Association between Rheumatoid Arthritis and Apical Periodontitis: A Cross-sectional Study

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ABSTRACT

Objective: The present cross-sectional study aimed to investigate possible association between Rheumatoid Arthritis (RA) and Apical Periodontitis (AP).

Methods: In table one it is mentioned 48 patients diagnosed with RA were included in the experimental group. Another 48 healthy age- and gender-matched participants who reported no history of any systemic disease were selected to form the control group. All the patients were examined radiographically and clinically to diagnose the presence of AP. The following data was recorded for all patients; the number of teeth present, the number of teeth with AP, the number of patients with AP, the number of patients with root canal treated teeth (RCT) and the number of patients with RCT + AP. The chi-square test and logistic regression analysis were used to determine the possible association between RA and AP.

Results: A total of 1026 teeth were examined in the RA group and 45 of them was diagnosed as AP. In the control group, 1025 teeth were examined and 21 teeth were diagnosed as AP. It was found that the prevalence of teeth with AP (4.3%) was significantly higher in the RA group than the control (2%) (odds ratio [OR]=2.193, P=0.003). Logistic regression analysis showed that RA is significantly associated with AP.

Conclusion: It can be concluded that patients with RA can be more prone to develop AP.

Keywords: Rheumatoid arthritis, apical periodontitis

HIGHLIGHTS

• This is the first study revealed that patients with Rheumatoid Arthritis can be more prone to develop Apical Periodontitis.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common form of inflammatory joint diseases affecting 1% of the world population. It is a chronic inflammatory disorder and is characterized by pain, stiffness, swelling, and progressive joint destruction (1). The exact mechanism of RA is still unknown but it is probably caused by a combination of infectious agents, autoimmunity and genetics (2).

In RA, it is well known that there is a continual expression of cytokines such as tumor necrosis factor α, interleukin-1 and interleukin-6 by macrophages (3). These cytokines may induce bone resorption and play a pro-inflammatory role in apical periodontitis (AP) (4-6). Additionally, it has been revealed that there is a link between increased systemic levels of inflammatory cytokines and AP (7). Although, several studies have revealed an association between RA and periodontitis (8-10), there is no evidence suggesting that there is an association between RA and AP. Previously, Jalali et al (11) conducted a retrospective study and compared the prevalence of periapical rarefying osteitis in the case of RA and control patients. They reported that there was no statistically significant difference between RA and control patients in terms of the prevalence of periapical rarefying osteitis. However, the association between RA and AP is still unclear since the authors evaluated radiographs to diagnose periapical rarefying osteitis, and did not undertake any clinical examination to diagnose AP. Therefore, in the present cross-sectional study, the aim was to investigate a possible association between RA and AP. The null hypothesis was that there would be no association between RA and AP.

MATERIALS AND METHODS

The sample size calculation was performed based on the data of a previous study that evaluated the prevalence of RA and periapical rarefying osteitis (11) with an effect size of 0.1, error of al-
The periapical index (PAI) was used to evaluate the periapical status. The teeth with normal periapical structure or with small changes in bone structure were categorized as healthy (PAI 1 and 2). The teeth with a widened periodontal ligament, periodontitis with a well-defined radiolucent area and/or severe periodontitis with exacerbating features (PAI 3, 4 and 5) were categorized as teeth with periapical pathology (12). The PAI score for multirotted teeth was determined by the highest score of all roots (13).

The chi-square test and logistic regression analysis were used to determine the possible association between RA and AP. The Student t test was used to compare the age variable between the groups. The statistical analysis was conducted using IBM® SPSS® Statistics 20 software (IBM SPSS Inc., Chicago, IL, USA) at a significance level of 5% (P=0.05).

RESULTS

A total of ninety-six patients with 2051 teeth were evaluated (Table 1). A total of 1.026 teeth were examined in the RA group and 45 of them was diagnosed as AP. In the control group, 1.025 teeth were examined and 21 teeth were diagnosed as AP. It was found that the prevalence of teeth with AP (4.3%) was significantly higher in the RA group than in the control group (2%) (odds ratio [OR]=2.193, P=0.003).

Logistic regression analysis showed that RA is significantly associated with AP. The prevalence of AP in at least 1 tooth was higher in the RA group (47.9%) than in the control (29.7%) (OR=3.087, P=0.027). This may indicate that AP is more likely in patients with RA than in the control subjects. At least 1 root canal treated tooth was found in 16 (33.3%) and 20 (41.7%) of

