

Research Article

The Relationship of Periodontal Disease with Rheumatoid Arthritis

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Abstract: Rheumatoid arthritis (RA) is a chronic multi-system, autoimmune disease. Periodontal disease is associated with alveolar bone resorption and eventual tooth loss and is commonly seen in RA patients. This study aimed to assess the prevalence and severity of periodontal disease in patients with RA. This historical cohort study was conducted on two groups of RA patients and age- and sex-matched healthy controls (n=50 each). Periodontal status of groups was compared by assessing the number of teeth, bleeding on probing (BOP), probing pocket depth (PPD), clinical attachment loss (CAL), alveolar bone loss (ABL) and plaque index (PI). Data were analyzed using SPSS version 19, t-test, and Mann Whitney test. Participants in each group included 45 females and 5 males with a mean age of 44.66 years in the case and 44.96 years in the control group. The overall CAL (P=0.000), relative frequency of areas with PPD>3mm (P=0.001), ABL (P=0.000), relative frequency of areas with CAL (P=0.010) and PI (P=0.010) were significantly higher in RA group compared to controls. No significant difference was found between the two groups in terms of BOP, number of teeth, and the relative frequency of areas with ABL (P>0.05). No significant association was found between any drug intake and periodontal parameters (P>0.05). RA patients had poorer periodontal status. Special care must be taken to prevent the progression of periodontitis in these patients.

Keywords: Rheumatoid arthritis, Periodontal disease, Plaque index, Bleeding on probing, Alveolar bone loss, tooth loss.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, multi-system disease of unknown etiology. It has a wide range of systemic manifestations but persistent synovial inflammation is pathognomonic for RA and usually involves peripheral joints symmetrically [1,2].

Rheumatoid arthritis has a prevalence of 1%; which increases by aging and Women are affected more than men [2,3]. Cartilage damage, bone destruction and changes in the articular structure due to synovial inflammation are the main signs of RA [1].

Specific symptoms manifest gradually when multiple joints particularly in the hands, wrists, knees and legs are symmetrically involved. Although asymmetric articular involvement may be seen in some patients, the symmetric pattern of involvement is more typical [4].

Periodontal disease is a hereditary or acquired disease of the tooth surrounding tissues and is categorized into gingivitis and periodontitis. These

conditions are caused by microflora pathogens present in dental plaque and microbial biofilm that form daily [5].

Several previous studies have reported the association of RA and periodontal disease [2,6-8]. Scher and Abramson in 2014 reported that periodontal disease was more prevalent in RA patients and also stated that periodontal disease played a role in the pathogenesis of RA [9].

According to Koziel et al, periodontal disease was twice more common in subjects with RA compared to healthy individuals. Moreover, the course of periodontal disease was more severe in subjects with RA irrespective of age, race, sex, or history of smoking. Furthermore, the destructive mechanisms responsible for chronic bone loss in RA and chronic gingival recession in periodontitis are similar between the two diseases in terms of inflammatory cells and proinflammatory cytokines [10].

Other studies in this field indicate greater bleeding on probing (BOP) [2,7,11], plaque index (PI)

[2,7, 11,12,13], clinical attachment loss (CAL) [2,7,12,13] and higher number of lost teeth [2,8,11] in RA patients.

Evidence shows that the severity of periodontal disease depends on the host inflammatory responses, and the immune response to pathogenic bacteria can aggravate the disease. Systemic diseases can also alter the tissue and physiological responses and impair the patients' defense mechanisms and aggravate the periodontal disease[7].

Some evidence exists regarding the correlation of RA with periodontal disease. Genetic factors guide the host responses and result in chronic diseases with a complex pathogenesis. Tumor necrosis factor alpha (TNF- α) is a proinflammatory cytokine that activates a cascade of inflammatory events and plays a role in both periodontitis and RA. Other common factors include matrix metalloproteinases, prostaglandin E₂, osteoprotegerin and NFkB (Nuclear Factor kappa B).

Some other conditions such as osteoporosis and cardiovascular diseases also have the same genetic pathways. Infection is the etiology of many diseases and it seems that *Porphyromonas gingivalis* plays a fundamental role in development of periodontal disease. Via the process of citrullination or deamination, *P. gingivalis* replaces arginine in proteins with citrulline and exposes periodontitis patients to citrullinated antigens leading to the production of anti-CCP specific antibody. This indicates similar pathogenesis of the two diseases and may explain the chronic process in both conditions [3].

