Research Article

JPIS Journal of Periodontal & Implant Science

J Periodontal Implant Sci 2012;42:67-72 • http://dx.doi.org/10.5051/jpis.2012.42.3.67

Effect of rheumatoid arthritis on periodontitis: a historical cohort study

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Purpose: Rheumatoid arthritis (RA) is a chronic multi-systemic disease that causes damage to the bone and connective tissues. This study was conducted in order to accurately measure the correlation between RA and periodontitis, and to obtain an unbiased estimate of the effect of RA on periodontal indices.
Methods: In this historical cohort study, which was conducted from February to May 2011 in Hamadan city, Iran, 53 exposed people (with RA) were compared with 53 unexposed people (without RA) in terms of clinical periodontal indices (the outcomes of interest) including 1) plaque index (PI), 2) bleeding on probing (BOP), and 3) clinical attachment loss (CAL).
Results: A sample of 106 volunteers were evaluated, 53 rheumatoid versus 53 non-rheumatoid subjects. There was a statistically significant correlation between RA and BOP ($P<0.001$) and between RA and CAL ($P<0.001$). However, there was no statistically significant correlation between RA and any of the periodontal indices. No correlation was seen between gender and any of the indices either. There was a strong positive correlation between age and all three periodontal indices ($P<0.001$).
Conclusions: The present study indicated a potential effect of RA on periodontal indices. However, much more evidence based on a prospective cohort study is needed to support the cause and effect relationship between RA and periodontal indices.

Keywords: Rheumatoid arthritis, Periodontitis, Periodontal index, Iran.

INTRODUCTION

Periodontitis is an infectious disease and a leading cause of chronic periodontal inflammation in which microbial plaque causes damage to alveolar bone and surrounding connective tissue; it is also a leading cause of tooth loss [1]. Rheumatoid arthritis (RA) is a chronic multi-systemic disease that causes damage to bone and joint connective tissue [2].

There is a similarity between the pathologic mechanisms of RA and those of periodontitis. In both diseases, an imbalance between pre-inflammatory and anti-inflammatory cytokines may lead to destruction of connective tissue. In addition, some bacterial infections play a role in the etiology of periodontitis and may be a trigger for RA [3]. Furthermore, incompetent hand performance among rheumatoid patients may lead to limitation in toothbrushing practice and thus reduction in oral hygiene, which in turn may cause periodontitis [4].

The correlation between RA and periodontal disease has been investigated by previous observational studies. However, these studies had limitations of their own. They were conducted either on the basis of data collated from a self-reported health questionnaire [5], or reported a single index for the periodontitis [6], or used a small sample size (75 subjects) [7],

Received: Mar. 13, 2012; **Accepted:** Apr. 16, 2012
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pISSN 2093-2278
eISSN 2093-2286

JPIS Journal of Periodontal & Implant Science

or enrolled other patients (osteoarthritis subjects) as a control group rather than healthy individuals [8]. However, the present historical cohort study was conducted in order to measure the correlation between the two diseases accurately and to obtain an unbiased estimate of the effect of RA on periodontal indices with a high significance level and a strong statistical power.

MATERIALS AND METHODS

The local Human Subject Review Board of Hamadan University of Medical Sciences approved this study. All of the patients participated voluntarily and provided informed consent. This historical cohort study was conducted from February to May 2011 in Hamadan city, Iran.

A previous local study in Iran [6] had reported the prevalence of periodontitis of about 60% and 16% among rheumatoid and non-rheumatoid subjects, respectively. Therefore, considering a 99% confidence level and a 99% statistical power, a sample of 53 exposed and unexposed sets was estimated to be needed. We enhanced both the significance level and statistical power in order to increase the sample size and thus decrease the possibility of random error.

