune cell

types, and proteinases lead to interactions which promote joint destruction and systemic complications (13).

Periodontitis is the destruction of periodontium, with subsequent bone loss, tooth mobility, and ultimately loss of teeth. Periodontitis is present in around 20% of the population and has multifactorial aetiology. The progression of periodontitis mainly involves bacterial species. Moreover, some periodontal bacteria, such as *Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, are suggested to play a crucial role in the link between periodontitis and RA (14).

In both entities, proinflammatory cytokines such as IL-1β, IL-6 and TNF-α are up-regulated, promoting inflammation of soft tissue and destruction of bone. Patients with established RA have a greater prevalence of periodontal diseases (15–17).

Several epidemiologic studies have suggested a bidirectional relationship between periodontitis and RA (17, 18). In the US population data, patients with RA showed a 1.8 times increased risk of periodontitis (15). The history of periodontitis was also associated with a mildly increased risk of RA in other population-based studies (10, 19, 20).

This study aimed to investigate the association of oral health status in RA patients compared with a healthy control group, with a null hypothesis (H_0) of no significant difference in the caries index DMFT and its individual components (Decayed, Missing and Filled Teeth) between patients with rheumatoid arthritis and a control group of healthy individuals, but a statistically significant difference between the groups is predicted in periodontal health.

MATERIALS AND METHODS

Study Population

The cross-sectional epidemiological case-control study of the First Department of Internal Medicine and First Department of Stomatology (Faculty of Medicine, Pavol Jozef Šafárik University and Louis Pasteur University Hospital in Košice) involved a total of 64 subjects. They were patients of the First Department of Internal Medicine with diagnosed rheumatoid arthritis (n = 14, 21.9%), 2 (14.3%) males and 12 (87.5%) females, and a control group of healthy patients (n = 50, 78.1%) which included 19 (38.0%) males and 31 (62.0%) females. The subjects with RA were recruited from individuals who attended the outpatient Department of Rheumatology. RA was diagnosed according to the 1987 American College of Rheumatology (ACR) Revised Criteria (21). According to the classification, subjects with RA have four of the following seven criteria: morning stiffness, arthritis of three or more joint areas, arthritis of hand joints, symmetric arthritis, rheumatoid nodules, serum rheumatoid factors, and radiographic changes. In 2022 (March–October) 14 subjects with RA (2 males and 12 females, mean age 55.93 years; median disease duration 24.21 years) provided informed consent and were enrolled into the study. The subjects with RA were taking non-steroidal anti-inflammatory drugs, low doses of corticosteroids (less than 7.5 mg of prednisone/day or its equivalent), conventional synthetic DMARDs, mostly methotrexate. The patients were also treated with biological DMARDs; we only selected patients on the anti-TNF treatment. In the group of selected patients with rheumatoid arthritis there was no additional disease (e.g. diabetes), and the DAS score mean at the time of study was 2.48.

The non-RA control group of 50 subjects (19 males and 31 females, mean age 53.12 years) was also examined. The controls were recruited from patients attending the general dental office of the Fist Department of Stomatology. Exclusion criteria for the cases and controls were a history of periodontal therapy or the use of antibiotics during the last three months prior to the examination, diabetes mellitus, pregnancy, and lactation. The study was approved by the Ethics Committee of the Louis Pasteur University Hospital in Košice (141/2022/OBVaKS). Written informed consent was obtained from all subjects prior to their enrolment. Both groups (RA and non-RA controls) were statistically stratified according to their smoking affinity (smoker, ex-smoker, non-smoker).

Assessment of Clinical Rheumatologic Parameters

Disease activity in the subjects with RA was assessed by the Disease Activity Score (DAS28) (22). The disease activity index ranges from 0 to 10 and includes a 28 tender-and-swollen joint count, the erythrocyte sedimentation rate (ESR, mm/hour), and the patient's assessment of disease activity measured with a visual analogue scale (100 mm). For example, DAS28 > 5.1 meant that the subject had a high disease activity, whereas DAS28 < 3.2 meant that the disease activity was low. Also, the Health Assessment Questionnaire (HAQ) score was recorded. It assesses a patient's level of functional ability involving fine movements of the upper extremity and locomotor activities of the lower extremity. Higher scores indicate more disability (0 ≥ without any difficulty; 1 ≥ with some difficulty; 2 ≥ with much difficulty; and 3 ≥ unable to do).

