#### **OBSERVATIONAL RESEARCH**





# Temporomandibular disorders in ankylosing spondylitis: a cross-sectional, monocentric study

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#### Abstract

There are contradictory results in the relevant literature about the relationship between objective determinants of craniocervical posture and temporomandibular disorder (TMD), whereas no study has worked on ankylosing spondylitis (AS) and TMD relationship. We conducted this study to test the predictors of TMD in AS patients and its relationship with craniocervical posture. AS patients aged between 18 and 50 years consecutively admitted to our outpatient clinics were recruited. TMD was diagnosed by 'Diagnostic Criteria for Temporomandibular Disorders (DC/TMD)'. Spinal mobility was assessed by BASMI; disease activity by ASDAS-CRP and neck disability by Neck Disability Index. Craniocervical posture was assessed on lateral cervical X-ray by measuring the craniocervical angle, cervical curvature angle, suboccipital distance, atlas–axis distance, and anterior translation distance. A total of 98 (58.2% female) patients with a mean age of  $37.4\pm8.2$  years were enrolled in this study. TMD was diagnosed in 58 (59.2%) patients. Spinal mobility and craniocervical posture measurements were similar among the two groups. Smoking, bruxism (in females), neck disability and AS disease activity (in males) were higher in TMD patients. Multivariate analysis revealed active smoking (aOR 6.9; 95% CI 1.8–25.6; p=0.004), bruxism in females (aOR 17.9; 95% CI 3.8–42.9; p < 0.001) as independent risk factors for TMD in AS patients. No relationship between the craniocervical posture measurements and TMD was found in AS patients. Active smoking, high disease activity in males, bruxism in females and neck disability were found as predictors of TMD in AS patients.

Keywords Temporomandibular disorders · Ankylosing spondylitis · Craniocervical posture · Disease activity

## Introduction

Temporomandibular disorders (TMD) are one of the most important public health problems which affect approximately 5–12% of the overall population. Temporomandibular disorders are a group of musculoskeletal problems that principally originated from temporomandibular joint (TMJ), masticatory muscles and neighbouring tissues [1]. Pain, crepitation, click, and locking are the most common symptoms. Trauma, para-functional habits, stress, bruxism, and malocclusion are potential risk factors for the development of TMD [2].

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<sup>1</sup> Department of Physical Medicine and Rehabilitation, Faculty of Medicine, Hacettepe University, Ankara, Turkey Ankylosing spondylitis (AS), commonly seen in males, is characterized by inflammatory back pain. It primarily involves sacroiliac joints and spine, less commonly peripheral joints may be affected. According to very little data, the prevalence of TMD is 4–35% in AS patients [3–5]. Although the underlying mechanisms are poorly defined, primary synovial involvement of TMJ, destruction of joint capsule or components of the disc, and postural changes related to AS have been postulated as possible mechanisms [5, 6].

Several studies proposed a relationship between craniocervical postural changes and TMD [7–9]. Projected mechanism of this association is that the distorted craniocervical posture may change the position of the chin by affecting surrounding muscle and tendons and resulting pressure overload on TMJ leading to TMD [10]. Contrarily, there are also some findings indicating no relation between craniocervical posture and TMD [11–13]. Cervical kyphosis is the most common cervical deformity in AS patients and causes headforward position. To the best of our knowledge, no data has

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The aims of this study are to determine the frequency of TMD in a group of AS patients, and to test whether there is a relationship between craniocervical posture and TMD and to determine the risk factors for the development of TMD in AS patients.

# **Patients and methods**

## **Patient enrollment**

In this cross-sectional observational study, we enrolled AS patients who consecutively admitted to the Departments of Physical Medicine and Rehabilitation and Rheumatology, Hacettepe University, Ankara, Turkey between September 2018 and April 2019. The patients with a diagnosis of AS according to the modified New York criteria [14] and aged between 18 and 50 years were included in this study. Modified New York criteria are the combination of 1 clinical component with the radiographic sacroiliitis. Clinical components are low back pain and stiffness which improves with activity for more than three months, limited range of motion of the lumbar spine in both forward and lateral bending and limitation of chest expansion relative to normal values correlated for age and sex. Radiographic criteria were the at least bilateral grade 2 sacroiliitis or unilateral at least grade 3 sacroiliitis [14]. Diagnosis of each patient was confirmed by UK and OO, independent of each other. The exclusion criteria were as follows: patients with neurological or cognitive deficits, presence of active dental or periodontal pain, history of orthodontic treatment, history of tumor, surgery, radiotherapy or trauma to head and neck region. Local Ethics Committee (Hacettepe University-GO 18/755, Date: 24 July 2018) approved the study protocol, and the written informed consents were obtained from all patients.