Other common factors found in both conditions include IL-1B and decreased IL-10 and TGF-B2 suppressing cytokines. Although the etiology of periodontal disease and RA appears to be different, their pathological mechanisms seem to be the same and there is a possibility that in subjects with concurrent RA and periodontitis, dysregulation of inflammatory pathways play a role[15]. On the other hand, inadequate oral hygiene due to physical disability in these patients further complicates the issue[11].

Considering the high prevalence of RA and young age of patients (even as early as in the third decade of life), further investigations about this condition are necessary. On the other hand, the chronic process of periodontal disease that mostly affects older

patients emphasizes the need for the assessment of periodontal disease in RA patients. If the prevalence of periodontal disease is proven to be higher in RA patients, necessary treatments should be initiated for these patients to prevent further destruction of tooth surrounding tissues by using adjunct oral hygiene aids and periodontal care.

This study aimed to assess the prevalence and severity of periodontal disease in RA patients by evaluating clinical periodontal parameters of PI, periodontal pocket depth (PPD), tooth loss (TL), alveolar bone loss (ABL) and CAL.

MATERIALS AND METHODS

This historical cohort study was conducted in 2013 at School of Dentistry of Qazvin University of Medical Sciences, Iran. The case group comprised of 50 males and females between 20-60 years suffering from RA who were randomly selected among patients whom diagnosis of RA was made by a rheumatologist based on clinical, laboratory and radiographic findings in accordance with the international guidelines. Those patients were referred by their rheumatologist for oral health routine examinations. Fifty healthy individuals were randomly chosen as the control group.

Patients were briefed about the study and signed written informed consent. The inclusion criteria for the case group were: suffering from RA for a minimum of five years and having no other autoimmune diseases. The inclusion criteria for the control group were not having RA or any other autoimmune diseases. The remaining inclusion criteria were similar for both groups and included presence of 16 teeth, no smoking, no pregnancy, not having systemic conditions affecting the periodontal status such as diabetes mellitus or cardiovascular diseases, not taking cyclosporine, nifedipine or phenytoin and no history of periodontal therapy in the past three months.

A questionnaire containing first and last name, age, sex, medical history, current general health status, duration of RA, medications used and duration of drug intake was filled out for each patient. Six radiographs including two right and left posterior bitewings, two periapical radiographs from the maxillary incisors and two periapical radiographs from the mandibular incisors were obtained from each patient according to their examination requirements by using lead apron and collar (Figure 1).

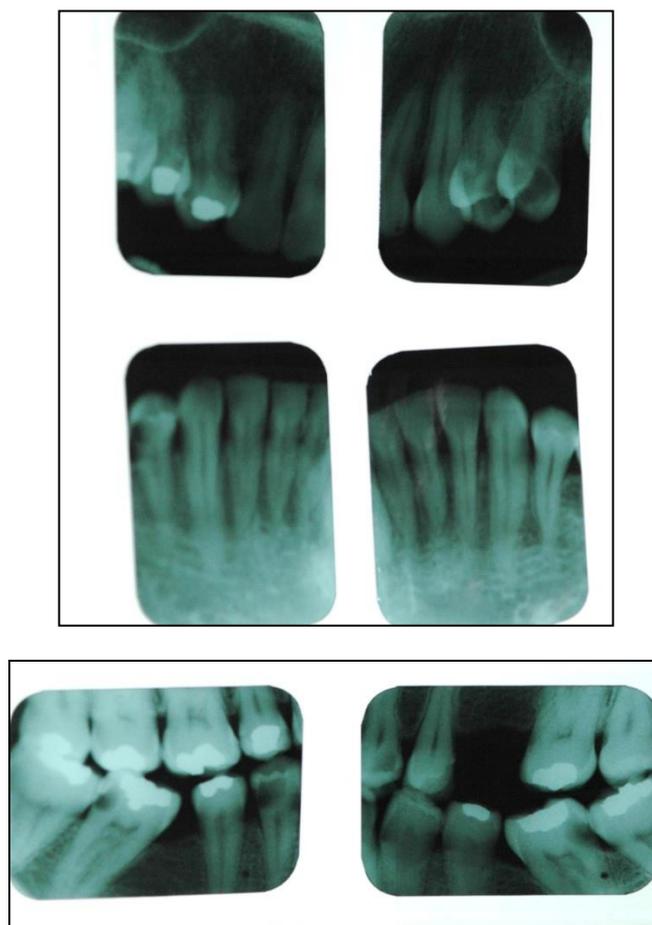


Fig-1: Radiographs obtained from a patient

By clinical examination and studying the radiographs, the following parameters were measured for each patient: BOP using the Gingival Bleeding Index (Ainamo and Bay)[16], PPD, CAL, PI using O'Leary's index [17] and alveolar bone height (ABH) using radiography. Data were analyzed using SPSS version 19.0, t-test and Mann Whitney test. P value<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

There were 45 females and 5 males in each group. The mean (\pm SD) age of subjects was 44.66 \pm 8.96 years in the RA and 44.96 \pm 10.64 years in the control group. The difference in this respect between the two groups was not significant. The duration of involvement with RA was 5-20 years with a mean (\pm SD) duration of 7.46 \pm 3.67 years.