Intraoral Examination

Oral and dental examinations were performed for all patients of the monitored group by one calibrated examiner, under standard conditions in a dental chair, using basic examination instruments: dental mirror, dental probe and periodontal WHO probe. The number of Decayed, Missing and Filled Teeth (DMFT) (23) and Community Periodontal Index of Treatment Need (CPITN) were recorded. The presence of caries was determined following the International Caries Classification and Management System (24). Periodontal status was assessed by the Community Periodontal Index (CPI) that measures the severity and degree of the disease (gingivitis, task deepness) according to the World Health Organization (WHO) recommendations (25). Each sextant was assigned a code number and the condition of the worst affected site in the sextant was recorded.

Caries lesions were diagnosed clinically and by observation. Radiography was not used at any stage of the study. Wisdom teeth on all four sides were excluded from the study. All periodontal measurements were assessed at four sites of each tooth (mesiobuccal, distobuccal, mesiolingual, and distolingual).

Statistical Analyses

Frequency distributions, means (AM), and standard deviations (SD) were determined to describe the data. Risk factors and dental variables were compared between the subjects with RA and non-

RA controls using the parametric Student's unpaired t-test and non-parametric Mann-Whitney U-test for continuous variables or the χ^2 (chi-square) test and the Fisher's exact test for categorical variables. The Fisher's exact test was used for comparison of categorical variables and the t-test and U-test were used for the comparison of continuous variables between the two groups. All statistical analyses were conducted using SPSS 21.0 and XLSTAT. P-value < 0.05 was considered statistically significant.

RESULTS

The study included patients with diagnosed rheumatoid arthritis (n = 14, 21.9%), 2 (14.3%) males and 12 (87.5%) females, and a control group of healthy patients (n = 50, 78.1%) which included 19 (38.0%) males and 31 (62.0%) females. Other demographic data are presented in Table 1.

The patients (n = 14) with diagnosed RA were adults between 31 and 68 years of age, mean age 55.93 (SD = 10.6). The subjects (n = 50) included in the control group were adults between 21 and 81 years of age, mean age 53.12 (SD = 13.8). There were no statistically significant differences in age mean between the group of RA patients and controls (t = 0.704, p = 0.484). The mean age of the RA patients is not significantly higher (AM = 55.93, SD = 10.6) than the mean age of the controls (AM = 53.12, SD = 13.8).

The mean disease duration of the RA patients was 24.21 years (SD = 9.5), with the minimum disease duration of 12.0 and maximum of 45.0 years. The mean DAS28 was 2.48 (SD = 1.3), with DAS28 minimum of 1.20 and maximum of 4.54. The mean HAQ was 0.93 (SD = 0.6) with the maximum of 2.0. Seven percent of RA patients were current smokers. The majority of the patients (n = 10, 71.4%) and subjects (n = 33, 66.0%) do not smoke; 21.4% of the RA patients were smokers in the past. No statistically significant difference (p = 0.256) was confirmed between the groups of RA and controls in the number of smokers, non-smokers and ex-smokers (Table 2).

When evaluating the DMFT caries index, an essential role is played by the analysis of its individual components to verify the assumption of normality of the distribution of DMFT to Decayed (D), Missing (M) and Filled (F) teeth, the Shapiro-Wilk normality test was used. Since the assumption of normality for the variables Decayed (p < 0.001) and Missing (RA: p = 0.040, control: p = 0.020) was not confirmed, in further analysis the non-parametric Mann-Whitney U-test was used to compare the median level of all DMF components between the RA patients and control group.

