Inter-Relationship between Rheumatoid Arthritis and Periodontal Disease: A Case Control Study

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Abstract

Background: There are some common similarities in the epidemiology and immunopathogenesis of periodontal disease and rheumatoid arthritis(RA). But the associations between their respective disease activities are less well documented. Hence, the present study was conducted to investigate the prevalence and severity of periodontal disease among RA patients. **Materials and Method:** The study included 40 subjects with RA and 40 healthy controls matched by age and gender. Oral hygiene and Periodontal health was assessed using plaque index (PI), gingival index (GI) and probing depth (PD). The severity of Rheumatoid arthritis was determined by TJC (Tender joints count), SwJC (Swollen joints count),VAS for pain (visual analogue scale), EMS (early morning stiffness), ESR (erythrocyte sedimentation rate),RA factor and DAS28 (disease activity scores). **Results:** Values of PI and GI were significantly higher in subjects with RA compared to control subjects (1.71versus 1.54, $P < 0.05$; 0.51versus 0.37, $P < 0.05$).Significant differences were also found in Pocket probing depth, PD (1.88 mm versus 1.71mm ; $P < 0.05$).These values remain more significant in older age groups. **Conclusion:** Patients with RA have an increased prevalence of periodontitis compared to other non-diseased individuals. Poor manual dexterity along with other parameters may be the potential mediators of this association.

Keywords: Periodontitis, Rheumatoid Arthritis, Oral Hygiene, Plaque Index, Periodontal Pocket.

Introduction

Periodontal disease is a destructive inflammatory disease and is one of the most common chronic disorders of infectious origin caused by specific microorganisms with a prevalence of 10-60% in adults based on the diagnostic criteria.[1] The degree of inflammation varies among different individuals with periodontal disease, independently of the degree of bacterial infection, suggesting that acceleration of immune function may substantially contribute to its extent. Factors such as smoking, education, and body mass index (BMI) are discussed as potential risk factors for periodontal disease.[2–4.]

Rheumatoid arthritis (RA) is a chronic destructive inflammatory autoimmune disease characterized by the accumulation and persistence of an inflammatory infiltrate in the synovial membrane that leads to synovitis and destruction of the joint architecture. About 1%

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of the world population is affected by rheumatoid arthritis and the female/male ratio is 3:1 and has a peak incidence of onset in women in the fourth and fifth decades of life. [5] Infact, Mercado et al reported that incidence of RA in periodontitis patients can be as high as 3.95%.[6]

Similarities exist in the epidemiology and immunopathogenesis of periodontitis and rheumatoid arthritis . Both the diseases are characterized by tissue destruction caused due to chronic inflammation. Proinflammatory cytokines such as tumor necrosis factor-alpha (TNFα) and interleukin (IL)-1, 6 as well as microbial enzymes and host matrix metalloproteinases (MMP-8, 9) appear to play important roles in both conditions. [7]

In addition, RA commonly affects the proximal interphalangeal and metacarpophalangeal joints[8],which may lead to substantial manual disability. Oral hygiene may be impaired in these patients, making them susceptible to plaque accumulation and inflammatory periodontal disease. Recently , it has been suggested that there is mild to moderate association between human periodontal disease and certain systemic disorders such as diabetes mellitus, pneumonia, heart disease and preterm birth and rheumatoid arthritis . But the relationship between periodontitis and rheumatoid arthritis is not clear. There are limited number of studies[9-16] that have examined the periodontal status in subjects with RA . So the present study examined the prevalence and severity of periodontal disease among subjects with RA and healthy controls.

Materials and Method

The study included total 80 subjects, 40 subjects with RA and 40 healthy controls . These patients were selected between the age group of 30 – 70 years and divided into 4 groups based on the age i.e. 31 – 40 years , 41 -50 years, 51 - 60 years , 61 – 70 years and equal no. of patients were kept in each group i.e 10 patients in each age group.

RA patients were selected from the Rheumatoid arthritis centre of the Indian Spinal Injuries Centre Hospital, Delhi. Healthy controls with no evidence of RA were selected from out-patient department of Periodontology & Oral Implantology, ITS Dental College, Ghaziabad.

Inclusion Criteria

RA was diagnosed according to the guidelines given by American Rheumatism Association (ARA)[17, 18]. According to the classification, patients with atleast four of the following seven criteria were included: morning stiffness, arthritis of three or more joint areas, arthritis of hand joints, symmetric arthritis, rheumatoid nodules, serum rheumatoid factor, and radiographic changes.

