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Research Article

Keywords: Rheumatoid Arthritis, Periodontitis, Attachment loss, Tooth loss, Pocket Depth

Posted Date: February 1st, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-149796/v1>

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Comparison of the Periodontal Status in the Patients with Active and Inactive Rheumatoid Arthritis

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Abstract

Introduction: Rheumatoid Arthritis (RA) is the most common chronic inflammatory joint disease. Periodontitis is also an inflammatory disease that affects the periodontal tissue. The former studies have been suggested probable relationship between them.

Objectives: The purpose of this study was to evaluate the relation of severity of Periodontitis and RA activity.

Materials and Methods: In this study 50 patients who referred to the Rheumatology Department of the Khatamolanbia clinic of Yazd considering inclusion criteria were enrolled in the study. After obtaining the informed consent, based on rheumatologic criteria such as Sedimentation (ESR and Clinical features they were divided into two groups; active and inactive RA. Topics were compared based on age, sex, Rheumatoid Factor, Erythrocyte Sedimentation Rate, Hemoglobin Level for RA Bleeding on Probing, Clinical Attachment Loss, Pocket Depth, and Tooth Loss for periodontitis.

Results: The results of this study showed that there was no significant relationship between the variables studied in the active and inactive RA subgroups ($p > 0.05$).

Conclusion: According to the present study while all RA patients show some degree of periodontitis, the periodontitis severity is not correlated with RA activity.

Key Words: Rheumatoid Arthritis, Periodontitis, Attachment loss, Tooth loss, Pocket Depth

Introduction:

Rheumatoid Arthritis (RA) is an autoimmune inflammatory disease that primarily affects the synovial membrane of the joints and is the most common chronic inflammatory joint disease. Moreover, Periodontitis is an inflammatory disease that affects the periodontal tissue and causes periodontal fibers destruction, gingival recession, alveolar bone resorption, packet formation and gingival bleeding, which ultimately results in mobility and loss of teeth [1].

Previous studies have investigated the prevalence of periodontitis in patients with RA and the association between the two diseases is considered possible. Although similarities have been observed in the epidemiology and pathogenesis of these two diseases, less studies have been dealing with the relationship between periodontitis with active or inactive Rheumatoid Arthritis. [1-4] Since in both disease, Rheumatoid Arthritis and Periodontitis, the balance between pro-inflammatory and anti-inflammatory cytokines appears to be impaired; hence, it caused tissue and bone destruction. [2]

Fathi et al. (2018), in a study of the clinical significance of periodontitis in patients with Rheumatoid Arthritis, concluded that periodontitis is common in the patients with RA, especially in early cases, and has a significant association with decreased function and disease activity. [2] Periodontitis, one of the most common oral disease, is a chronic plaque-dependent inflammatory disease that virulence of microorganisms, risk factors and host immune status are important in its development and progression.[3] Gingival diseases are more common in individuals with chronic conditions such as Rheumatoid Arthritis or immunosuppressants medications consumption because of defects in the immune systems. [1]

Rheumatoid Arthritis is the most common chronic inflammatory disease with autoimmune origin, usually involving the small joints of the arms and legs, leading to progressive destruction, deformity, and limited motor mobility of the affected joint. [1]

Since periodontal fibers union the tooth-bone junction as the joint contents, the aim of this study was to compare the severity of periodontitis in patients with active and inactive Rheumatoid Arthritis.

The pathophysiology of chronic periodontitis and RA has some similarities, and in both diseases, extensive degeneration of collagen-rich tissues such as gum, periodontal ligament, bone and cartilage occurs which indicate importance role of matrix metalloproteinases. [4]

Materials and Method:

This study was approved by the Ethics Committee of Semnan University of Medical Sciences. (IR.SEMUMS.REC.1399.193) Written informed consent were obtained from the 50 patients referred to Khatamolambia Rheumatology Clinic of Yazd, Iran. The patients don't have any other

systemic diseases. All methods were conducted in accordance with the ethical standards of the declaration of Helsinki.

Diagnosis of RA

The diagnosis of active rheumatoid arthritis was based on the American College of Rheumatology classification criteria. According to the classification, individuals 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.[5] For each patient the number of swollen joints, number of tender joints, and ESR (erythrocyte sedimentation rate) level were documented. For recording Pain score visual analog scale (VAS) was used, which has 10 scores (0–10) from no pain to the worst possible pain. The disease activity score (DAS28 index) was designed by placing these recorded factors in a specific formula in an automated calculator application. Disease activity in the patients with RA was evaluated by the Disease Activity Score (DAS28).[6] This disease activity index ranges from 0 to 10 and contains a 28 tender-and-swollen joint count, the erythrocyte sedimentation rate (ESR, mm/hour) [7], and the patient's assessment of disease activity measured with a visual analog scale (100 mm). For example, DAS28 <3.2 showed a low disease activity, whereas DAS28 >5.1 meant that disease activity was high.