The DMFT index mean in the RA patient group was 19.21 (SD = 6.95) and 17.72 (SD = 6.19) in the control sample. Despite the fact that a higher caries index level measured by DMFT was found in the RA patients compared to the control group, the difference was not statistically significant (U = 387.5, p = 0.547).

The RA patients presented a lower mean of decayed teeth than the control group (AM = 0.36, SD = 0.63 vs. AM = 1.46, SD = 2.32, p = 0.078), showing that the patients in the control group had more active caries. Despite this fact, no statistically significant difference was found between the two groups in the frequencies of untreated dental caries.

At the same time, the mean of filled teeth was lower in the RA group compared to the control one (AM = 8.79, SD = 4.49 vs. AM = 10.62, SD = 5.36, p = 0.397). No statistically significant difference was found between the two groups in the frequencies of filled teeth. In frequencies of extracted teeth (Missing), the group of the RA patients represents a higher value, 52% of the total value of DMFT (AM = 10.07, SD = 8.86), than the control group with 32% of missing teeth (AM = 5.64, SD = 4.05). No statistically significant difference was found in the frequencies of missing teeth (p = 0.126) between the groups (Table 3).

Table 1. *Selected demographic data*

Sex	RA group (n = 14) n (%)	Control group (n = 50) n (%)
Male	2 (14.3)	19 (38.0)
Female	12 (85.7)	31 (62.0)
Ratio (male/female)	0.2	0.6

RA – rheumatoid arthritis

Table 2. *Demographic characteristics, data on RA patients and control group*

Parameter	RA group (n = 14)	Control group (n = 50)	p-value
Age (years), mean (SD)	55.93 (10.6)	53.12 (13.8)	0.484
Min–max	31.0–68.0	21.0–81.0	
Disease duration, mean (SD)	24.21 (9.5)		
Min–max	12.0–45.0		
DAS28, mean (SD)	2.48 (1.3)		
Min–max	1.20–4.54		
HAQ, mean (SD)	0.93 (0.6)		
Min–max	0.0–2.0		
Smoker			
Yes, n (%)	1 (7.1)	12 (24.0)	0.256
No, n (%)	10 (71.4)	33 (66.0)	
In the past, n (%)	3 (21.4)	5 (10.0)	

RA – rheumatoid arthritis; DAS – Disease Activity Score; HAQ – health assessment questionnaire

The assessment of periodontal health was performed by determining the percentage of persons with the highest CPITN score according to the WHO for both groups (Table 4).

Not a single individual showed the maximum score – 0 (healthy periodontium) in both examined samples; 14.3% of the RA patients showed a maximum CPI score 1, while in the group of controls a marginal periodontal inflammation was found in 16.0% of those examined (p = 0.003).

Score 2 (deposits of supra and/or subgingival dental calculus with the presence or absence of gingival bleeding upon examination) was identified in 7.1% of the RA patients, while in the control group this parameter was identified in 50.0% of the examined controls (p = 0.003).

Score 3 (presence of shallow periodontal pockets, mild periodontitis) was diagnosed in 42.9% of the RA patients and in 22.0% of the examined controls (p = 0.003).

The presence of deep periodontal pockets (CPI = 4) was diagnosed in 21.4% of the RA patients and in 12.0% of the controls (p = 0.003).

Score X (sextant not evaluable for teeth loss) was found in 14.3% of the patients with rheumatoid arthritis and in no individual of the control sample. A statistically significant difference at the 0.05 level was confirmed between the groups.

DISCUSSION

The aim of this research was to study the association between oral health and rheumatoid arthritis, focused on dental caries prevalence and presence of periodontal disease in rheumatoid arthritis patients in Slovakia compared with a healthy control group. DMFT and CPI indices, as a basic epidemiological indices of oral health monitoring were used to identify the state of oral health in both groups.

Dental Health

Dental caries is characterized by the progressive demineralization of the enamel caused by the fermentation of carbohydrates by acidic bacteria. One of the main bacteria associated with dental caries is the *Streptococcus mutans*, however, a wide variety of microorganisms that intervene in dental caries have been identified by various researchers (9, 26).

