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Cervical spine instability in axial spondyloarthritis: prevalence, patterns, and predictive factors in a high-risk cohort

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Objective: Although axial spondyloarthritis (axSpA) is an inflammatory disease primarily affecting the spine, studies investigating cervical spine instability (CSI) are limited, and no research has comprehensively evaluated all forms of CSI. This study aimed to determine the frequency and associated factors of CSI in axSpA patients.

Method: This retrospective cross-sectional study, conducted in a single tertiary rheumatology unit, included adult axSpA patients with inflammatory back pain duration of > 10 years and receiving biological or targeted synthetic therapy. Patients with any concomitant disease that could affect the spine were excluded. CSI lesions were assessed using lateral neutral, full extension, full flexion, and open-mouth anteroposterior cervical radiographs. Radiographs were evaluated by two blinded rheumatologists.

Results: In total, 159 axSpA cases (ankylosing spondylitis: 89.3%; non-radiographic axSpA: 10.7%) were included in the study; 57.9% were male, mean age was 47 years, and mean disease duration was 17 years. A total of 33 CSI lesions was detected in 31 patients (19.5%); the most common was anterior atlantoaxial subluxation (54.5%), followed by subaxial (33.3%) and vertical subluxation (6.1%). In univariate logistic regression analysis; disease duration ($p = 0.004$), age at first symptom ($p = 0.02$), uveitis ($p = 0.049$), and sacroiliitis stage ($p = 0.039$) were associated with CSI. In multivariate analysis, disease duration was identified as a potential independent predictor of CSI ($p = 0.027$).

Conclusion: These results highlight the need for increased clinical awareness of CSI in axSpA, and support consideration of cervical imaging in patients with prolonged disease duration, severe sacroiliitis, or uveitis.

Axial spondyloarthritis (axSpA) is a group of chronic, inflammatory rheumatic diseases that primarily affect the spine and sacroiliac joints, typically beginning in the third decade of life. This disease spectrum includes the subtypes ankylosing spondylitis (AS: radiographic axSpA) and non-radiographic axial spondyloarthritis (nr-axSpA). AS is the prototype disease of this group, with a prevalence of 0.5% and occurring three times more frequently in men. The prevalence of nr-axSpA ranges between 0.32% and 1.4%, and it is seen equally in both sexes (1). Although all segments of the spine can be affected in cases of AS, cervical vertebra involvement is more frequently observed in patients with symptomatic and structural damage (2).

One of the most prominent and consistent clinical features of the disease is slowly progressing spinal inflammation. axSpA can lead to direct vertebral lesions such as spondylitis, spondylodiscitis, and facet joint arthritis in the spine, as well as ossification of the spinal ligaments. Over time, structural damage in the vertebral column, syndesmophyte formation resulting from new bone growth, and ankylosis in the spine may occur. Chronic progressive spinal inflammation can affect not only the lumbar and thoracic regions but also the cervical spine, leading to reduced spinal mobility and postural changes over time (3). The majority of the spinal damage caused by the disease occurs within the first 10 years, and 10–40% of nr-axSpA cases progress to AS within 10 years (4, 5).

In rheumatology practice, cervical spine instability (CSI) is associated with inflammatory arthritis group diseases and has been linked to several mechanisms, such as chronic synovitis, ligamentous laxity, and bone erosions in the occiput–atlas (C0–C1) and atlas–axis (C1–C2) joints (6). Different types of lesion exist within CSI, including anterior atlantoaxial subluxation (aAAS), posterior atlantoaxial subluxation (pAAS), lateral atlantoaxial subluxation (lAAS), subaxial subluxation (SAS), and vertical subluxation (VS) (7). Clinically, CSI can range across a broad spectrum,

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from being asymptomatic to causing mild neurological complications or life-threatening neurological complications that may require surgical intervention (8).