The diagnosis of TMD has been established according to the Diagnostic Criteria for Temporomandibular Disorders (DC/TMD) which is the most recent criteria set published in 2016 [15]. The study population was divided into two main groups: TMD (+) and (-) groups. Demographic, clinical and radiographical parameters were compared between two groups.

#### **Clinical assessment**

Demographic and clinical features including age, gender, smoking history, comorbidities confirmed by both medical records and patient interviews, AS disease duration, current medications and presence of self-reported bruxism were recorded. Ankylosing Spondylitis Disease Activity Score-C-reactive protein (ASDAS-CRP) was used to assess AS disease activity. Cut-off values of ASDAS-CRP score for inactive, low, and high/very high disease activity were 1.3, 2.1 and 3.5, respectively [16].

To assess spinal mobility; chin–sternum distance (measured according to ASAS) and the components of Bath Ankylosing Spondylitis Metrology Index (BASMI) score (lateral spinal flexion, tragus–wall distance, modified Schober test, maximal intermalleolar distance, and cervical rotation angle) were measured [17].

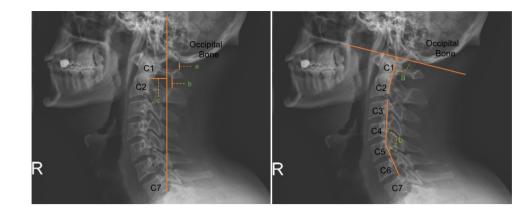
The Turkish version of Neck disability index (NDI) was used to assess how much does the neck pain affect the patients' daily activities of living. This index is composed of ten questions with a maximum score of 50. Zero to four points indicate no disability, 5–14 points indicate mild disability, 15–24 points indicate moderate disability, 25–34 points indicate severe disability and 35–50 points indicate complete disability [18].

### **Radiological assessment**

Craniocervical posture was assessed by measuring suboccipital, atlantoaxial and anterior translation distances (in millimeter), craniocervical and cervical curvature angle on lateral cervical X-ray which was taken while the patient was standing up, holding his or her head high and shoulders low. All these measurements were performed by the same researcher blinded to the patients' clinical data. In accordance with previous studies, radiographic measurements were defined as follows: suboccipital distance (in millimeter); vertical distance between the base of occipital bone and posterosuperior point of first vertebrae, atlantoaxial distance (in millimeter); vertical distance between the most inferoposterior point of posterior arch of atlas and the most posterosuperior point of the spinous process of axis, anterior translation distance (in millimeter); horizontal distance between the vertical line passing by the superoposterior point of C2 vertebral body and vertical line passing by the posteroinferior point of C7 vertebral body, craniocervical angle; the angle between the McGregor plane and the line tangential to the backside of the odontoid apophysis, cervical curvature angle; the angle between the straight lines passing on the posterior borders of body of third and sixth vertebrae (Fig. 1a, b) [7, 8, 10]. Also, modified Stoke AS spine score (mSASSS) was calculated to compare the degree of spinal involvement of AS [19].

#### Sample size

We calculated the sample size based on the primary objective of the study. With the assumption that the rate of TMD is 10% in general population, we hypothesized the rate of Fig. 1 For the assessment of cranicervical posture; suboccipital distance  $(\mathbf{A}(a))$ , atlanto-axial distance  $(\mathbf{A}(b))$  anterior translation distance  $(\mathbf{A}(c))$ , craniocervical angle  $(\mathbf{B}(a))$ , and cervical curvature angle  $(\mathbf{B}(b))$  were measured on standardized lateral X-rays



TMD in AS as 20% in light of the previous studies [3, 5, 20, 21]. We used G power 3.1 computerized system with type 1 error of 0.05 and type 2 error of 0.20. At least 78 patients were needed to test our hypothesis.

