

Evaluating the association of oral health with quality of life in Ankylosing Spondylitis patients: A case control study

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Abstract

Background: Periodontitis is a chronic inflammatory disease that affects the tissues surrounding the teeth, leading to the destruction of the bone and connective tissue supporting them. The relationship between Ankylosing spondylitis (AS) and periodontitis has been an area of debate in recent studies.

Objectives: According to the recent conflicting studies that have been conducted on the periodontal indicators of patients bearing AS, some have reported the existence of a relationship, and others have reported the absence of a relationship. Considering that there are few studies related to oral and dental health and its relationship with quality of life in AS patients, and the results of the existing studies are controversial, we investigated this issue in the present study.

Methods: This study employed a case-control design. The study participants consisted of 108 individuals, 54 of whom were in the patient group and 54 in the control group, which comprised healthy individuals. The patients were divided into three groups based on the severity of the disease (mild, moderate, severe). The patients were selected from among people referring to dental clinics in Isfahan (Iran) in 2022. Oral health behaviors, clinical attachment loss (CAL), periodontal pocket depth, gingival bleeding on probing, and DMFT index were measured in the studied individuals.

Results: The value of the CPI index was significantly higher in people with severe disease compared to those with mild disease ($p = 0.030$) and healthy cases ($p < 0.001$). The CAL index in individuals with severe disease was significantly higher than in patients with mild disease ($p = 0.011$), moderate disease ($p = 0.047$), and healthy participants ($p < 0.001$). A significant difference was observed in the comparison of the DMFT index between healthy individuals (16.78 ± 4.03) and case groups with mild (16.17 ± 5.61), moderate (12.94 ± 5.72), and severe (17.67 ± 6.45) disease ($p = 0.021$).

Conclusion: AS patients had more serious periodontal conditions than the control group; based on the results, it seems that this serious condition is more tangible in patients with severe disease activity.

Keywords: Gingivitis; Gum disease; Oral health; Periodontitis; Seronegative spondyloarthropathy.

1. Background

Seronegative spondyloarthropathy is a group of rheumatic and joint disorders that include five categories of diseases, namely Ankylosing spondylitis, Psoriatic arthritis,

Inflammatory bowel disease with arthritis, Reactive arthritis, and Undifferentiated spondyloarthritis (1).

Patients suffering from seronegative spondyloarthropathy have common

etiological and clinical indicators, such as axial and peripheral joint inflammation, joint swelling, and extra-articular manifestations. They are also closely related to the presence of the HLA B-27 epitope (2). According to recent studies, ankylosing spondylitis (AS) is the most prevalent among subtypes of seronegative spondyloarthropathy. This chronic, complex, and debilitating disease turns into chronic bilateral sacroiliac joint inflammation within a few years. In these people, the quality of life is very low due to disabilities, back and hip pains, and stiffness of the spine joints (3, 4).

Based on this, it has been demonstrated that the frequency of HLA-B27 in Asian populations, particularly in the Iranian population, ranges from 0.3% to 70%. Therefore, given the close relationship between AS and HLA B-27, the frequency of AS may vary in the Iranian population (5).

There are various methods to measure the severity of the disease and its effect on the patient's function, which are widely used in the study of spondyloarthropathy, especially the Bath AS Disease Activity Index (BASDAI) for measuring the severity of AS, and the AS disease activity score (ASDAS); both of which are measures of disease activity. In these patients, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) also increase (6, 7).

Inflammatory conditions of the gums and supporting tissues cause progressive destruction of the periodontal ligament and alveolar bone in periodontitis. In most cases, gingivitis precedes periodontitis, and gingivitis inflammation occurs only in the gingiva, while periodontitis inflammation extends into the periodontal tissues. Among the primary characteristics of this disease are bleeding gums, bone loss, formation of periodontal pockets, and tissue inflammation. (8).

In epidemiological studies, there are three main criteria for diagnosing

periodontitis: 1) bleeding on probing (BOP), 2) clinical attachment loss (CAL), and 3) pocket depth (PD) (9, 10).