Our overall mean of the DMFT index in the rheumatoid arthritis cases was slightly higher than in the healthy individuals (19.21 vs. 17.72, respectively) but with no significant difference between the groups (p = 0.547). There have only been two studies using the DMFT index to assess caries in RA patients and controls, and both reported no significant differences between the groups – 11.84 vs. 10.56, respectively (27), and 17.61 vs. 16.03, respectively (28). Although the DMFT index is generally used in dental caries epidemiological studies, it is only focused on determining caries experience during the subject's life (29). In the study conducted by Sánchez-Medrano et al., there was also no significant difference between the group of RA patients and controls concerning DMFT (9).

The analysis of the DMFT index components shows that the amount of tooth decay in the rheumatoid arthritis cases was lower than in the healthy individuals (0.36 vs. 1.46, respectively) with no significant difference between the groups (p = 0.078), which is not consistent with a comparable study (29). The number of filled teeth in the healthy individuals was higher than in the RA patients (10.62

***Table 3**. Oral status measured by DMFT index and its components*

Parameter	RA group (n = 14) Mean (SD)	Control group (n = 50) Mean (SD)	p-value
DMFT	19.21 (6.95)	17.72 (6.19)	0.547
Decayed, mean (SD)	0.36 (0.63)	1.46 (2.32)	0.078
%	2.0	8.0	
Missing, mean (SD)	10.07 (8.86)	5.64 (4.05)	0.126
%	52.0	32.0	
Filled, mean (SD)	8.79 (4.49)	10.62 (5.36)	0.397
%	46.0	60.0	

RA – rheumatoid arthritis; DMFT – Decayed, Missing and Filled Teeth

***Table 4.** Periodontal health according to the highest CPI score (N = 64)*

Parameter	RA group (n = 14) n (%)	Control group (n = 50) n (%)	p-value
Healthy CPI = 0	0 (0.0)	0 (0.0)	0.003
Bleeding CPI = 1	2 (14.3)	8 (16.0)	
Calculus CPI = 2	1 (7.1)	25 (50.0)	
Shallow pockets CPI = 3	6 (42.9)	11 (22.0)	
Deep pockets CPI = 4	3 (21.4)	6 (12.0)	
No teeth CPI = X	2 (14.3)	0 (0.0)	

RA – rheumatoid arthritis; CPI – Community Periodontal Index

vs. 8.79, respectively) with no significant difference between the groups, which is consistent with the studies by Sánchez-Medrano et al. and Martinez-Martinez et al. (9, 29). The presence of more than 20 natural teeth has a fundamental role in maintaining a satisfactory nutritional status. Missing teeth could lead to altered dietary intake and poor nutritional status, which could contribute to increased risk of developing chronic diseases. The number of missing teeth in RA patients in the present study was higher than in healthy individuals (10.07 vs. 5.64) but with no significant difference ($p=0.397$). The finding does not corelate with a study by Mehdipour et al. with the mean number of missing teeth between RA and control groups (9.09 vs. 5.47, $p=0.026$), where the difference was statistically significant (10). Our findings corelate with a study conducted by Sánchez-Medrano et al. where no significant difference in missing teeth was found between the group of patients with rheumatoid arthritis ($n=13$) and subjects without rheumatoid arthritis ($n=16$) (9). Our null hypothesis in relation to the caries index, that there is no significant difference between RA patients and controls in all DMFT index parameters, was confirmed.

An increased number of missing teeth is a risk factor for RA occurrence. De Pablo et al. showed that in patients with RA there was higher prevalence of tooth loss, and the association with complete tooth loss was robust in patients with seropositive RA (15). Tooth loss is a consequence of complex causes, including periodontal diseases, old age, smoking, comorbidities, and medication usage (7, 8, 29).