#### **Statistical analysis**

The variables were investigated using visual (histogram, probability plots) and analytic methods (Kolmogorov-Smirnov, skewness and kurtosis) to determine whether they are normally distributed. The data of descriptive analysis were expressed as either mean  $\pm$  standard deviation (SD) or the median (interquartile range). Categorical variables were compared with the Chi-square test or Fisher's exact test where appropriate. The Student's t test was used to compare the normally distributed continuous data between two groups, Mann-Whitney U test was used to compare the non-normally distributed continuous data between two groups. For multivariate analysis, univariate analyses with a p value lower than 0.20 and detected interactions (effect modifications) were entered firstly with "Backward LR", then "Enter" for the final model to determine independent predictors of TMD development in AS patients. Hosmer-Lemeshow goodness-of-fit statistics were used to assess model fit. A 5% Type-I error level was used to infer statistical significance. Statistical analysis was performed using the Statistical Package for the Social Sciences software (version 23.0; IBM Corporation, Armonk, NY, USA).

## Results

## Study population

We recruited a total of 98 consecutive AS patients with a mean age of  $37.4 \pm 8.2$  years. Fifty-seven (58.2%) of them were female and 33.7% were active smokers. Approximately 45% of the patients had at least one concomitant disease, the most common ones were familial Mediterranean fever

(13 patients, 13.2%) and hypertension (11 patients, 11.2%). The mean duration of AS disease was  $8.1 \pm 5.7$  years. Self-reported bruxism was present in 61 (62.2%) of all patients.

Of 98 patients, the diagnosis of TMD has been established in 58 (59.2%) patients (TMD (+) group). Age, gender, presence of comorbidities, AS disease duration, current AS treatment were similar between TMD (+) and (-) groups. The percent of active smokers (43.1% vs. 20.0%) and self-reported bruxism (74.1% vs. 45.0%) were significantly higher in TMD (+) group (p = 0.017 and 0.003, respectively). When the interaction between gender and bruxism was investigated, it has been found that there was no significant difference in the presence of TMD whether the patients had bruxism or not (56.0% vs. 37.5%, p = 0.24) in males, however TMD was more prevalent in patients with bruxism (80.6% vs. 42.9%, p = 0.004) in females.

Details of the demographic and clinical features of the study population are given in Table 1.

## Measurements related to ankylosing spondylitis and craniocervical posture

Tragus–wall distance, cervical rotation, chin–sternum distance, BASMI, and mSASSS were similar in both groups. ASDAS-CRP was significantly higher in TMD (+) group [2.9 (2.0–3.2) vs. 1.9 (1.4–2.5), p < 0.001, respectively (Table 2); rate of high-very high ASDAS-CRP: 70.5% vs. 29.5%, p=0.003, in TMD (+) and (–) groups, respectively]. An interaction between gender and AS disease activity was found. While TMD was more frequent in male patients with higher disease activity (high-very high ASDAS vs low-inactive ASDAS; 73.7% vs. 27.3%, p=0.005), the frequency of TMD was similar in female patients with high-very high ASDAS or low-inactive ASDAS AS (69.0% vs. 60.0%, p=0.52).

No significant difference in the radiographic measurements of craniocervical posture were found between TMD (+) and (-) groups (Table 2).