The mean (\pm SD) number of teeth was 24.04 \pm 4.41 in the RA and 24.48 \pm 3.94 in the control group. The mean (\pm SD) percentage of areas with BOP was 32.76 \pm 19.34% in RA and 28 \pm 16.76% in the control group. According to the t-test, the difference in these variables between the two groups was not significant (P>0.05).

The mean(\pm SD) percentage of areas with mild CAL was 17.42 \pm 12.75% in the RA and 11.32 \pm 14.40%

in the control group; this difference between the two groups was statistically significant (P=0.003). The mean (\pm SD) percentage of areas with moderate CAL was 19.44 \pm 16.34% in the RA and 15.46 \pm 15.93% in the control group; which were not significantly different (P>0.05). The mean (\pm SD) percentage of areas with severe CAL was 14.09 \pm 9.58% in the RA and 9.91 \pm 5.50% in the control group; which were significantly different (P=0.038).

Overall, the mean (\pm SD) percentage of areas with CAL was 46.44 \pm 28.42% in the RA and 31.82 \pm 26.95% in the control group; this value was significantly different between the two groups (P=0.01).

The mean (\pm SD) percentage of areas with PPD>3mm was 9.62 \pm 9.38% in the RA and 7.36 \pm 4.78% in the control group; which were significantly different (P=0.001). The mean (\pm SD) percentage of areas with radiographic ABL was 42.56 \pm 35.40% in the RA and 28.80 \pm 31.27% in the control group; this parameter was not significantly different between the two groups.

Of all interdental (proximal) areas that should have been seen on the radiographs, 14.04 \pm 8.69% in the RA group and 13.60 \pm 9.31% in the control group were not clear due to the overlapping of proximal contacts as

the result of incorrect horizontal angulation or cone-cuts; the difference in this regard between the two groups was not significant.

The mean (\pm SD) radiographic ABH was 2.78 \pm 1.76 mm in the RA and 2.43 \pm 1.23 mm in the control group; the difference in this respect between the two groups was statistically significant ($P=0.000$). The mean (\pm SD) PI was 73.56 \pm 17.46 in the RA and

69.48 \pm 12.71 in the control group; this difference between the two groups was statistically significant ($P=0.010$).

According to the Mann Whitney test, no significant association was found between any drug intake and number of teeth, BOP, CAL, PPD>3mm, ABH and PI. The results are summarized in Table 1.

Table -1: Comparison of the mean (\pm SD) periodontal parameters between the case (RA) and control groups

Parameter	RA patients	Control group	P value
Age	44.66 \pm 8.96	44.96 \pm 10.64	0.879
Female/male	0.11	0.11	1
Number of teeth	24.04 \pm 4.41	24.48 \pm 3.94	0.60
BOP	32.76 \pm 19.34	28 \pm 16.76	0.217
Mild CAL	17.42 \pm 12.75	11.32 \pm 14.40	0.003
Moderate CAL	19.44 \pm 16.34	15.46 \pm 15.93	0.167
Severe CAL	9.58 \pm 14.09	5.50 \pm 9.91	0.038
Overall CAL	46.44 \pm 28.42	31.82 \pm 26.95	0.010
PPD>3mm	9.38 \pm 9.62	4.78 \pm 7.36	0.001
ABL	42.56 \pm 35.40	28.80 \pm 31.27	0.067
Radiographic ABH	2.78 \pm 1.76	2.43 \pm 1.23	0.000
PI	73.56 \pm 17.46	69.48 \pm 12.71	0.010

Although the etiology of periodontal disease and RA appears to be different, their pathological mechanisms seem to be the same and there is a possibility that in subjects with concurrent RA and periodontitis, dysregulation of inflammatory pathways play a role because the progression of both conditions is associated with presence of inflammatory agents[18] .