To evaluate oral health conditions, various indicators have been established, including the decayed, missing, and filled teeth (DMFT), CAL, PD, and BOP index. In addition, it is essential to evaluate the patient's behaviors that affect oral health, such as smoking habits, as well as their oral and dental hygiene practices, including the use of toothbrushes and dental floss (11).

The DMFT is an index used to evaluate the overall condition of the teeth in terms of the number of dental caries, filled teeth, and lost teeth due to caries. The DMFT index is one of the simplest and most commonly used indices in epidemiologic surveys of dental caries. It quantifies dental health status based on the number of carious, missing, and filled teeth (12).

2. Objective

According to the recent conflicting studies that have been conducted on the periodontal indicators of patients bearing AS, some have reported the existence of a relationship, and others have reported the absence of a relationship. Considering that there are few studies related to oral and dental health and its relationship with quality of life in AS patients, and the results of the existing studies are controversial, we investigated this issue in the present study.

3. Methods

Selection of patients

This cross-sectional study was conducted in the Azad University of Isfahan branch from January 2022 to December 2022. The patients were selected from among people referring to dental clinics in Isfahan (Iran). The sampling method was convenience sampling. The study participants consisted of 108 individuals, 54 of whom were in the patient group and 54 in the control group,

comprising healthy individuals. The patients were divided into three groups based on the severity of the disease (mild, moderate, severe).

Inclusion and Exclusion criteria

The inclusion criteria included patients with AS who had been diagnosed for at least two years, had a medical record, and were undergoing treatment. The age range was 30 to 60 years in both groups. Exclusion criteria include Patients with a history of taking anticoagulant drugs, completely edentulous patients, patients with a history of recent periodontal surgery, pregnant patients, and patients with underlying diseases.

BASDAI index:

A six-question questionnaire has been designed to evaluate the BASDAI index, and patients score these questions on a scale of 1 to 10. In the next step, the points given by the patient to the questions were checked by the rheumatologist, and he/she determined a score based on the overall assessment of the patient's condition and the treatment process, which was finally the sum of the first four questions plus the average of questions 5 and 6. Dividing by five gives us the final number of the BASDAI index. In this study, patients were divided into three types: silent or mild ($BASDAI < 2$), moderate ($BASDAI > 2$), and severe or active ($BASDAI > 4$) (13).

Clinical examination

The goal of the clinical examinations was to evaluate BOP and periodontal probing depth (PPD). For this purpose, the Community Periodontal Index (CPI) was used. In this index, the dental system is divided into six sextants: 1. Posterior upper right (from tooth 17- 14), 2. Upper incisor (13-23), 3. Posterior upper left (24-27), 4. Posterior lower left (34-37), 5. Lower incisor (33-43), 6. Posterior lower right (44-47), and

the following items are checked:

Code 0: Healthy periodontium

Code 1: Bleeding after gentle probing,

code 2: The presence of calculus (subgingival or supragingival bleeding may or may not be present),

code 3: 4-5 mm periodontal pocket depth

Code 4: 6 mm or more periodontal pocket depth

Code 9: A sextant in which there are no teeth or the number of teeth is less than two.

The WHO has suggested that among adults over 20 years of age, only the teeth numbered 17, 16, 11, 26, 27, 36, 37, 31, 46, and 47 should be examined, and the highest score should be recorded for each one. If there is no teeth index, all the remaining teeth in that sextant should be checked (14-16). Each tooth is examined in the mesial, distal, mid-buccal, and lingual/palatal regions. The force applied to the periodontal probe for examining the periodontium should not be more than 20 grams.

To check the CAL, the dentition was divided into six groups, including 1. Posterior upper right (from tooth 17- 14), 2. Upper incisor (13-23), 3. Posterior upper left (24-27), 4. Posterior lower left (34-37), 5. Lower incisor (33-43), and 6. Posterior lower right (44-47). The results are also interpreted as follows: code 0 indicates no analysis and loss of adhesion, code 1 represents $1\text{mm} > \text{CAL} > 2\text{mm}$, code 2 represents $3\text{mm} > \text{CAL} > 4\text{mm}$, and code 3 represents $\text{CAL} > 5\text{mm}$. The highest score recorded for each quadrant is then averaged.