There are currently no imaging recommendations for CSI in cases of axSpA. Sufficient data regarding the association with CSI are lacking in this rheumatological disease, where spinal inflammation is present in 100% of cases. The data in the literature are generally in the form of case reports, and there have been very few studies involving large patient groups (9). There are too few studies investigating the frequency and associated factors of CSI lesions in patients with axSpA, and no single study has investigated all forms of CSI simultaneously. Our aim in this study is to determine the frequency of CSI and any associated factors by examining all CSI lesions in a homogeneous axSpA cohort with a long disease duration and high disease activity requiring targeted therapy.

Method

Patient selection and study design

Our single-centre, cross-sectional retrospective study was conducted in 2024 with adult patients diagnosed with axSpA who presented to the rheumatology unit of Hatay Mustafa Kemal University Hospital, Turkiye, a tertiary care centre, with a disease duration of > 10 years and a history of using targeted therapy for at least 6 months. Demographic, clinical, laboratory, and treatment data were recorded from electronic patient files. Patients were classified as 'axSpA' according to the 2010 Assessment of SpondyloArthritis international Society (ASAS) criteria (10). The diagnosis of AS was established according to the modified New York criteria (11). Patients with inflammatory rheumatic diseases that can cause cervical spine involvement (e.g. rheumatoid arthritis, psoriatic arthritis, and enteropathic arthritis), non-inflammatory diseases that can cause cervical spine involvement (e.g. diffuse idiopathic skeletal hyperostosis and ochronosis), a history of trauma or surgery that compromises cervical spine integrity, and patients with spinal restriction severe enough to prevent functional cervical radiography were excluded from the study. Biological disease-modifying anti-rheumatic drugs (bDMARDs) and targeted synthetic disease-modifying anti-rheumatic drugs (Janus kinase inhibitors: tsDMARDs) were defined as 'targeted therapy'.

Assessments

The degree of sacroiliitis was assessed using the Ferguson view and defined according to the modified New York criteria (11); the highest-grade sacroiliitis lesion was noted. Syndesmophyte formation was evaluated as the presence of new bone formation leading to bridging by connecting two adjacent vertebrae (12); the presence of a syndesmophyte was defined as finding at least one syndesmophyte at any level of the spine. CSI lesions were assessed on four different X-rays: lateral cervical neutral, full-extension, and full-flexion radiographs, and an open-mouth anteroposterior cervical radiograph. The radiographs examined within the past year were evaluated by two rheumatologists blinded to the patients. Complete agreement was sought between the readers for the radiographic findings; in case of disagreement, the radiographs were re-evaluated and a final decision was made. Interobserver agreement for the presence of CSI lesions was assessed using Cohen's kappa coefficient.

CSI lesions were examined under five categories: (i) aAAS: a distance (anterior atlantodental interval) > 3 mm between the anterior surface of the odontoid process of C2 and the posteroinferior aspect of the C1 tubercle on a lateral cervical radiograph (13); (ii) pAAS: the posterior surface of the anterior arch of the atlas being displaced posterior to the anterior C2 line owing to erosion of the dens, as observed on a lateral radiograph (14); (iii) lAAS: displacement of C1 over C2 by > 2 mm on an open-mouth view (15); (iv) VS: Chamberlain's line (the distance between the hard palate and the posterior edge of the foramen magnum) being > 3 mm (16); and (v) SAS: horizontal displacement of one vertebra relative to an adjacent vertebra by > 2 mm without osteophyte formation (17).

Peripheral arthritis was confirmed by rheumatologist examination. Hip joint arthritis was detected by a rheumatologist and confirmed by ultrasonography (US) or magnetic resonance imaging (MRI). Uveitis was diagnosed by an ophthalmologist with more than 10 years of experience. Elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) was defined as ESR > 28 mm/h or CRP > 5 mg/L in a peripheral venous blood sample, provided that the elevation was detected on at least two visits. All radiographs were obtained in the same radiology department using standard protocols for cervical imaging, including lateral neutral, flexion, extension, and open-mouth odontoid views. Images were acquired by experienced radiology technicians trained in musculoskeletal radiography.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp, Armonk, NY, USA). Continuous variables were expressed as mean ± sd, and categorical variables as numbers with percentages (%). The distribution of the data was examined using the Kolmogorov–Smirnov test. For comparisons between groups, the independent samples t-test was used for normally distributed data, the Mann–Whitney U-test for non-normally distributed data, and Pearson's chi-squared or Fisher's exact test

for categorical variables. To determine the factors affecting the development of CSI, a univariate logistic regression analysis was first performed, and subsequently, variables found to be significant were included in a multivariate (generalized linear model – binomial logit) regression analysis. In all analyses, a p value of < 0.05 was considered statistically significant.