In this study we evaluated the periodontal status of RA patients and since the two groups were matched in terms of age and sex, the confounding effects of these two factors were non-existent. Although medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs) can affect the progress of periodontal disease, we could not eliminate this confounding factor since these medications had to be regularly taken by the patients and could not be discontinued. Lack of a significant difference in BOP, which indicates the presence of inflammation in oral tissues, between the two groups may falsely hide the inflammatory state of periodontal tissue in RA patients. The reason may be that control subjects were also selected among those presenting to dental school and could possibly have dental hygiene issues and oral conditions. Also, most RA patients in this study were taking NSAIDs due to their condition and this could have resulted in less gingival inflammation in these patients. This finding was in accord with the results of Ishi[8] and Garib[2] but in contrast to those of Torkbazan[7] ,Santiago[6] , Joseph[19] , Taheri[11] and Pischon[13] It should be noted that the methodology of the mentioned studies was different from the methodology of the current study; which may explain the difference between their

results and ours. . For instance, Joseph used Silness-Löe plaque index [19] and Taheri used the Muhleman-Saxer index[11] whereas, in our study O'Leary's pocket index was used.

The mean percentage of areas with pocket in our study was significantly different between the two groups, which was in accord with the results of Joseph [19] and Ams[12]. The mean CAL was significantly different between the two groups, which was in line with the findings of Torkzaban[7] , Santiago[6], Joseph[19],Garib[2], Ams[12]and Pischon[13]. Also, our study showed that the difference in percentage of areas with non-normal CAL was significant between the two groups. We also evaluated the frequency of periodontal disease based on the percentage of areas with non-normal CAL in the two groups, which was found to be 46.44 in the case and 32.81 in the control groups and this difference was statistically significant. Such increased prevalence and severity of periodontal disease in patients with RA may be due to higher PI in this group. However, there is a greater possibility that unknown inflammatory mechanisms play a role as underlying factors aggravating both conditions. Some genetic factors are also related to periodontal disease and RA such as specific HLA (human leukocyte antigen) s, presence of a series of pro-inflammatory cytokines such as IL-6, IL-1b and TNF-a and a reduction in anti-inflammatory factors such as IL-10 and TGF-B, which are similarly seen in both conditions[19].

The mean radiographic ABL was significantly different between the two groups in the current study. This finding was in accord with the results of Garib[2]

may be due to the osteoporosis related to this condition. ABL was not evaluated in studies by Torkbazan[7], Santiago[6], Joseph[19], Taheri [11], Ams [12], Pischon[13] and Ishi[8] and assessment of this parameter was a strength of our study. Moreover, in the current study we calculated the frequency percentage of areas with non-normal ABL and this has not been done in any of the above mentioned studies.

The mean PI in our study was similar to that in studies by Taheri[11], Ams[12], Pischon[13] and Ishi[8]. In all the afore-mentioned studies, the mean PI in the case group was significantly higher than that in the control group. This may also indicate poorer oral hygiene in patients with RA, which may be due to the impaired hand skills of these patients secondary to the problems in their interphalangeal joints complicating tooth brushing by these patients. However, we minimized the effect of this confounding factor by excluding patients with significantly compromised hand skills. The mean PI in studies by Torkbazan [7], Garib[2] and Sayyar[18] was greater in cases than controls; but not significantly. The PI was not calculated in some other studies[6,20].

In a study by Joseph *et al.*, oral hygiene index-simplified (OHI-S) was used instead of PI. OHI-S calculates the amount of debris and calculus and cannot be compared with the PI used in our study [19].

Since most patients in our study were on NSAIDs and DMARDs, we expected less periodontal destruction in these patients. However, higher rate of periodontal disease in this group indicated the great impact of RA on periodontal disease.

Other autoimmune and chronic diseases such as diabetes mellitus and cardiovascular diseases as well as smoking also affect the periodontal status. Thus, these patients were excluded from this study to eliminate the confounding effects of these factors.

However, in our study, we could not completely match the two groups mainly due to the limited number of RA patients and also high number of confounders, which could not be adjusted. Thus, future studies with a larger sample size and ideal matching of case and control groups are recommended to assess the relationship of factors such as rheumatoid factor, erythrocyte sedimentation rate and C-reactive protein, which indicate the severity of disease, with periodontal parameters.

CONCLUSION

Rheumatoid arthritis seems to have the same pathogenesis with the periodontal disease. Due to its destructive nature, it significantly affects the joints. These factors along with patients' inability to follow a precise oral hygiene practice can explain the higher

prevalence and severity of periodontal disease in RA patients.

Our study showed that the relative frequency distribution of clinical periodontal parameters (BOP, CAL, PPD and PI) and the intensity of periodontal disease (ABL and CAL) were higher in RA patients than healthy controls indicating the need for greater preventive and therapeutic measures in this regard for these patients.

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