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].
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%).

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 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-
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 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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**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             |               |                 |     |               |
| Rheumatoid arthritis   |               |                 |     |               |
| Absent                 | 53            | 71.95           | 8.76| 0.923         |
| Present                | 53            | 71.71           | 15.18| 0.448         |
| Gender                 |               |                 |     | 0.187         |
| Female                 | 58            | 70.39           | 13.50| 0.374         |
| Male                   | 48            | 73.57           | 10.64| 0.374         |
| Age (year)             |               |                 |     | <0.001        |
| 30-39                  | 45            | 66.41           | 8.83 | <0.001        |
| 40-49                  | 32            | 75.04           | 17.66| <0.001        |
| 50-59                  | 29            | 76.70           | 8.28 | <0.001        |

SD: standard deviation.

4Comparisons 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             |               |                         |     |               |
| Rheumatoid arthritis   |               |                         |     |               |
| Absent                 | 53            | 29.29                   | 18.45| 0.061         |
| Present                | 53            | 36.61                   | 21.22| <0.001        |
| Gender                 |               |                         |     | 0.497         |
| Female                 | 58            | 31.73                   | 19.66| 0.284         |
| Male                   | 48            | 34.42                   | 20.79| 0.284         |
| Age (year)             |               |                         |     | <0.001        |
| 30-39                  | 45            | 18.14                   | 13.41| <0.001        |
| 40-49                  | 32            | 43.13                   | 18.49| <0.001        |
| 50-59                  | 29            | 44.70                   | 15.62| <0.001        |

SD: standard deviation.

4Comparisons of means between the groups adjusted for all other variables in the table using 3-way analysis of variance at 0.01 significance level.

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

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 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  |
|--------------------|---------------|--------------------------------|------|----------|
| Rheumatoid arthritis |               |                               |      |          |
| Absent             | 53            | 0.90                          | 0.53 | 0.161    |
| Present            | 53            | 1.05                          | 0.59 | <0.001   |
| Gender             |               |                               |      |          |
| Female             | 58            | 0.91                          | 0.51 | 0.192    |
| Male               | 48            | 1.05                          | 0.62 | 0.089    |
| Age (year)         |               |                               |      |          |
| 30-39              | 45            | 0.54                          | 0.29 | <0.001   |
| 40-49              | 32            | 1.27                          | 0.48 | <0.001   |
| 50-59              | 29            | 1.32                          | 0.51 |          |

SD: standard deviation.

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     | 0.082| 7.920  | <0.001  | 0.489     | 0.974     |
| Age group (50-59/30-39 year)| 0.794     | 0.089| 8.020  | <0.001  | 0.534     | 1.054     |
| Constant           | 0.307       | 0.083| 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.

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REFERENCES

1. Novak MJ. Classification of Diseases and Conditions Affecting of Periodontium. In: Newman MG, Takei H, Klokkevold PR, Carranza FA, editors. Carranza’s clinical periodontology. 10th ed. Philadelphia: Saunders; 2006. p.100-9.
2. Lipsky PE. Rheumatoid Arthritis. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, et al., editors. Harrison’s principles of internal medicine. 17th ed. New York: McGraw Hill; 2008. p.2083-92.
3. Mercado FB, Marshall RI, Bartold PM. Inter-relationships between rheumatoid arthritis and periodontal disease. J Clin Periodontol 2003;30:761-72.
4. Pischon N, Pichon T, Kroger J, Gulmez E, Kleber BM, Bernimoulin JP, et al. Association among rheumatoid arthritis, oral hygiene, and periodontitis. J Periodontol 2008;79:979-86.
5. Mercado F, Marshall RI, Kestov AC, Bartold PM. Is there a relationship between rheumatoid arthritis and periodontal disease? J Clin Periodontol 2000;27:267-72.
6. Bakhtiari S, Taheri JB, Abbasi F. Association between rheumatoid arthritis and moderate to severe periodontitis in Iranian adults. J Dent (Teheran) 2009;6:145-9.
7. Pinho Mde N, Oliveira RD, Novaes AB Jr, Voltarelli JC. Relationship between periodontitis and rheumatoid arthritis and the effect of non-surgical periodontal treatment. Braz Dent J 2009;20:355-64.
8. Dissick A, Redman RS, Jones M, Rangan BV, Reimold A, Griffiths GR, et al. Association of periodontitis with rheu-
matoid arthritis: a pilot study. J Periodontol 2010;81:223-30.

9. Perry DA. Plaque Control for the Periodontal Patient. In: Newman MG, Takei HH, Klokkevold FR, Carranza FA, editors. Carranza’s clinical periodontology. 12th ed. Missouri: WB Saunders; 2012. p.552-60.

10. Ishi Ede P, Bertolo MB, Rossa C Jr, Kirkwood KL, Onofre MA. Periodontal condition in patients with rheumatoid arthritis. Braz Oral Res 2008;22:72-7.

11. Kasser UR, Gleissner C, Dehne F, Michel A, Willershausen-Zonnchen B, Bolten WW. Risk for periodontal disease in patients with longstanding rheumatoid arthritis. Arthritis Rheum 1997;40:2248-51.