Exposed subjects (with RA) were compared with unexposed subjects (without RA) in terms of periodontal indices. The rheumatoid patients were selected randomly from the clinical records of Shaheed Beheshti Hospital, an educational hospital affiliated with Hamadan University of Medical Sciences. The patients had already been diagnosed by a rheumatologist based on clinical and serological criteria. Members of the non-exposed group (without RA) were selected from among non-relative spouses of rheumatoid patients.

The inclusion criteria for enrolling the subjects in the study included: 1) 30 to 80 years of age, 2) having at least seven teeth, 3) no history of systemic diseases such as diabetes or Sjögren's disease, 4) no history of using antibiotics during the previous three months, 5) no history of treatment for periodontal disease for the previous three months, 6) not using immunosuppressive drugs, 7) and non-smoker. Additional criteria for RA patients included having more than one inflamed joint, C-reactive protein level >5 mg/L, and at least a 3-year history of RA. Additional inclusion criteria for non-RA subjects included no obvious history of RA in the past and no close relation with the spouse. In addition, the performance capability of the subjects' hands for brushing teeth in different directions was measured qualitatively. For this purpose, we asked the patients to simulate the method of toothbrushing as they usually did. Patients who were not able to brush their teeth properly were excluded from the study.

The outcome of interest was periodontal disease. The three clinical indicators considered for assessment of periodontitis included: 1) plaque index (PI), 2) bleeding on probing (BOP), and 3) clinical attachment loss (CAL).

For evaluation of the PI and oral hygiene, a staining method was used in which a chewable disclosing tab was given to the subjects to wipe over all parts of their teeth by moving their tongues. Then the subjects were asked to wash their mouths. In order to measure the extent of discoloration, the sites of each tooth were divided into four parts including mesial, distal, buccal, and lingual parts. Then, the extent of the discoloration was assessed and recorded for each part separately and reported as a percentage [9]. Based on the PI, the oral hygiene of the subjects was divided into three groups: 1) good hygiene (zero to 30%), 2) moderate hygiene (31 to 50%), and 3) poor hygiene (51 to 100%). The PI was not measurable for teeth without a clinical tooth crown. These teeth were excluded from the analysis and calculation of the PI.

In order to estimate the extent of oral inflammation, BOP based on the percentage of sites for all teeth of a subject other than teeth without clinical crowns was measured 30 seconds after probing the sites. Bleeding was recorded as point, linear, or drop bleeding. Then, the data were averaged to create a subject mean, which was reported as a percentage (Fig. 1).

In order to assess the severity of periodontitis, the CAL was measured using a Williams color-coded probe. The distance between the cementoenamel junction and the apical end of the probe was measured in millimeters for each tooth at six different sites: the mesial, distal, and midbuccal on the buccal side, and the mesial, distal, and midlingual on the lingual side (Fig. 2). The CAL was not measurable for teeth with calculus or cervical caries or without a clinical tooth crown. These teeth were excluded from the analysis and calculation of the CAL.

Three-way analysis of variance was used to compare the mean of the periodontal indices between subjects with and without RA. A linear regression model was also used to pre-

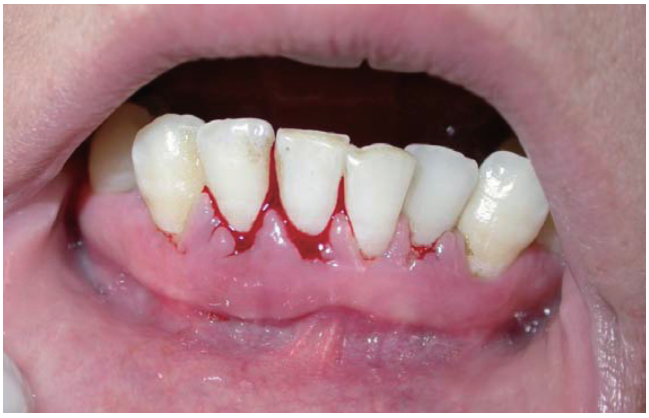

Figure 1. Method of assessment of bleeding on probing.