Periodontal Health

Recent literature highlights the relationship between rheumatoid arthritis and periodontitis. Several clinical, epidemiological, and serologic studies have shown a bidirectional association between periodontitis and RA (15, 20, 30). In both entities, proinflammatory cytokines such as IL-1β, IL-6 and TNF-α are upregulated, promoting inflammation of soft tissue and destruction of bone (31, 32). Furthermore, patients with PD have a greater risk of various systemic inflammatory diseases such as atherosclerosis, diabetes mellitus and RA. The risk of progression of periodontitis is 1.82 times higher in patients with RA than in healthy people (17). Moreover, RA often causes mental and physical impairment affecting interphalangeal and metacarpophalangeal proximal joints; oral health may cause disorders in these patients and result in plaque accumulation and subsequently periodontal inflammatory disease (17, 33, 34). There is a significant association described between the 'eating' category of the HAQ with average probing pocket depth. This suggests that RA patients with nutrition issues may be more predisposed to PD (28).

In our study a periodontal condition most frequently found in the group of RA patients was the presence of shallow pockets – moderate periodontitis, 42.9% vs. 22.0% in the non-RA group and the presence of deep periodontal pockets – severe periodontitis found in 21.4% of RA group vs. 12.0% in the non-RA group. The difference between the groups was statistically significant ($p=0.003$). Our null hypothesis in relation to periodontal health, which predicted statistically significant difference in the presence of periodontal diseases between RA patients and controls was confirmed. The results of our study confirm a significantly higher incidence of periodontitis in the group of RA patients compared to the control group.

The association between RA and PD has been examined in a few studies with inconsistent results. Although most earlier studies did not find positive associations of RA with PD (35, 36), more recent evidence suggests that subjects with RA have higher odds of PD compared to non-diseased individuals (1, 37). Our results are in line with other recent case control studies in RA/PD patients, which showed higher odds ratios of PD prevalence in established RA patients (15, 17, 38, 39). Although our study did not provide evidence for a clear connection between periodontitis or tooth loss and the development of RA, some basic research supports this association. Some periodontal bacteria that are crucial in the development of periodontitis have been suggested to induce autoimmunity in RA. The detection of antibodies against periodontal pathogens and DNA from periodontal bacteria in serum and synovial fluid of patients with RA supports this idea (14, 40).

Moreover, association between oral care behaviour and disease was reported in patients with RA. Khare et al. identified that a group that received nonsurgical periodontal therapy, such as scaling, root planning, and oral hygiene instructions, showed significant improvement in all RA parameters compared with a group that did not (41). The result of our study is the confirmation of the predicted relationship between periodontitis and RA, as well as subsequent knowledge that better oral hygiene behaviour reduces the risk of developing RA in the targeted population group.

Limitations of the Study

There are some limitations. The major limitations of our study are the limited RA patient number, where from the dental medicine point of view, it is a rare and unique disease, the limited patient number did not allow analysis of PD severity as a factor of variance, the patients with RA received anti-rheumatic medication that might have affected the oral microbiota and our study design cannot suggest a causal relationship as a retrospective observational study.

CONCLUSION

The present study suggests that patients with RA have an increased prevalence of periodontitis compared to non-diseased individuals. An increased number of missing teeth and presence of periodontitis may be risk factors for the occurrence of rheumatoid arthritis. Several studies point to a significant relationship between periodontitis and rheumatoid arthritis. Patients with RA suffer from limited movements of hands, elbows and shoulders, which leads to poor or no oral hygiene and consequently to an increased incidence of periodontitis. The results indicate the fact that patients with RA do not receive consistent dental care, or the emphases is dominantly placed on the treatment of general disease. People with RA have unique oral health perceptions and experience significant challenges with personal and professional oral health care due to their arthritis. Adapting oral hygiene recommendations and professional oral care delivery to the needs of those with arthritis are patient priorities and are required to improve satisfaction regarding their oral health. To achieve this, a close collaboration among physicians, dentists, and dental hygienists when treating patients with RA is needed.

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Conflicts of Interest

None declared

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