To evaluate the BOP, the periodontal probe was gently moved laterally in the depth of the pocket, and then bleeding was checked; this was sometimes done immediately after probing and sometimes after a few seconds, during which bleeding from the gums occurred. For this reason,

30-60 seconds after completing the probing of the teeth, bleeding from the gingiva was evaluated.

DMFT index:

To assess the DMFT index, a table was prepared that examined all teeth except the third molars (wisdom teeth). The teeth were scored as follows: decayed teeth were assigned code 1, restored teeth that required replacement or had secondary decay were assigned code 2, and restored teeth were assigned code 3. Missing teeth were scored with code 4, and any crown, implant, bridge, or veneer was scored with code 5. The total number of decayed, filled, and missing teeth was calculated and recorded. All numbers were then added together to obtain the DMFT index. Based on the obtained data, the necessary analysis was performed. It should be noted that the transillumination test was used to detect interdental caries in both the control and case groups, and dental explorers were employed to evaluate the caries on smooth surfaces (Class V) and the occlusal surface.

Statistical Analysis and Sample Size:

The analysis was done on two descriptive and inferential levels. At the descriptive level, frequency distribution tables and mean and standard deviation indices were used to describe the situation of the sample in each of the two groups. At the inferential level, after controlling for the presumption of normality of the data using the Shapiro-Wilk test, if the assumption was established, the one-way ANOVA, along with Bonferroni's post hoc test, was used. Otherwise, the Kruskal-Wallis and Mann-Whitney tests were used. To compare the qualitative variables between patients with different severities of the disease, chi-square or Fisher's exact test was used. Analyses were performed at the 5% error level using SPSS software version 24.

The sample size for comparing different

clinical indicators of oral health among patients with seronegative spondyloarthropathy was categorized by severity into mild, moderate, and severe. To perform a two-sided test, at a significance level of 5% ($\alpha=0.05$), with a test power of 80% ($\beta=0.2$), and to detect a difference at least equal to the standard deviation, was calculated according to the following formula, with 16 cases in each group (severity).

$$n = \frac{2\sigma^2(z_{1-\alpha/2} + z_{1-\beta})^2}{\delta^2} = \frac{2\sigma^2(1.96 + 0.84)^2}{(1.0\sigma)^2} \cong 16$$

N= Sample size

The Z-score equals the standard normal distribution function

α = Equal to the amount of type I error and equal to 0.05

β = Equal to the amount of type II error and equal to 0.2 (1-beta equals the power of the test and is equal to 80 percent)

S= Standard deviation

δ = Equal to the minimum significant difference between the means of two groups, which is considered as accuracy.

4.Result

Demographical information

Eighty patients with AS in a private practice were selected as the cases, and the severity of the disease was determined based on the BASDAI index; the patients were divided into three categories: mild, moderate, and severe. An equal number of patients from each group (mild, moderate, and severe) were included in the study, and 63 people were randomly assigned to the control group.

The mean age was 43.54 ± 9.08 years in patients with AS and 41.91 ± 8.58 years in the control group. The result of the one-way analysis of variance did not show any significant differences in the mean age based on the severity of the disease ($p = 0.792$). Additionally, according to the

independent t-test, the mean age of patients and healthy individuals was not significantly different ($p = 0.340$). The demographic and past medical history variables of the patients in the two groups are summarized in Table 1. Based on the results of the chi-square test, there was no significant difference between patients with mild, moderate, and severe disease severity

in terms of the use of sulfasalazine ($p = 0.054$), Methotrexate ($p = 0.221$), and biological drugs ($p = 0.237$). Additionally, the results of Fisher's exact test revealed no significant difference between the three patient groups in terms of NSAIDs ($p = 0.783$), Prednisolone ($p = 0.916$), and Hydroxychloroquine ($p = 0.099$).