Diagnosis of periodontitis

Periodontal status was surveyed by a periodontist in order to selecting individuals who had at least 20 teeth and had generalized moderate-to-severe chronic periodontitis. Regarding to 1999 workshop of periodontology, in the generalized periodontitis, more than 30% of sites were involved; its moderate form was considered as the presence of sites with 3–4 mm of attachment loss and severe as the presence of sites with ≥ 5 mm of attachment loss. In order to checking the periodontal status, the probing depth (PD) and bleeding on probing (BOP) were assessed. Oral health conditions were measured using O'Leary plaque index (PI) in all the participants. [8]

Study design

Participant patients based on rheumatologic criteria such as ESR and Clinical features, were divided in active and inactive groups. The first group consisted of individuals with inactive Rheumatoid Arthritis (n = 13), the second one contained 14 new case of active arthritis rheumatoid and the third case group (23 patients) with recurrent active RA. Regarding to Age, they were divided into two groups: below 40 years and over 40 years. Finally, these three groups were

compared based on age, sex, Rheumatoid Factor (RF), Erythrocyte Sedimentation Rate (ESR), Hemoglobin level (Hb), Bleeding on Probing (BOP), Clinical Attachment Loss (CAL), Packet Depth (PD), and Tooth Loss (TL). Demographic data was collected from the records or during interviews; RF, ESR and hemoglobin levels were recorded from patients' blood tests and under the supervision of a rheumatologist. Oral examinations of the patients with RA and of the control group were performed by the same inspector with a manual periodontal probe, and the readings were documented to the nearest 1 mm. All periodontal measurements were assessed at mesio-buccal, disto-buccal, mesiolingual, and disto-lingual aspect of each tooth. Plaque Index was measured based on Silness and Loe[9] and the gingival index (GI) was assessed according to Loe.[10] . PI was calculated from four sites per tooth: 0, absence of plaque on the tooth surface; 1, plaque revealed after running a periodontal probe along the gingival margin; 2, noticeable plaque gathering; and 3, abundance of plaque. GI was calculated from four sites per tooth: 0, complete absence of visual signs of inflammation in the gingiva; 1, minor alteration in gingival color and texture; 2, visual inflammation contained redness, edema, and glazing; bleeding predilection after a probing along the gingival margin; and 3, obvious inflammation as noticeable redness and edema, ulcerations, tendency to spontaneous bleeding. Probing depth (PD) was defined as the distance from the free gingival margin to the bottom of the sulcus or periodontal pocket. Each tooth divided to 4 dental surfaces (mesiobuccally, buccal, distolingual, lingual) to determine areas of bleeding (BOP) by standard Williams probe as bleeding present or absent 10 seconds following probing.[11] The depth of the packet was measured and recorded at 4 levels of each tooth. Furthermore; Clinical attachment loss (CAL) was measured by determining the distance of CEJ to the depth of the packet at the mentioned surfaces. Periodontal disease was defined as a mean CAL >4.0. The number of missing teeth was also recorded. After calculating the mean of each of the above items in each three groups separately, data were entered into SPSS19 software. Then, the data were analyzed and compared by Pearson correlation, Chi-square, Mann-Whitney tests.

Results:

Fifty patients with Rheumatoid Arthritis participated in this study. They were divided into three active, recurrent and inactive groups according to rheumatologist opinion. The first group included patients with inactive Rheumatoid Arthritis (n = 13), the second group of patients with newly diagnosed active Rheumatoid Arthritis (n = 14) and the third group of patients with recurrent active Rheumatoid Arthritis (n = 23).

Topics were also divided into two age groups below 40 and over 40 and were compared based on age, sex, Rheumatoid Factor, Erythrocyte Sedimentation Rate (ESR), Hemoglobin level, Bleeding on Probing (BOP), Loss of Clinical Adhesion. (CAL), Pocket Depth (PD) and Tooth Loss (TL) finally.

3 (23.1%) out of 13 patients with inactive RA were under 40 years and 10 (76.9%) were over 40 years. In the 14-person` active RA group, 4 (28.6%) were under 40 years and 10 (71.4%) were over 40 years, and the patients with active relapsed RA were 23 patients, 9 (39.1%) were under 40 and 14 (60.9%) were over 40 years.