Ethics

The study was conducted in accordance with the principles of the Declaration of Helsinki and was ethically approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee at its meeting on 19 February 2025 (meeting number 03, decision number 36).

Results

In total, 159 patients (17 with nr-axSpA and 142 with AS) were included in the study. The mean age of the patients was 47 ± 11.3 years, and approximately 58% were male. The mean disease duration was 17.1 ± 9.1 years, and human leucocyte antigen (HLA)-B27 was positive in 80.5% of the cases. Among the targeted therapies currently used by the patients, secukinumab ranked first (22%), followed by adalimumab at 19%.

CSI was present in 19.5% (n = 31) of our study group; the total number of CSI lesions was 33 owing to the presence of mixed-type lesions in two patients. While 54.6% of all CSI lesions were aAAS (n = 18), the second most common lesion was SAS at 33.3% (n = 11). VS was present in two cases, while pAAS and lAAS were present in only one case each. Table 1 presents the demographic, clinical, laboratory, and treatment data of the study population. Figure 1 shows an example patient radiograph with aAAS in our study cohort. None of the patients with CSI had signs of myelopathy, whereas 14 patients reported neck pain. Patients with CSI were referred to the neurosurgery department, and no surgical intervention was indicated.

When the study group was compared as two groups, CSI-positive and CSI-negative, the CSI-positive group exhibited a longer mean disease duration (21.6 ± 9.1 years vs 16.1 ± 8.8 years; p = 0.002), an earlier age of first symptom onset (24.2 ± 8.6 years vs 29.3 ± 11.1 years; p = 0.032), a higher prevalence of peripheral arthritis (25.8% vs 11.7%; p = 0.045), and a higher prevalence of stage 4 sacroiliitis (51.6% vs 32%; p = 0.036) (Table 2). The interobserver agreement for detecting CSI lesions was substantial [$\kappa = 0.78$; 95% confidence interval (CI) 0.71–0.84].

In the univariate logistic regression analysis, uveitis [odds ratio (OR) = 2.82; 95% CI 1.01–7.90; p = 0.049], disease duration (OR = 1.07; 95% CI 1.02–1.11; p = 0.004), age at first symptom (OR = 0.95; 95% CI 0.91–0.99; p = 0.02), and sacroiliitis stage (OR = 1.46; 95% CI 1.02–2.09; p = 0.039) were found to be significantly associated with CSI. However, in the multivariate logistic regression analysis, which included disease duration, peripheral arthritis, uveitis, and sacroiliitis stage, only the disease duration was identified as a potential independent predictor of CSI (OR = 1.05; 95% CI 1.01–1.10; p = 0.027). Although the presence of peripheral arthritis and uveitis increased the risk of CSI by approximately 1.9 and 2.1 times, respectively, this result did not reach statistical significance (Table 3). Although a possible correlation between age and disease duration should be considered, age was not included in the multivariate model because it was not statistically significant in the univariate analysis. Owing to the limited number of events in our study, the number of variables included in the multivariate model was kept low reduce the risk of overfitting. In addition, evaluation of model fit indices showed that the deviance/df and Pearson χ^2/df ratios were close to 1, suggesting that the model demonstrated an acceptable fit to the data.