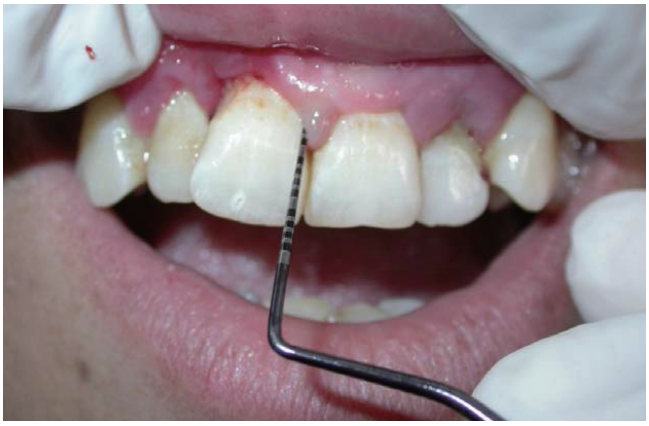

Figure 2. Assessment of clinical attachment loss using a Williams probe.

dict the risk of periodontitis among the two groups by sex and age group. All analyses were performed at the 1% significance level ($P<0.01$) using the statistical software STATA release 11 (StataCorp LP., College Station, TX, USA).

RESULTS

In this study, 106 volunteers participated, including 53 individuals with RA arthritis as the exposed group and 53 individuals without RA as the unexposed group, among them 58 females and 48 males. The mean age of the exposed group was 41.5 years old (range, 30 to 58 years) and that of the unexposed group was 43.5 years (range, 31 to 57 years) ($P=0.220$).

The comparison of the mean percent of sites manifesting PI between the groups is shown in Table 1. Oral hygiene was poor in all participants (PI>50%). There was no significant difference in the means between RA and non-RA subjects nor between males and females. However, the difference in the means of PI between age groups was statistically significant ($P<0.001$).

The comparison of the mean percent of sites manifesting BOP between the groups is shown in Table 2. The mean BOP between the RA and non-RA subjects was not statistically significant on crude analysis ($P=0.061$) but was strongly significant after adjustment for other variables ($P<0.001$). There was no significant difference in the mean BOP between males and females whereas the difference in the mean BOP between the age groups was statistically significant ($P<0.001$).

The comparison of mean percent of sites manifesting CAL between the groups is shown in Table 3. The mean CAL between the RA and non-RA subjects was not statistically significant on crude analysis ($P=0.161$) but was strongly significant after adjustment for other variables ($P<0.001$). No difference was seen between the mean CAL among males and females. However, the difference in the mean CAL between

Table 1. Comparison of means of plaque index (%) by rheumatoid arthritis (absent/present), gender (female/male) and 10-year age groups.

Variable	No. (n=106)	Plaque index (%)	SD	*P*-value	
				Unadjusted[a]	Adjusted[b]
Rheumatoid arthritis				0.923	0.448
Absent	53	71.95	8.76		
Present	53	71.71	15.18		
Gender				0.187	0.374
Female	58	70.39	13.50		
Male	48	73.57	10.64		
Age (year)				<0.001	<0.001
30-39	45	66.41	6.83		
40-49	32	75.04	17.66		
50-59	29	76.70	8.28		

SD: standard deviation.
[a]Comparisons of means between the groups unadjusted (crude) for other variables using analysis of variance. [b]Comparisons of means between the groups adjusted for all other variables in the table using 3-way analysis of variance at 0.01 significance level.

Table 2. Comparison of means of bleeding on probing (%) by rheumatoid arthritis (absent/present), gender (female/male) and 10-year age groups.