Table 1The clinical anddemographical data of the studypopulation

Table 2Comparison ofAS-related and craniocervicalpostural assessments

Parameter	TMD $(+)$ $(n=58)$	TMD $(-)$ $(n=40)$	p value
Gender (female) <sup>a</sup>	38 (65.5)	19 (47.5)	0.076
Age <sup>b</sup>	40 (11)	38 (14)	0.60
Smoking <sup>a</sup> Smoker Non-smoker	25 (43.1) 33 (56.9)	8 (20.0) 32 (80.0)	0.017
$\begin{array}{l} Comorbidity^{a} \\ \geq 1 \\ 0 \end{array}$	29 (50.0) 29 (50.0)	15 (37.5) 25 (62.5)	0.22
AS disease duration (year) <sup>b</sup>	6.5 (8)	8.0 (6)	0.46
AS treatment <sup>a</sup> NSAID Regular On-demand Sulphasalazine Anti-TNF agents	8 (13.8) 31 (53.4) 24 (41.4) 33 (56.9)	5 (12.5) 18 (45.0) 14 (35.0) 26 (65.0)	0.52 0.67 0.42
Bruxism <sup>a</sup> Present Nighttime Daytime Whole day Absent	43 (74.1) 11 (25.6) 10 (23.3) 22 (51.2) 15 (25.9)	18 (45.0) 7 (38.9) 5 (27.8) 6 (33.3) 22 (55.0)	0.003

Anti-TNF anti-tumor necrosis factor, AS ankylosing spondylitis, NSAID nonsteroidal anti-inflammatory drugs

<sup>a</sup>n (%); Chi-square was used for comparison

<sup>b</sup>Median (IQR); Mann–Whitney U test was used for comparison

Parameter	TMD $(+)$ $(n=58)$	TMD $(-)$ $(n = 40)$	p value**
AS-related measurements			
ASDAS	2.9 (1.2)	1.9 (1.1)	< 0.001
Male	2.5 (1.5)	1.5 (0.7)	0.004
Female	3.0 (0.7)	2.4 (0.9)	0.19
Tragus-wall distance (cm)	11 (1.0)	11 (1.25)	0.70
Cervical rotation (angle)	75 (10.0)	75 (10.0)	0.75
Chin-thorax distance (cm)	2.0 (2.0)	2.0 (2.0)	0.50
BASMI	1.8 (1.2)	1.6 (0.8)	0.93
mSASSS	2.0 (4.0)	2.0 (4.0)	0.99
Measurements of craniocervical posture			
Craniocervical angle	79 (16.0)	82 (13.0)	0.34
Cervical curvature angle	165 (21.0)	166 (17.0)	0.99
Suboccipital distance (mm)	5.7 (6.0)	6.1 (6.0)	0.56
Atlas-axis distance (mm)	5.0 (3.7)	5.0 (3.6)	0.62
Anterior translation distance (mm)	12.3(18.4)	8.5 (19.6)	0.27
Neck disability index $(n, \%)$			< 0.001
No disability	9 (15.5)	24 (60.0)	
Mild to severe disability	49 (84.5)	16 (40.0)	

AS ankylosing spondylitis, ASDAS Ankylosing Spondylitis Disease Activity Score, BASMI Bath Ankylosing Spondylitis Metrology Index, mSASSS Modified Stoke AS Spine Score, mm millimeter

p values in bold indicate statistical significance

Data presented as median (IQR), otherwise specified

\*\*Mann-Whitney U

Neck disability was more prevalent in TMD (+) group when compared to TMD (-) group (84.5% to 40.0%, p < 0.001). In TMD (+) group; 32 (55.2%), 12 (20.7%) and 5 (8.6%) patients had mild, moderate and severe disability, respectively. However, in the TMD (-) group; 16 (40%) patients had a mild disability, none of them had moderate or severe disability (Table 2).

#### Univariate and multivariate analyses

A multivariate logistic regression analysis was performed to determine the independent effects of each parameter which had been determined by univariate analyses including gender, smoking, presence of self-reported bruxism, high ASDAS and presence of neck disability. As interactions were found between gender and bruxism and also between gender and high ASDAS, we included the following parameters to multivariate analysis: gender, smoking status, presence of bruxism and interaction of bruxism and gender, high ASDAS and interaction of high ASDAS and gender, and presence of neck disability.

As shown in Table 3, final multivariate analysis revealed active smoking (aOR 6.9; 95% CI 1.8–25.6; p = 0.004), presence of bruxism in females (aOR 17.9; 95% CI 2.0–159.2; p = 0.01), high ASDAS in males (aOR 11.8; 95% CI 1.2–122.5; p = 0.038), and presence of neck disability (aOR 12.7; 95% CI 3.8–42.9; p < 0.001) as independent risk factors for TMD in AS patients. Model fit was tested by Hosmer–Lemeshow test (p = 0.55).