Exclusion Criteria

- Patients having < 7 teeth were kept excluded.
- Patients with history of periodontal therapy or the use of antibiotic during the last 3 months prior to examination were kept excluded.
- Pregnant and lactating mothers were also kept excluded from this study.

Assessment Of Clinical Rheumatoid Parameters

Disease activity in subjects with RA was assessed by the Disease Activity Score (DAS28)[19].This disease activity index ranges from 0 to 10 and includes a 28 tender-and-swollen joint count, the erythrocyte sedimentation rate (ESR, mm/hour)[20], early morning stiffness (EMS) , Rheumatoid factor

(RF) and the patient's assessment of disease activity measured with a visual analog scale (0 to 100). Also, the Health Assessment Questionnaire (HAQ)[21] score was recorded based on the disability index . HAQ was based on self-reports and assessed the subject's disabilities (e.g., dressing, arising, eating, walking, hygiene, and common activities). The disability index is scored from 0 to 3 :

"0" No assistance needed

"1" Assistance required in few regular activities

"2" Use of an aid or device (cane, walker wheelchair)

"3" Assistance from another person

Intraoral Examination:

Intraoral examination of the subjects with RA and the control subjects were performed by the same examiner for Plaque index , Gingival Index and for pocket probing depth using a manual periodontal probe (Williams periodontal probe). All periodontal measurements were assessed at four sites of each tooth (mesio-buccal, disto-buccal, mesio-lingual, and disto-lingual). The plaque index (PI) was evaluated according to Turesky Gilmore Glickman modification of Quingley Hein plaque index[22] and the gingival index (GI) was assessed according to Loe And Silness[23]. Pocket Probing depth (PD) was defined as the distance from the free gingival margin to the bottom of the sulcus or periodontal pocket.

Statistical Analysis

Frequency distributions, means, and standard deviations were determined to describe the data. Student unpaired t test was used to compare data between the test and control groups. ANOVA test and Post-hoc Comparison - Bonferroni Multiple Comparisons test was used to compare data between different age groups of RA patients. All P values presented are two-tailed, and P values <0.05 were considered statistically significant. Analyses were performed using a statistical program SPSS ver. 14.0.

Results

Subject Distribution

For this study 40 RA patients were compared to an age, gender and socioeconomical status matched group of 40 non – rheumatoid subjects (Control group). The mean age and standard deviation of the subjects in test group was 50.8 ± 11.1 years and for the control group it was 51.1 ± 11.4 years. The test group included 32 females and 8 males , where as the control group included 31 females and 9 males.

Table I. shows the comparison of dental variables between the test group (RA)and control group for Plaque index , Gingival index and Pocket probing depth. PI and GI were significantly higher in subjects with RA compared to control subjects (1.71 ± 0.44 versus 1.54 ± 0.30 , $P<0.05$; 0.51 ± 0.02 versus 0.37 ± 0.19 , $P < 0.05$) . Significant differences were also found in Pocket probing depth, PD (1.88 ± 0.50 mm versus 1.71 ± 0.53 mm ; $P < 0.05$).

Plaque Index, Gingival Index and Pocket Probing Depth were also compared stepwise according to age within the Test Group (Table II, III, and IV) . Though, no statiscally significant difference was found for Plaque index between different age groups, significantly higher gingival inflammation and pocket probing depth was found in patients in the age group of 61-70 years. Tables V and VI show the relationship of rheumatological parameters within different age groups in RA

patients. On comparison it was seen that values for Disease Activity Score (DAS) and Rheumatoid factor (RF) were significantly higher for age group 61 years to 70 years. When relationship of early morning stiffness (EMS), visual analog scale (VAS) and erythrocyte sedimentation rate (ESR) were determined for different age groups , the data remained insignificant for all age groups .