Variable	No. (n=106)	Bleeding on probing (%)	SD	*P*-value	
				Unadjusted[a]	Adjusted[b]
Rheumatoid arthritis				0.061	<0.001
Absent	53	29.29	18.45		
Present	53	36.61	21.22		
Gender				0.497	0.284
Female	58	31.73	19.65		
Male	48	34.42	20.79		
Age (year)				<0.001	<0.001
30-39	45	18.14	13.41		
40-49	32	43.13	18.49		
50-59	29	44.70	15.62		

SD: standard deviation.
[a]Comparisons of means between the groups unadjusted (crude) for other variables using analysis of variance. [b]Comparisons of means between the groups adjusted for all other variables in the table using 3-way analysis of variance at 0.01 significance level.

age groups was statistically significant ($P<0.001$).

The correlations between RA and periodontal indices adjusted for gender and age are shown in Table 4. According to these results, the mean percent of sites manifesting PI was 1.969-fold higher in the RA group than the non-RA group ($P=0.448$), 2.384-fold higher in males than in females ($P=0.374$), 8.572-fold higher in the 40 to 49 year age group than in the 30 to 39 year age group ($P=0.002$), and 9.901-fold higher in the 50 to 59 year age group than in the 30 to 39 year age group

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(P=0.001).

Based on the results shown in Table 4, the mean percent of sites manifesting BOP was 11.989% higher in the RA group than the non-RA group (P=0.001), 3.693% higher in the males than in the females (P=0.284), 24.826% in the 40 to 49 year age group than in the 30 to 39 year age group (P=0.001), and 27.848% in the 50 to 59 year age group than in the 30 to 39 year age group (P=0.001).

According to the results shown in Table 4, the mean percent of sites manifesting CAL was 0.310 mm greater in the RA group than the non-RA group (P=0.001), 0.158 mm greater in the males than in the females (P=0.089), 0.731 mm greater in the 40 to 49 year age group than in the 30 to 39 year age group (P=0.001) and 0.794 mm greater in the 50 to 59 year age group than in the 30 to 39 year age group (P=0.001).

Table 3. Comparison of means of clinical attachment loss (mm) by rheumatoid arthritis (absent/present), gender (female/male) and 10-year age groups.

Variable	No. (n=106)	Clinical attachment loss (mm)	SD	*P*-value	
				Unadjusted[a]	Adjusted[b]
Rheumatoid arthritis				0.161	<0.001
Absent	53	0.90	0.53		
Present	53	1.05	0.59		
Gender				0.192	0.089
Female	58	0.91	0.51		
Male	48	1.05	0.62		
Age (year)				<0.001	<0.001
30-39	45	0.54	0.29		
40-49	32	1.27	0.48		
50-59	29	1.32	0.51		

SD: standard deviation.
[a]Comparisons of means between the groups unadjusted (crude) for other variables using analysis of variance. [b]Comparisons of means between the groups adjusted for all other variables in the table using 3-way analysis of variance at 0.01 significance level.

DISCUSSION

The results of the present study revealed a significant correlation between RA and mean percent of BOP, which is a clinical indicator for oral inflammation, and RA and the mean percent of CAL, which is a clinical indicator for progression of periodontitis. However, no significant correlation was evident between RA and the mean percent of PI, which is a clinical indicator for oral hygiene. A reason for this finding is that the status of oral hygiene was poor (PI>50%) among all subjects with and without RA. Therefore, the difference between the two groups was not statistically significant. This issue was an important limitation of this study and might obscure the real correlation between RA and PI.

The mean percent of BOP and CAL were not statistically significant between the RA and non-RA groups, while the differences became statistically significant after adjustment

Table 4. Linear regression analysis for comparison of plaque index (PI), bleeding on probing (BOP), and clinical attachment loss (CAL) among exposed group with rheumatoid arthritis (RA) and unexposed group without rheumatoid arthritis adjusted for gender and age.