Discussion

To the best of our knowledge, this is one of the very few studies that comprehensively evaluates all forms of CSI in a homogeneous axSpA cohort with long-standing disease. By systematically assessing all radiographically detectable CSI types, our study expands the current understanding of CSI in axSpA and suggests that the overall burden of CSI may be underestimated when only aAAS is considered. In our study, we investigated the prevalence and associated factors of CSI in axSpA cases whose disease duration exceeded the initial 10 years – during which the majority of spinal damage occurs – and who were using bDMARD/tsDMARDs because of high disease activity. We applied these criteria to select a high-risk group for CSI involvement, aiming to determine an upper limit for CSI prevalence. In a total of 159 axSpA cases, we found the prevalence of CSI to be 19.5%. In this study, which is unique in the literature for examining all CSI lesions, 54.5% of the CSI lesions were aAAS, while 45.5% consisted of non-aAAS lesions. Therefore, when investigating CSI in axSpA cases, lesions other than aAAS must also be reviewed. In our retrospective analysis, disease duration, age at first symptom, history of uveitis, and sacroiliitis stage were found to be associated with the presence of CSI. However, after multivariable adjustment, only disease duration remained independently associated with axSpA-related CSI.

The study with the largest number of patients among those investigating the association between CSI and axSpA cases in the literature was conducted by JS Lee et al (18). In the study group, the mean disease duration was 13.3 years, and anti-tumour necrosis factor-α usage

Table 1. Demographic, clinical, laboratory, and treatment characteristics of the study population.

Total patients	159
Non-radiographic axSpA	17 (10.7)
Ankylosing spondylitis	142 (89.3)
Age (years)	47 ± 11.3
Male sex	92 (57.9)
Female sex	67 (42.1)
Smoking history	82 (51.6)
Body mass index (kg/m^2)	27.8 ± 5.5
Hypertension	29 (18.2)
Diabetes mellitus	13 (8.2)
Chronic kidney disease	3 (1.9)
Coronary artery disease	9 (5.7)
Disease duration (years)	17.1 ± 9.1
Age at first symptom (years)	28.3 ± 10.8
Peripheral arthritis	23 (14.5)
Hip arthritis	74 (46.5)
Uveitis	19 (11.9)
Elevated ESR	103 (64.8)
Elevated CRP	135 (84.9)
HLA-B27 positivity	128 (80.5)
Syndesmophyte	53 (33.3)
Sacroiliitis	
Grade 0	5 (3.2)
Grade 1	28 (17.6)
Grade 2	36 (22.6)
Grade 3	33 (20.8)
Grade 4	57 (35.8)
Targeted therapy	159 (100)
Etanercept	23 (14.5)
Infliximab	16 (10.1)
Adalimumab	31 (19.5)
Certolizumab pegol	15 (9.4)
Golimumab	23 (14.5)
Secukinumab	35 (22)
Tofacitinib	5 (3.1)
Upadacitinib	11 (6.9)
Patients with cervical spine atlantoaxial instability	31 (19.5)
Total atlantoaxial instability lesions	33 (100)
Anterior atlantoaxial subluxation	18 (54.6)
Posterior atlantoaxial subluxation	1 (3)
Lateral atlantoaxial subluxation	1 (3)
Vertical subluxation	2 (6.1)
Subaxial subluxation	11 (33.3)

Data are shown as n, n (%), or mean ± sd.
axSpA, axial spondyloarthritis; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; HLA, human leucocyte antigen.

was 38.3%. The frequency of aAAS was found to be 14.1%. In multivariate logistic regression analysis, elevated CRP, peripheral arthritis, and resistance to nonsteroidal anti-inflammatory drugs/conventional synthetic disease-modifying anti-rheumatic drug treatment were identified as independent predictive factors for the frequency of aAAS in AS patients. The study by JS Lee et al only examined aAAS among the CSI lesions, whereas our study investigated a total of 5 different forms. The frequency of aAAS in our study is lower than in their study (11.3% vs 14.1%), but when all CSI lesions are considered, the rate is higher than in their study (19.5% vs 14.1%). Approximately 10% of the cases in our study were nr-axSpA, and only one of the CSI-positive cases had a diagnosis of nr-axSpA; this factor may have contributed to the difference in aAAS between the two studies. In both studies, disease duration was identified as an independent predictive factor for CSI (18).