Table I: Comparison of PI, GI, PD between test and control group (* P < 0.05)

	Groups	Number	Mean	S.D.	P value*
PI	**Test (RA)**	40	1.71	0.44	**0.049***
	Control	40	1.54	0.30	
GI	**Test (RA)**	40	0.51	0.23	**0.003***
	Control	40	0.37	0.19	
PD	**Test (RA)**	40	1.88	0.50	**0.004***
	Control	40	1.71	0.53	

Table II. Post-hoc Bonferroni Multiple Comparisons test showing Comparison of Plaque index between different age groups in Test group (* Statistically Significant at P< 0.05)

Dependent Variable	Age	Age	Mean Difference	P value*
PLAQUE INDEX (PI)	31-40 yrs	41-50 yrs	-0.011	1.000
		51-60 yrs	0.103	1.000
		61-70 yrs	-0.214	1.000
	41-50 yrs	31-40 yrs	0.011	1.000
		51-60 yrs	0.114	1.000
		61-70 yrs	-0.203	1.000
	51-60 yrs	31-40 yrs	-0.103	1.000
		41-50 yrs	-0.114	1.000
		61-70 yrs	-0.32	0.755
	61-70 yrs	31-40 yrs	0.214	1.000
		41-50 yrs	0.203	1.000
		51-60 yrs	0.317	0.755

Table III. Post-hoc Bonferroni Multiple Comparisons test showing Comparison of Gingival index between different age groups in Test group (* Statistically Significant at P< 0.05)

Dependent Variable	Age	Age	Mean Difference	P value*
GINGIVAL INDEX (GI)	31-40 yrs	41-50 yrs	-0.18	0.284
		51-60 yrs	-0.13	0.682
		61-70 yrs	-0.45	0.000
	41-50 yrs	31-40 yrs	0.179	0.284
		51-60 yrs	0.053	1.000
		61-70 yrs	-0.270	0.039*
	51-60 yrs	31-40 yrs	0.127	0.682
		41-50 yrs	-0.053	1.000
		61-70 yrs	-0.32	0.003*
	61-70 yrs	31-40 yrs	0.450	0.000*
		41-50 yrs	0.270	0.039*
		51-60 yrs	0.320	0.003*

Table IV : Post-hoc Bonferroni Multiple Comparisons test showing Comparison of Probing depth between different age groups in Test group(* Statistically Significant at P< 0.05)

Dependent Variable	Age	Age	Mean Difference	P value*
Probing depth (PD)	31-40 yrs	41-50 yrs	-0.093	1.000
		51-60 yrs	-0.355	0.090
		61-70 yrs	-1.13	0.000*
	41-50 yrs	31-40 yrs	0.093	1.000
		51-60 yrs	-0.261	0.408
		61-70 yrs	-1.440	0.000*
	51-60 yrs	31-40 yrs	0.355	0.090
		41-50 yrs	0.261	0.408
		61-70 yrs	-0.775	0.000*
	61-70 yrs	31-40 yrs	1.137	0.000*
		41-50 yrs	1.037	0.000*
		51-60 yrs	0.775	0.000*

Table V. Post-hoc Bonferroni Multiple Comparisons test showing Comparison of DAS between different age groups in Test group (* Statistically Significant at P< 0.05)

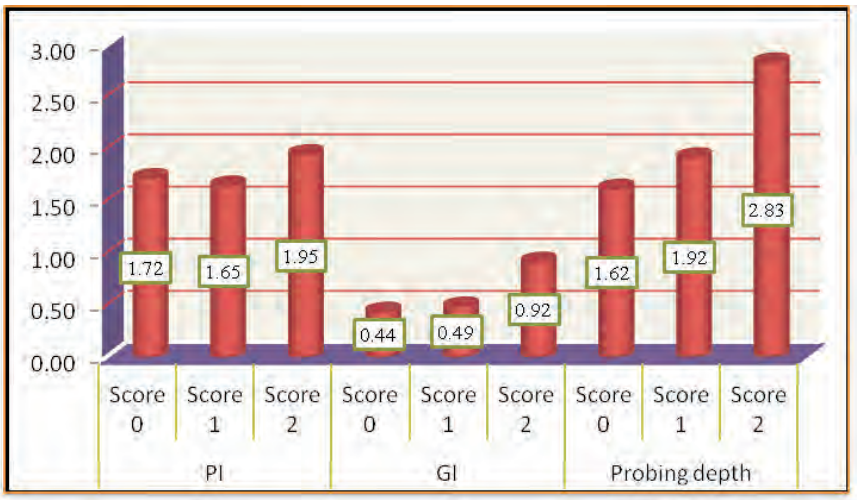
Dependent Variable	Age	Age	Mean Difference	P value*
DAS	31-40 yrs	41-50 yrs	-0.96	0.491
		51-60 yrs	-0.58	1.000
		61-70 yrs	-2.18	0.003*
	41-50 yrs	31-40 yrs	0.96	0.491
		51-60 yrs	0.37	1.000
		61-70 yrs	-1.22	0.023*
	51-60 yrs	31-40 yrs	0.58	1.000
		41-50 yrs	-0.37	1.000
		61-70 yrs	-1.59	0.024*
	61-70 yrs	31-40 yrs	2.18	0.003*
		41-50 yrs	1.22	0.023*
		51-60 yrs	1.59	0.024*