Table 1. Demographic and past medical history variables in the two groups

		Disease Severity			χ^2	F	p-value
		Mild N (%)	Moderate N (%)	Severe N (%)			
Gender	Male	9(50)	9(50)	9(50)	00		1.00
	Female	9(50)	9(50)	9(50)			
Mean age		44.17 ± 8.47	43.28 $\pm$ 9.59	43.17 $\pm$ 9.62		0.347	0.792
Duration of disease		9.94 $\pm$ 5.55	7.44 $\pm$ 5.27	7 $\pm$ 4.54		1.719	
Sulfasalazine	Yes	7(38.9)	14(77.8)	9(50)	3.018		0.054 b*
	No	11(61.1)	4(22.2)	9(50)			
Methotrexate	Yes	9(50)	4(22.2)	7(38.9)	3.018		0.221 b*
	No	9(50)	14(77.8)	11(61.1)			
NSAID	Yes	15(83.3)	13(72.2)	13(72.2)	-		0.783 a*
	No	3(16.7)	5(27.8)	5(27.8)			
Prednisolone	Yes	3(16.7)	5(27.8)	4(22.2)	-		0.916 a*
	No	15(83.3)	13(72.2)	14(77.8)			
Biologic drugs	Yes	10(55.6)	8(44.4)	13(72.2)	2/878		0/273 b*
	No	8(44.4)	10(55.6)	5(27.8)			
Hydroxychloroquine	Yes	0	0	3(16.7)	-		0/099 a*
	No	18(100)	18(100)	15(83.3)			

Calculated based on (a) Fisher's exact and (b) chi-squared test

Evaluation of habits and behaviours between two groups

In the comparison between the case and control groups, a significant difference was observed in the use of toothpaste and the frequency of dental visits. According to the results of Fisher's exact test, favourable behaviour in using toothpaste was significantly higher in healthy individuals compared to patients ($p = 0.031$).

Additionally, the Chi-square test revealed that dental visits were significantly higher among patients with AS ($p = 0.024$). No significant difference was observed between healthy and AS-bearing patients in other oral habits, including brushing teeth ($p = 0.845$), using dental floss ($p = 0.278$), eating sweet snacks ($p = 0.390$), and smoking ($p = 0.588$). (Table 2)

Table 2. Comparison of habits and behaviours affecting oral and dental health between two groups

		Case group N (%)	Control group N (%)	X2	p-value
Teeth brushing	Favourable	31(57.4)	32(59.3)	0.038	0.845 a*
	Unfavourable	23(42.6)	22(40.7)		
Use toothpaste	Favourable	46(85.2)	53(98.1)	-	0.031 b*
	Unfavourable	8(14.8)	1(1.9)		
Use dental floss	Favourable	17(31.5)	12(22.2)	0.278	1.179 s b*
	Unfavourable	37(68.5)	42(77.8)		
Last visit to the dentist	Favourable	23(42.6)	12(22.2)	0.024	5.791 a*
	Unfavourable	31(57.4)	42(77.8)		
Eating sweet snacks	Favourable	41(75.9)	37(68.5)	0.738	0.39 b*
	Unfavourable	13(24.1)	17(31.5)		
smoking	Favourable	45(83.3)	47(87)	0.293	0.588 b*
	Unfavourable	9(16.7)	7(13)		

Calculated based on (a) chi-squared test and (b) Fisher's exact

Evaluation of the DMFT index of research units based on disease severity

A significant difference was observed in the comparison of the DMFT index between healthy individuals and case groups with mild, moderate, and severe disease ($p = 0.021$). The result of the Mann-Whitney post hoc test with the Bonferroni adjustment showed that the DMFT index was significantly higher in healthy individuals

with moderate disease conditions ($p = 0.017$). However, there was no significant difference between individuals with mild and severe disease ($p > 0.05$). (Table 3)

The Mann-Whitney test was used to compare the DMFT index between the two groups. There was no significant difference in the DMFT index between the control and case groups. (Table 3).