| TABLE 1. Distribution of the analyzed variables in patients with rheumatoid arthritis and control group |
|------------------------------------------------|
| Rheumatoid arthritis | Control | P value | Odds ratio |
|----------------------|---------|---------|------------|
| N                     |         |         |            |
| Patients             | 48      | 48      | -          |            |
| Teeth                | 1026    | 1025    | -          |            |
| Mean age             | 47.69±10.6 | 47.19±10.7 | 0.82      | -          |
| Gender               |         |         |            |
| Female               | 33      | 33      | -          | -          |
| Male                 | 15      | 15      | -          | -          |
| Smoking habit        |         |         |            |
| Present              | 13 (27.1%) | 10 (20.8%) | 0.321      | 1.655      |
| Absent               | 35 (72.9%) | 38 (79.2%) |            |            |
| Number of teeth with AP, n (%) | | | | |
| Present              | 45 (4.3%) | 21 (2%) | 0.003      | 2.193      |
| Absent               | 981 (95.7%) | 1004 (98%) |            |            |
| Patients with AP n (%)|         |         |            |
| Present              | 23 (47.9%) | 14 (29.7%) | 0.027      | 3.087      |
| Absent               | 25 (52.1%) | 34 (70.3%) |            |            |
| Patients with RCT, n (%) |         |         |            |
| Present              | 16 (33.3%) | 20 (41.7%) | 0.538      | 0.733      |
| Absent               | 32 (66.7%) | 38 (58.3%) |            |            |
| Patients with RCT+AP, n (%) | | | | |
| Present              | 5 (10.4%) | 6 (12.5%) | 0.375      | 0.473      |
| Absent               | 43 (89.6%) | 42 (87.5%) |            |            |

Patients with AP; at least 1 tooth with apical periodontitis (Absent/ Present); Patients with RCT; at least 1 root canal treated tooth (Absent/ Present); Patients with RCT+AP; at least 1 root canal treated tooth with apical periodontitis (Absent/ Present). Values in bold indicate statistical significance at P<0.05. AP: Apical periodontitis, RCT: Root canal treated teeth.
RA and control patients, respectively. The prevalence of one or more root canal treated teeth between the RA and the AP groups did not show any statistically significant difference (P>0.05). At least 1 root canal treated tooth with AP was found in 5 (10.4%) and 6 (12.5%) of the RA and the AP patients, respectively. The difference between the groups in terms of the prevalence of one or more root canal treated teeth with AP was not statistically significant (P>0.05). There was no statistically significant association between smoking habits and the presence of AP (P>0.05).

**DISCUSSION**

Literature shows positive relationship between RA and periodontitis (9, 14, 15). Since AP shares similar microbiota and cytokine profiles with chronic periodontitis (16, 17), the present cross-sectional study aimed to evaluate the possible association between the RA and AP. The result of the study showed that there was a statistically significant association between RA and AP. Thus the null hypothesis was rejected.

The RA is characterized by the increased production of proinflammatory cytokines such as interleukin-1, interleukin-6, interleukin-17 and tumor necrosis factor alpha (18). These cytokines are predominant in the pathobiology of both RA and AP. The similar pathobiology of both diseases could explain the significant association between them. Additionally, the progression of both diseases include bone resorption process through the activation of the receptor activator of nuclear factor kB (18). Moreover, it has been reported that there is a positive correlation between the presence of the Immunoglobulin G rheumatoid factor in periapical lesions and rheumatoid disease (19). Another possible explanation is that the drugs used in the treatment of RA have an immunosuppressive effect which makes patients with RA predisposed to AP (20).

Previously, association between RA and periapical rarefying osteitis has been studied, and it has been reported that there is no association between periapical rarefying osteitis and RA (11). This is inconsistent with the result of the present study. This may be attributed to the difference in the methodology of the studies. In the present study, all patients were examined radiographically and clinically to diagnose the presence of AP. In contrast, the previous study used radiographs to diagnose teeth with periapical rarefying osteitis (11). Periapical rarefying osteitis could be associated with the presence of AP. However, without clinical confirmation, a radiographic examination may not be enough to diagnose AP. This is because radiographic changes in cancellous bone cannot be detected until the bone loss reach the cortical plate (21). Thus, in the previous study, it is possible that some of the teeth with periapical rarefying osteitis may not have been diagnosed.

In the present study, there were several confounding factors that may affect the results. Previously it has been reported that health conditions significantly affect the healing of AP (22). Therefore, in the present study, patients without any history of systemic disease except RA were included. Additionally, it is well known that age and gender does not influence the outcome (23). However, to obtain standardization between the groups, an age and gender matched study design was performed. A limitation of the present study could be that, the oral hygiene of the patients that may affect the number of teeth with AP was not evaluated. Previously, it has been reported that the incidence of AP development is higher for patients with periodontal disease compared with patients without periodontal disease (24). Another limitation of the present study was that the quality of root canal filling or coronal restoration were not evaluated. The quality of root canal filling and coronal restoration can influence the outcome of root canal treatment (25). However, according to the result of the present study, there was no significant difference between the groups in terms of the number of patients with RCT+AP. Therefore, the impact of the quality of root canal filling and coronal restoration on the outcome of RCT did not differ for both groups.

**CONCLUSION**

According to the results of the present study, RA is significantly associated with an increased prevalence of AP. Patients with RA can be more prone to develop AP. However, RA did not affect the response to root canal treatment because there was no significant difference between the RA and control groups in terms of RCT teeth with AP.

**Disclosures**

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