In a study where radiographs were evaluated by two radiologists in AS patients with long disease duration, JH Lee et al compared the group with atlantoaxial ankylosis with the group with aAAS (19). They found that the mean modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) in the atlantoaxial ankylosis group was significantly higher than in the aAAS cases,

Table 2. Comparison of the study population according to atlantoaxial instability status.

Variable	CSI-positive group (n = 31)	CSI-negative group (n = 128)	p
Age (years)	47 ± 10.9	47 ± 11.4	0.855†
Male sex	16 (51.6)	76 (59.4)	0.432‡
Smoking history	17 (54.8)	65 (50.8)	0.685‡
Body mass index (kg/m^2)	26.4 ± 5.5	28.1 ± 5.4	0.09‖
Type of axSpA			
Non-radiographic axSpA	1 (3.2)	16 (12.5)	0.198§
Ankylosing spondylitis	30 (96.8)	112 (87.5)	
Disease duration (years)	21.6 ± 9.1	16.1 ± 8.8	0.002‖*
Age at first symptom (years)	24.2 ± 8.6	29.3 ± 11.1	0.032‖*
Peripheral arthritis	8 (25.8)	15 (11.7)	0.045‡*
Hip arthritis	18 (58.1)	56 (43.8)	0.152‡
Uveitis	7 (22.6)	12 (9.4)	0.061§
Elevated ESR	22 (71)	81 (63.3)	0.421‡
Elevated CRP	27 (87.1)	108 (84.4)	0.999§
HLA-B27 positivity	25 (80.6)	118 (80.4)	0.126§
Syndesmophyte	14 (45.2)	39 (30.5)	0.119‡
Sacroiliitis			
Grade 0	0 (0)	5 (3.9)	0.036‖*
Grade 1	3 (9.7)	25 (19.5)	
Grade 2	7 (22.6)	29 (22.7)	
Grade 3	5 (16.1)	28 (21.9)	
Grade 4	16 (51.6)	41 (32)	

Data are shown as mean ± sd or n (%).
CSI, cervical spine instability; axSpA, axial spondyloarthritis; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.
†Independent samples t-test; ‡Pearson's chi-squared test; §Fisher's exact test; ‖Mann–Whitney U-test.
*Statistically significant difference ($p < 0.05$).

Table 3. Univariate and multivariate (generalized linear model – binomial logit) analysis.

Variable	β coefficient (95% CI)	OR (95% CI)	p
Univariate analysis			
Peripheral arthritis	0.963	2.620 (0.995–6.899)	0.051
Uveitis	1.037	2.819 (1.006–7.902)	0.049*
Male sex	–0.315	0.730 (0.332–1.605)	0.433
Disease duration	0.064	1.066 (1.021–1.114)	0.004*
Age at first symptom	–0.051	0.950 (0.910–0.992)	0.02*
Age	–0.001	0.999 (0.965–1.035)	0.975
Body mass index	–0.063	0.939 (0.867–1.017)	0.121
Grade of sacroiliitis	0.379	1.460 (1.019–2.092)	0.039*
Multivariate analysis			
Disease duration	0.051	1.052 (1.006–1.101)	0.027*
Peripheral arthritis	0.658	1.931 (0.674–5.527)	0.220
Uveitis	0.742	2.1 (0.680–6.484)	0.197
Grade of sacroiliitis	0.269	1.308 (0.909–1.883)	0.148

CI, confidence interval; OR, odds ratio.
*Statistically significant ($p < 0.05$).