## Discussion

In this study, active smoking, high disease activity in males, bruxism in females and neck disability were found as predictors of TMD in AS patients, also we did not find any relationship between the objective determinants (measurements) of craniocervical posture and TMD in AS patients. In current literature, there are case reports related to TMJ involvement in AS [5, 20] and a few cross-sectional studies giving data about TMD symptoms in AS patients [3, 4].

The prevalence of TMD varies between studies due to the differences in study populations and the diagnostic criteria. In previous population-based studies, the prevalence of TMD was found to be between 5 and 12% [21–24]. Data related to TMD in AS patients are very little and the frequency of TMD in these patients has been reported as 4 to 37% [3–5, 24–27]. However, standardized diagnostic criteria set for TMD was applied in none of these studies. In a study by Helenius and colleagues, 37% of AS patients reported TMD symptoms including tenderness of masticatory muscles, tenderness, clicking and crepitation of TMJ and this rate was higher than the rates in rheumatoid arthritis (RA)

Variables	Univê	Univariate analyses		Multivariate analyses (initial model)	alyses (initial n	nodel)	Multivariate	Multivariate analyses (final model)	model)
	OR	95% CI $p$ value	<i>p</i> value	Adjusted OR 95% CI	95% CI	<i>p</i> value	Adjusted OR	95% CI <i>p</i> value	<i>p</i> value
Female gender	2.1	0.9-4.8	0.076	1.4	0.4-4.9	0.57			
Active smoking	3.0	1.9–7.7	0.017	4.3	1.2-15.1	0.024	6.9	1.8 - 25.6	0.004
Bruxism	3.5	1.1 - 8.3	0.003	1.9	0.6 - 5.5	0.24			
Bruxism (in females)	5.5	1.7-18.2	0.004	8.3	1.05-72.8	0.05	17.9	2.0-159.2	0.010
High/very high ASDAS-CRP	3.5	1.5 - 8.2	0.003	2.6	0.9–7.8	0.08	2.6	0.9–7.8	0.075
High/very high ASDAS-CRP (in males)	7.5	1.7-29.8	0.005	9.7	1.1 - 90.7	0.047	11.8	1.2-122.5	0.038
Neck disability	8.2	3.1-21.1	< 0.001	11.4	3.2-40.6	< 0.001	12.7	3.8-42.9	< 0.001

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p values in bold indicate statistical significance

and mixed connective tissue disease patients enrolled in this study [3]. Locher et al. reported the frequency of radiographical involvement of TMJ as 22% in 50 AS patients [25]. In another study including 79 patients with various rheumatic diseases (39 with RA, 17 with AS, 23 with Sjögren's syndrome), the frequency of subjective TMD symptoms reported by AS patients was 76.5% and this rate was significantly higher than healthy controls [4]. We found that 59.2% of our patients have TMD and this prevalence is higher than the general population.

Conflicting data are available about the relationship between the craniocervical posture changes and TMD. While a bunch of studies confirms the possible linkage [8, 9, 28, 29], others deny [11-13]. In a study comparing 32 TMD patients with 34 healthy controls, it has been reported that cervical curvature angle was higher in patients with muscle disorders, and atlantoaxial distance was higher in patients with disc displacement [7]. However; in a recent study conducted with 30 female TMD patients and 30 healthy controls, the craniocervical angles and atlantoaxial distances were found to be similar [30]. Overall, a recent review concluded that due to the methodological inadequacy and scantiness of relevant data, it is impossible to either approve or reject any relationship between craniocervical posture changes and TMD [31]. In our study, we found no significant association between the measurements of craniocervical posture and TMD in AS patients. To the best of our knowledge, this is the first study investigating the relationship between craniocervical posture and TMD diagnosed according to DC/TMD criteria set in patients with AS.

Age, gender, disease duration and medications were similar for TMD (+) and (-) groups. The frequency of active smoking, presence of bruxism (in females), AS disease activity (in males) and neck disability were significantly higher in TMD (+) group. As gender interacted with disease activity and bruxism, we analyzed these parameters according to gender.