Table VI. Post-hoc Bonferroni Multiple Comparisons test showing Comparison of RF between different age groups in Test group(* Statistically Significant at P< 0.05)

Dependent Variable	Age	Age	Mean Difference	P value*
Rheumatoid factor (RF)	31-40 yrs	41-50 yrs	-28.44	0.329
		51-60 yrs	-25.67	0.317
		61-70 yrs	-76.95	0.000*
	41-50 yrs	31-40 yrs	28.44	0.329
		51-60 yrs	2.78	1.000
		61-70 yrs	-48.51	0.019*
	51-60 yrs	31-40 yrs	25.67	0.317
		41-50 yrs	-2.78	1.000
		61-70 yrs	-51.29	0.004*
	61-70 yrs	31-40 yrs	76.95	0.000*
		41-50 yrs	48.51	0.019*
		51-60 yrs	51.29	0.004*

Also the relationship of the disability index (HAQ scoring) with the PI, GI, PD for test group was evaluated and it was found that patients with higher disability i.e disability index scoring also had higher values for PI , GI and for PD. (Graph I)

Graph I. Relationship of the HAQ scoring with the PI, GI , PD in test group



Discussion

In this study, RA patients had higher prevalence and more severe periodontal disease compared to control subjects. This association was independent of demographic and lifestyle characteristics, including age, gender, education, smoking status and alcohol consumption.

The association between RA and periodontal disease has been examined in a few studies with inconsistent results. Although earlier studies did not find any positive associations of RA with periodontal disease[12, 14, 15], but more recent evidence shows that subjects with RA have higher prevalence of periodontal disease compared to non diseased individuals [9,10,11, 24, 25] which is in agreement with our results.

The mechanisms of alveolar bone destruction in PD and articular surfaces in RA are similar. There is an overproduction of a variety of cytokines and MMPs that appear to be common in both diseases. PD and RA both have persistent high levels of proinflammatory cytokines, including IL-1b and tumor necrosis factor alpha (TNF-α), and low levels of cytokines that suppress the immunoinflammatory response such as IL-10 and transforming growth factor-β (TGF-β). These cytokines, together with low levels of metalloproteinases inhibitors (TIMPs), and high levels of MMPs and prostaglandin E2 (PGE2) are associated with disease activity.[7]

In the present study, a significantly higher value of PI , GI and PD were observed in RA patients compared to the control group. Moreover patients between the age group of 61 to 70 had more severe form of the disease and higher significant values of GI , PI , PD and HAQ score as compared to other age groups . Functional upper limb disabilities in patients with RA contribute to poor manual dexterity with the toothbrush and a lower oral hygiene status and may be an important reason for the results seen in our study. [26]

In this study RA subjects with varying degrees of duration and severity of disease were included. However, among subjects with RA, disease duration and clinical and laboratory parameters of disease severity were not significantly related to PI, GI and PD in most of the age group. Subjects with RA were taking disease- modifying antirheumatic drugs, non-steroidal anti-inflammatory drugs, corticosteroids, and/or tumor necrosis factor-alpha antagonists at the time of the investigation which may mask any potential effect of disease severity on the odds of having periodontal disease.

In older age group poor periodontal status was observed specially in female patients. Menopause occurs in females above 50 years of age. Also the subjects with RA, were on medication such as glucocorticoids, these drugs are a known cause of osteoporosis, and decreased systemic bone mineral density due to osteoporosis might predispose to further bone loss in RA and periodontitis. [27,28]

Conclusion

Periodontitis and Rheumatoid arthritis have many pathological features in common. The present study suggests that patients with RA have an increased prevalence of periodontitis compared to other non-diseased individuals. RA as a chronic inflammatory joint disease has numerous characteristics and pathogenetic similarities to periodontal diseases. However, poor manual dexterity along with other parameters may be the potential mediators of this association. Thus, further studies with larger sample size are required to confirm any

causal relationship between the two diseases.

Acknowledgement

The authors would like to thank Dr. Sanjeev Kapoor, Rheumatologist and Dr. Neeraj Goyal, Orthopaedics, Indian Spinal Injuries Centre for their valuable help and contribution in conducting the study.

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