The frequency distribution of age and sex in all three study groups is presented in Table 1.

Table 1: The relationship between age and sex variables with Rheumatoid Arthritis subgroups based on Pearson Chi-square test

Groups	Age		Sex	
	40>	40<	Female	Male
Group1	3(23.1%)	10(76.9%)	2(15.4%)	11(84.6%)
Group2	4(28.6%)	10(71.4%)	2(14.3%)	12(85.7%)
Group3	9(39.1%)	14(60.9%)	1(4.3%)	22(95.7%)
P value	0.58		0.46	

There was no significant difference in age, sex, RF, BOP and hemoglobin between the three groups and the study groups were matched for age and sex (p.value 0.58, 0.46, 0.27, 0.15, 0.81 respectively)

Mann-Whitney test was used to examine the relationship between ESR, AL, PD and TL variables with no significant difference in all three groups (p.value > 0.05). (Table 2).

The results of this study showed that there was no significant relationship between the variables studied including age, sex, Rheumatoid Factor, Erythrocyte Sedimentation Rate (ESR), Hemoglobin level, Bleeding on Probing (BOP), Attachment Loss (AL), Pocket Depth (PD) and Tooth Loss (TL) were not found in three groups ($p > 0.05$).

The only significant assessment was in the Kruskal-Wallis test, with a significant difference in ESR between the three groups ($P = 0.016$), which is noticeable in Table 2.

Table 2: Relationship between Hb, BOP, RF, ESR, TL, PD, AL variables with Rheumatoid Arthritis subgroups.

Group 1 included patients with inactive Rheumatoid Arthritis, group 2 patients with newly diagnosed active Rheumatoid Arthritis, and group 3 patients with recurrent active Rheumatoid Arthritis.

Groups based on age		40<	40>	P value
AL	Group1	3(4.17)	10(7.85)	0.30
	Group2	4(5.50)	10(8.30)	
	Group3	9(10.61)	14(12.89)	
PD	Group1	3(4.00)	10(7.90)	0.63
	Group2	4(6.50)	10(7.90)	
	Group3	9(11.44)	14(12.36)	
TL	Group1	3(5.33)	10(7.50)	0.14
	Group2	4(4.88)	10(8.55)	
	Group3	9(10.22)	14(13.14)	
ESR	Group1	3(33.4)	10(7.80)	0.63
	Group2	4(6.63)	10(7.85)	
	Group3	9(9.33)	14(13.71)	
RF(%)	Group1	5(38.5)	8(61.5)	0.27
	Group2	3(21.4)	11(78.6)	
	Group3	11(47.8)	12(52.2)	
BOP(%)	Group1	6(46.2)	7(53.8)	0.15
	Group2	8(57.1)	6(42.9)	
	Group3	6(26.1)	17(73.9)	

Hb	Group1	13(12.86)	0.81
	Group2	14(12.95)	
	Group3	23(13.16)	

based on Mann-Whitney test

Discussion:

Various studies have emphasized the existence of common genetic factors between these two diseases. [1-4 and 8] In human, the regulator genes of the monocytic cytokine response are located in the HLA-DR region of chromosome 5 in the TNF- β area. This gene is found in the both chronic periodontitis and Rheumatoid Arthritis. [1]

Previous studies have shown that Peptidyl Arginine Deiminase (PAD) is involved in causing autoimmune damage in Rheumatoid Arthritis and is produced by some human cells, such as lung cells, as well as the microorganism, *Porphyromonas gingivalis*, which confirms the association between periodontitis and Rheumatoid Arthritis. On the other hands, it has also been reported [12, 13] the concentration of Anti-Citrullinated Protein Antibody (ACPA) and Rheumatoid Factor (RF) is elevated in the serum of the patients with Rheumatoid Arthritis that affected by chronic periodontitis. [4]

The results of the current study showed that there was no significant difference in age, sex, Rheumatoid Factor, Hemoglobin, Bleeding on Probing, CAL, PD, and TL among the three study groups with Rheumatoid Arthritis. While ESR analysis showed a significant difference that confirms whether RA was active or not among the groups.

Cetinkaya B. et al. (2013) and Silosi I. et al. (2015) measured plaque index, BOP, and CAL in Rheumatoid Arthritis patients and concluded that there was no significant difference between patients and healthy individuals, that was consistent with current study [14, 15]

According to the results of the study of Mercado et al. (2001), RA patients had a high percentage of PD, TL, and AL, and also had a close association between bone loss and inflamed joint with CRP and ESR levels. Therefore, they found the relationship between periodontitis and Rheumatoid Arthritis to be significant. The inconsistency between this study and ours maybe due to different method and sample size [16].