Table3. Comparison of the DMFT index of research units based on disease severity

		Min-Max	Median	Mean $\pm$ SD	χ^2	Z	P-value
DMFT index	Mild	4-27	15.5	16.17 $\pm$ 5.61	9.74		0.021 a*
	moderate	4-28	13.5	12.94 $\pm$ 5.72			
	Severe	5-28	16.5	17.67 $\pm$ 6.45			
	Healthy	5-24	17	16.78 $\pm$ 4.03			
DMFT index	Case	4-28	15	15.59 $\pm$ 6.16		-1.625	0.104 b*
	Control	5-24	17	16.78 $\pm$ 4.03			

Calculated based on Kruskal-Wallis test (a) and Mann-Whitney test (b)

The Mann-Whitney test showed that the average number of decayed teeth in the healthy group was (3.77 ± 8.33) more than in the case group (5.24 ± 4.01), and the mean number of missing teeth in the healthy group (1.85 ± 2.29) was less than in

the case group (3.72 ± 4.93). There was no significant difference between the mean number of filled teeth between the case (6.7 ± 5.8) and the healthy group (6.59 ± 4.09) (Figures 1 and 2).

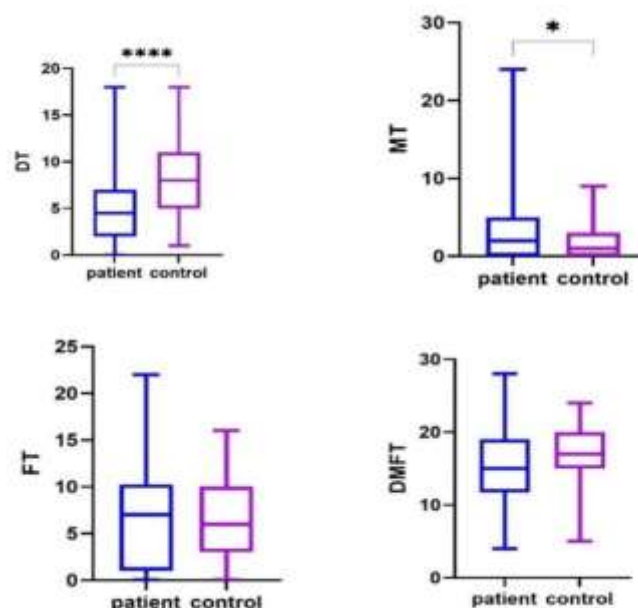


Figure1. DMFT index comparison between research units in the two groups. In each group, the middle line was equal to the median value of observations. Groups with significant differences have been marked with *.

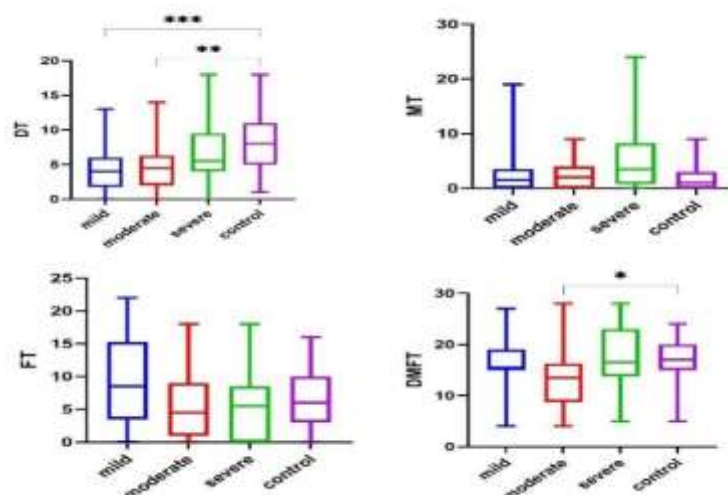


Figure2. Comparison of the DMFT index of research units based on disease severity. In each group, the middle line was equal to the median value of observations. Groups with significant differences have been marked with *

Evaluation of CPI index in research units based on disease severity

Among the participants with severe disease, the most significant percentage (44.4%) had a CPI index of 4 (deep pocket). The result of the Kruskal-Wallis test showed a significant difference between healthy individuals and those with mild, moderate, and severe disease in terms of the CPI index ($p < 0.001$). The result of the Mann-Whitney post hoc test with the Bonferroni adjustment showed that the CPI index in

people with severe and moderate disease ($p = 0.249$), moderate and mild disease ($p = 0.310$), and healthy individuals and mild patients ($p = 0.163$) did not exhibit a significant difference. The value of the CPI index was significantly higher in individuals with severe disease compared to those with mild disease ($p = 0.030$) and healthy individuals ($p < 0.001$). The value of the CPI index for patients with moderate disease was significantly higher than that for healthy participants ($p = 0.008$) (Table 4).