Variable	Coefficient	SE	*t*-test	*P*-value	99% CI	
Plaque index (%)						
RA (present/absent)	1.969	2.587	0.760	0.448	-4.823	8.761
Gender (male/female)	2.384	2.668	0.890	0.374	-4.620	9.387
Age group (40-49/30-39 year)	8.572	2.676	3.200	0.002	1.547	15.597
Age group (50-59/30-39 year)	9.901	2.868	3.450	0.001	2.371	17.432
Constant	64.471	2.685	24.010	<0.001	57.422	71.520
Bleeding on probing (%)						
RA (present/absent)	11.989	3.328	3.600	<0.001	3.251	20.726
Gender (male/female)	3.693	3.432	1.080	0.284	-5.317	12.703
Age group (40-49/30-39 year)	24.826	3.442	7.210	<0.001	15.789	33.864
Age group (50-59/30-39 year)	27.848	3.690	7.550	<0.001	18.160	37.536
Constant	10.171	3.454	2.940	0.004	1.103	19.239
Clinical attachment loss (mm)						
RA (present/absent)	0.310	0.089	3.470	0.001	0.076	0.545
Gender (male/female)	0.158	0.092	1.720	0.089	-0.084	0.400
Age group (40-49/30-39 year)	0.731	0.092	7.920	<0.001	0.489	0.974
Age group (50-59/30-39 year)	0.794	0.099	8.020	<0.001	0.534	1.054
Constant	0.307	0.093	3.310	0.001	0.064	0.550

SE: standard error, CI: confidence interval.

for gender and age. This issue revealed the negative confounding effect of gender and age on the correlation between RA and periodontitis. This confounding effect diluted the real correlation between RA and periodontitis. It should be remembered that the difference in CAL between groups was not clinically significant although it was statistically significant.

There was no correlation between gender and any of the periodontal indices. It seems that gender neither attenuates nor accentuates periodontitis. However, both crude and adjusted correlation between age and all periodontal indices was highly significant. These findings confirm that the probability of periodontitis increases with age with or without RA.

Oral hygiene status could affect the extent of CAL [6]. However, the status of oral hygiene was poor in both groups based on the PI. Hence, the difference in the extent of the CAL seen between the two groups cannot be attributed to the status of oral hygiene but can be attributed to the effect of other variables such as RA and age. This finding was confirmed by evidence from previous studies [5,7].

The limitation in capability of RA patients' hands for brushing teeth may play an important role in making patients prone to periodontitis [8]. In addition, some chronic diseases such as Sjögren's disease and diabetes, as well as smoking, can cause or exacerbate periodontitis. Furthermore, using immunosuppressive drugs may affect periodontitis [10,11]. In order to avoid these confounding effects on the correlation between RA and periodontitis, we excluded from the study population those patients whose hands did not have enough capability for toothbrushing. Furthermore, the subjects who had chronic disease or used immunosuppressive drugs or were smoker were excluded from the study as well. Accordingly, the observed association between RA and periodontitis should not have been confounded by these variables.

This study had a number of limitations. First, since smoking may play a role as a non-genetic risk factor for RA, by excluding smokers from the study, the external generalizability of the study results was limited. Second, the teeth without a clinical tooth crown were excluded from the analysis and calculation of the PI and CAL. This may raise the possibility of selection bias. Third, individuals with RA are possibly more likely to have periodontal disease and also to seek periodontal therapy. Thus, exclusion of participants undergoing periodontal therapy from this study might have raised the possibility of selection bias. Consequently, the results may have diluted or underestimated the probability of periodontitis among RA patients. Despite its limitations, an important strength of this study was that the control group was selected from the spouses of RA patients. This issue helped increase the similarity of individuals in the control and case groups regarding many characteristics such as socioeconomic status, lifestyle, and nutrition.

The present study indicated a potential effect of RA on periodontal indices. However, much more evidence based on a prospective cohort study is needed to support the cause and effect relationship between RA and periodontal indices.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This article is a part of an MD thesis supported by the Hamadan University of Medical Sciences. We would like to thank the Deputy of Education as well as the Deputy of Research and Technology of the Hamadan University of Medical Sciences for financial support of this study.

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