As an oral para-functional habit, smoking has been proposed as an independent risk factor for the development of TMD [32, 33]. Sanders et al. reported approximately four-fold increase in TMD occurrence, the increase was substantially higher in young smokers—a similar age group to our study [32]. Smoking-related inflammation, especially by interleukin-1 and macrophage chemoattractant protein-1, and nicotine-related hyperalgesia has been suggested as the potential mechanisms of this association [34, 35]. In our study, we found an approximately sevenfold increase in the risk of TMD in AS patients who are active smokers.

Another para-functional habit, bruxism has been largely studied in TMD patients. In a well-designed study from Brazil, the rate of bruxism was found as 52% in TMD patients and bruxism-related TMD risk was reported as twofold. However, they reported no gender difference [36]. In our study, we found an approximately 18-fold increase in the risk of TMD occurrence in female AS patients who have bruxism. However, the confidence interval is large and this could be mediated by the high discordance of the bruxism rate between two groups. Although we found a strong relationship, numbers should be interpreted cautiously.

According to the results of our study, high AS disease activity, especially in men, was defined as a risk factor for the development of TMD in AS patients for the first time in literature. There is no other study trying to explain this association. However, in our results, ASDAS-CRP levels were higher in females. But females with and without TMD both had high ASDAS-CRP levels. This may explain why the disease activity was not found as a strong factor statistically predicting TMD in females. To explain higher disease activity in females compared to males, we also analyzed the TNF use, comorbidities and other possible factors, but no relevant factor was found. Limitations of ASDAS-CRP, psychosocial factors may be counted as reasons but all need to be verified with prospective studies. Although biologic DMARD utilization was similar in males and females, we did not exactly determine how long they are on these treatments and about their treatment compliance. On the other hand, we found no association between tragus-wall, chin-thorax distances and cervical rotation and indicators of structural damage like BASMI and mSASSS with TMD. Therefore, we may speculate that the relationship between AS and TMD is based on the inflammation rather than the mechanical and postural changes. Also, prospective studies are needed to see whether suppressing the disease activity also heals TMD or not to elucidate the relationship between disease activity and TMD.

Furthermore, we found that neck disability is a strong and reliable factor for predicting TMD in AS patients. Silveria et al. reported that the score of NDI was significantly higher in 20 TMD patients compared to 20 healthy controls. Thus, they stated that the assessment of neck dysfunction should be considered in the diagnosis and treatment of TMD [37]. Another study with 154 patients, a strong correlation as 82% was found between TMD and NDI [38]. In addition, manual therapy for TMD resulted in significant improvement of NDI [39]. Similar to bruxism, the confidence interval is large, and this is because of the high discordance of the neck disability between two groups, thus numbers should be interpreted cautiously. Further studies are needed to test the availability and validity of NDI score for TMD assessment in AS patients.

Our study has some limitations and strengths. About 60% of our study group comprises females, this may be unusual when we consider the high prevalence of AS in males. This issue may be seen as a selection bias. However, during recruitment period, we asked all AS patients who consecutively applied to our departments to take part in the study,

not all of them agreed. So, we did not select patients, we "enrolled" the "voluntary patients" and females volunteered to participated more. In fact, this situation could result from referral center bias. As a tertiary center, our patient profile is different from regular population. Because of referral bias, there seems an accumulation on female gender and this may create a selection bias-like picture. As the overlapping high frequency and discordance of predicting factors in TMD (+) patients compared to (-) patients and selection bias could explain the large confidence intervals. To overcome this bias, we have checked all possible modifier effects of gender and included the relevant interactions to the final model. Secondly, a control group would have strengthened our results. On the other hand, blinded assessment of lateral X-rays and being the first study that applied the most recent TMD diagnostic criteria to AS patients may be counted as strong aspects of this study.

In conclusion, we found a high prevalence of TMD in AS patients. Clinicians should assess for TMD in AS patients during routine daily practice. We found active smoking, high disease activity in males, bruxism in females and neck disability as predictors of TMD in AS patients. No relationship between the objective determinants (measurements) of craniocervical posture and TMD in AS patients was found. Gender seems to have a role, and our results should be interpreted gender-selectively. Further studies with higher number of patients are needed to elucidate the possible underlying mechanisms that favor TMD development in AS patients.

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