Table 4. Comparison of CPI index in research units based on disease severity

		Disease severity			Healthy N (%)		
		Mild N (%)	Moderate N (%)	Sever N (%)		χ^2	p-value
CPI index	Healthy	0	0	1(5.6)	9(16.7)	19.227	<0.001
	Bleeding	0	0	0	11(20.4)		
	Calculus	13(72.2)	9(50)	4(22.2)	19(35.2)		
	Pocket 4-5mm	4(22.2)	6(33.3)	5(27.8)	10(18.5)		
	Pocket >6mm	1(5.6)	3(16.7)	8(44.4)	5(9.3)		

Evaluation of the BOP index in research units based on disease severity

According to the chi-square test, regarding the BOP index, there was no significant difference between the healthy participants and patients with mild,

moderate, and severe disease conditions ($p = 0.633$). There was also no significant difference between the BOP index of healthy participants and patients. $p=0.214$) (Table 5).

Table5. Comparison of the BOP index in research units based on disease severity

		Case group			Healthy N (%)		
		Mild N (%)	Moderate N (%)	Severe N (%)	N (%)	χ^2	p-value
BOP index	Positive	14(77.8)	13(72.2)	13(72.2)	34(63)	1.717	0.633
	Negative	4(22.2)	5(27.8)	5(27.8)	20(37)		

Calculated based on the Chi-square test

Evaluation of the CAL index in research units based on disease severity

Among the people with severe disease, the most significant percentage of the participants (55.6%) had a CAL index equal to 3 (severe adhesion). The result of the Kruskal-Wallis test showed a significant difference between the healthy group and groups with mild, moderate, and severe disease in terms of CAL index value ($p = 0.001$). The result of the Mann-Whitney post-hoc test with the Bonferroni adjustment showed that the CAL index in people with mild and moderate disease ($p =$

0.567), as well as in healthy people and mild patients ($p = 0.367$) and healthy people and moderate patients ($p = 0.109$), did not reveal a significant difference. The CAL index in individuals with severe disease was significantly higher than in those with mild disease ($p = 0.011$), moderate disease ($p = 0.047$), and healthy participants ($p < 0.001$) (Table 6). The Mann-Whitney test was used to compare the CAL index between the two groups. Based on the results of this test, the CAL index was significantly higher in the case group ($p = 0.002$).

Table 6. Comparison of the CAL index in research units based on disease severity.

		Disease severity			HealthyN(%)	χ^2	p-value
		Mild N (%)	Moderate N (%)	Sever N (%)			
CAL index	Normal	10(55.6)	8(44.4)	5(27.8)	37(68.5)	16.700	<0.001
	Mild	5(27.8)	7(38.9)	3(16.7)	11(20.4)		
	Moderate	2(11.1)	1(5.6)	0	5(9.3)		
	Severe	1(5.6)	2(11.1)	10(55.6)	1(1.9)		

Calculated based on the Kruskal-Wallis test

5. Discussion

Within the limitations of the study, which was the limited access to patients with seronegative spondyloarthropathy due to the low prevalence of this illness, the results of this study on the behaviors affecting oral and dental health showed that visits to the dentist were significantly higher in patients with seronegative spondyloarthropathy. This finding is attributable to the fact that patients are often worried that the disease will become active and out of control after experiencing minor health problems. In other words, the disease conditions have become intertwined with the patient's life, changing their lifestyle. Therefore, patients should undergo regular medical follow-ups to ensure a successful treatment process.