Pischon et al. (2008) examined the association between RA, oral hygiene, and periodontitis in 57 patients with active RA and 57 healthy individuals with regards to the age and sex. Oral status assessment included CAL, PD, GI, PI. On the other hand, risk factors of periodontitis such as smoking, alcohol consumption and BMI, as well as chronic RA-related diseases and periodontitis were assessed through a questionnaire. After reviewing the results, patients with RA had more severe periodontitis than the control group. [17] Finally, they declared that the patients with RA have significantly increased periodontal attachment loss. They concluded that oral hygiene may only partially account for this association. The differences between the conclusions of Pischon' study with ours probably because of differences in the methods of periodontitis assessment.

Dissick et al. (2010) surveyed the relationship between periodontitis and RA in their study. They studied 69 patients with RA and 35 healthy individuals and assessed their PD and panoramic radiographs. They claimed the prevalence of moderate to severe periodontitis in patients with RA were higher than controls, which was unrelated to the age, sex, smoking and diabetes mellitus. [1] This study was consistent with our study about age and sex of RA patients with periodontitis.

Although, Kim et al (2018) found no association between chronic periodontitis and Rheumatoid Arthritis in the Korean population, they concluded that RA was associated with tooth loss in younger adults. In their study 157 out of 20297 participants, had Rheumatoid Arthritis. [12] Their conclusion was similar to our study.

While many studies have emphasized the relationship between these two diseases and found a significant relationship between CAL, PI, BOP and PD [18-21], some studies found no noteworthy relationship between periodontitis and Rheumatoid Arthritis. [14, 15], which may have been due to the small sample size.

Therefore, further studies are needed to confirm the association between these two diseases and it is recommended that future researches will be done into the diagnosis of periodontitis and the presence of serum ACPA and its association with the clinical manifestations of Rheumatoid Arthritis, as well as the relationship between the treatment of periodontitis and the reduction of the risk of Rheumatoid Arthritis with ACPA positive.[4]

Since the data interval is highly dispersed for the gender and BOP variables, and the probability of correlating these variables with others is low; therefore, there is no significant relationship between active and inactive subgroups in the present study and it is suggested that future studies

isolate the variables and also examine them in similar groups to expect a meaningful relationship between them.

To assess the accurate impact of Hb deficiency (anemia) on autoimmune status, anemia should be performed at higher levels (Hb <10) as well as clinically. Also, at levels below 12 it will not have a statistically significant effect. Consequently, Hb <10 must be checked for signification.

Finally, considering the cross-sectional study and its results and also other limitations mentioned, although tooth loss in recurrent active group (23.36%) was higher than inactive group (12.83%), there was no statistically significant difference, so it was not possible to determine whether periodontitis was a factor in activating Rheumatoid Arthritis, but based on results from previous studies and significant systemic problems in Rheumatoid Arthritis patients, such as joint involvement, this Patients do not have the ability to maintain good dental and oral health and they need more timely dental examinations and treatments. Therefore, considering the controversies in previous studies, the purpose of the current study was to compare the severity of periodontitis in patients with active and inactive RA in order to prevent the progression of active RA disease by periodontal control.

Conclusion:

Generally, apart from in the present study all RA patients show some degree of periodontitis, the periodontitis status is not correlated with RA activity significantly. As the oral cavity is an important part of the human and its diseases affect the whole body; therefore, it is appropriate that the RA patients have a regular oral and dental examinations by oral medicine specialist. Furthermore, a close collaboration among physicians and dentists is essential in order to treat patients with RA.

Declarations:

Ethics approval and consent to participate

Informed consent was obtained from all participants. This research project (ref no: IR.SEMUMS.REC.1399.193) was approved by the ethics committee of Semnan University of medical science, Yazd, Iran. All methods were conducted in accordance with the ethical standards of the declaration of Helsinki.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this published article (and its supplementary information files)

Consent for publication: All authors agree for publication this article in BMC Oral Health Journal.

Competing interests: Authors mention that there is no conflict of interest in this study.

Funding: No funding support in this study.

Authors' contributions: F.O designed the study and edited the manuscript. M.J wrote the main manuscript draft and submit the final manuscript. E.K gathered data and Sh.S cooperated in writing manuscript.

Acknowledgements: We would like to express our special thanks to Dr Ali Dehghan, who helped us with useful knowledge and guidance in advancing this study.

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