Additionally, the use of toothpaste during brushing was more prevalent in the control group. No significant differences were observed in other oral health habits, such as smoking, consumption of sweet snacks, brushing, and flossing, between the two groups. The results of this study appear to conflict with those of Ziebolz et al., who found that AS patients have poorer oral hygiene than the control group due to movement disorders caused by the disease (17).

Regarding the DMFT index, the results showed that there was no significant difference between the two groups; however, a significant difference was observed among the different severities. This difference between the healthy and patient groups was determined to be

moderate in severity. In another comparison, it was concluded that the number of decayed teeth in the healthy group and the number of missing teeth in the case group were higher. Also, no significant difference was observed in the number of filled teeth between the two groups. It cannot be concluded that the incidence of caries in the control group has necessarily been higher; the cause of this issue can be a greater extent of caries in the patient's group, to the extent that when the patient refers to the dentist for examination, usually, teeth cannot be maintained and must be extracted. A significant amount of caries in AS patients was classified as class 5 caries; this may be due to the change in the composition of the saliva of these individuals compared to the controls, as also mentioned in previous investigations (18).

The results obtained regarding the DMFT index were similar to those of the study conducted by Ziebolz et al. in 2018; however, the number of decayed teeth in the case group was higher compared to the control group, which may be due to cultural and ethnic differences between the two studies (17). Most studies, including those by Helenius et al. and Pischen et al., have reported 3-6 teeth lost in patients.

Among periodontal indices, we used the CPI index. In the comparison between the two groups, we concluded that the CPI index in the patients showed significantly higher codes than in the healthy individuals. This finding was similar to the study by

Helenius et al.; in the cited study, the case group showed significantly more numbers of 3 and 4 in the CPI index than the control group, indicating worse periodontal conditions (18).

In the BOP index, there was no difference between patients in the moderate, severe, and mild groups and the control group. In the comparison between the CAL index in the control and patient groups, it appears that CAL was significantly higher in patients. In comparison to the control, moderate, and mild groups, we demonstrated greater CAL than 5 mm in more areas.

The obtained results were similar to those reported by Bisnaz et al. in 2016. They reported that people with severe disease activity had a significantly worse periodontal condition than the control group (19). There are studies conducted by Pischon et al. and Sezer et al., in which it is pointed out that Disease-modifying antirheumatic drugs (DMARDs), which are used to treat chronic inflammatory diseases, may increase the risk of periodontal disease (20, 21)

In the studies conducted by Soppiah et al., Kang et al., Douglas et al., Schmalz et al., and Helenius et al., a positive relationship was shown between periodontitis and seronegative spondyloarthropathy diseases (17, 18, 22-24). In another study conducted by Bautista et al. and Molano et al. on the Colombian race population, periodontitis was more common in the control group (25).

Additional studies on AS are also needed to determine whether preventive measures and periodontal treatment can control the progression of the disease. If this is proven, periodontal treatment can be a highly effective and cost-effective way to improve and prevent the progression of seronegative spondyloarthropathy.

6. Conclusion

Based on the obtained results, it seems that

AS patients have more serious periodontal conditions than the control group, even though it can be said that this serious situation is more tangible in patients with severe disease activity. It is important for patients with AS to undergo a dental examination; it can be recommended to patients by rheumatologists. They should undergo a periodontal evaluation and examination, as they may have a greater risk of developing periodontitis. Both diseases can significantly impact a person's quality of life. A crucial factor to consider is the degree to which AS and PD impact the patient's quality of life. Furthermore, it appears that a collaborative approach between rheumatologists and dentists is necessary for managing AS to determine whether routine periodontal treatments can modulate disease activity by reducing cytokines and pro-inflammatory factors.

However, the role of different AS-related parameters, periodontal health conditions, and their relationship seems unclear, and further investigations on larger populations are demanded to elucidate their connection. Additionally, it is recommended to conduct studies using a periodontal treatment approach to evaluate whether these treatments can alleviate the disease's activity.

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committee of Isfahan University of Medical Sciences (IR.IAU.KHUISF.REC.1401.038) and the 1964 Helsinki Declaration. Written informed consent was secured from all participants.

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