particularly in the cervical region (40.1 vs 16.5), and they demonstrated that there was no relationship between disease duration and atlantoaxial ankylosis versus aAAS (19). Suarez-Almazor and Russell, on the other hand, detected aAAS in six out of 17 patients (35%) with spondylitis and peripheral arthritis, but in none of the patients in the control group of 21 individuals with only axial involvement (20). However, most of the cases in the peripheral arthritis group in this study had psoriasis, Reiter's syndrome, or inflammatory bowel disease. Consequently, the researchers concluded that aAAS might be a common complication in spondyloarthritis (SpA) cases with peripheral arthritis, and this condition could occur in approximately one-third of the patients (20). Although peripheral arthritis was significantly more frequent in the CSI-positive group in our study population, this effect was lost in the regression analysis. HS Lee et al, in their study investigating

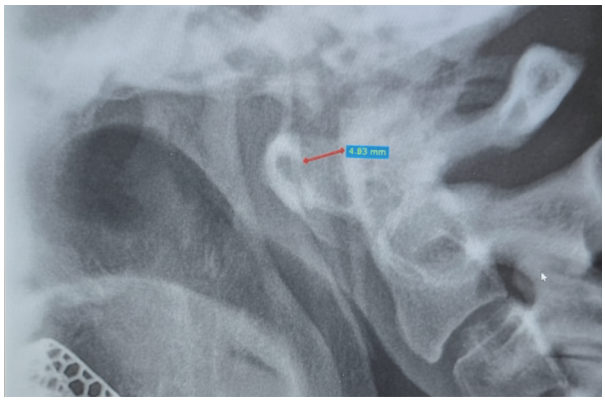


Figure 1. Example radiograph of a patient with anterior atlantoaxial subluxation.

cervical spine changes in AS cases (21), radiographically detected aAAS in 11.7% of 112 adult AS cases with a mean disease duration of 10.7 years; discovertebral (35.7%) and apophyseal joint involvement (28.6%) stood out as the most frequently detected cervical spine changes. Advanced age, long disease duration, cervical symptoms, lumbar and hip joint changes, and severe sacroiliitis were found to be predictive factors for all cervical spine lesions (21).

Kim et al evaluated the cervical radiographs of 544 AS patients, with a mean disease duration of 12 years (22). In this study, the frequency of aAAS was found to be 13.5% (22). Ramos-Remus et al prospectively followed 103 AS patients, with a mean disease duration of 10 years, for atlantoaxial subluxation (AAS) and neurological involvement (23). In the radiographic evaluation, they found the frequency of aAAS and VS to be 21% and 2%, respectively. The researchers found an association between radiographic aAAS and the degree of radiographic sacroiliitis, and suggested that the aAAS group might constitute a subgroup with more severe axial enthesopathy. In our study, the stage of sacroiliitis was also a predictive factor for the development of CSI (23). Laiho and Kauppi examined the radiographs of 72 AS cases, and reported that the most frequent lesion was apophyseal joint ankylosis (n = 32), followed by VS (n = 5) (24). In this study, among the CSI lesions, VS was the most common, detected in 11 cases, while aAAS was found in eight cases and pAAS in one case (24). In our study, the most frequently detected CSI lesions were aAAS and SAS, respectively. JY Lee et al detected AAS in approximately 17% (n = 11) of 61 AS patients. Among these 11 cases, aAAS was detected in five, lAAS in three, VS in two, and aAAS + lAAS in one. The researchers found that the disease duration was significantly higher in CSI-positive AS cases than in CSI-negative cases (25). In a study by Yalçınkaya et al investigating craniocervical junction involvement in inflammatory arthritis using computed tomography (CT) or MRI, in 200 SpA cases; VS was detected in 20 cases, AAS in 10 cases, and SAS in four cases. However, the relationship between CSI lesions and disease parameters was not evaluated in this study (26).

Currently, there are no recommendations for the routine screening of CSI lesions in patients with axSpA. The primary prerequisite for the development of CSI lesions is cervical spine inflammation. AS is a disease that affects the spine through ascending inflammation, starting from the sacroiliac joints. Cervical spine involvement increases with age and disease duration; it is more frequently observed in patients with symptomatic and structural damage (2). This patient group is highly likely to constitute the primary group in which CSI lesions should be investigated and suspected. The risk factors defined in the aforementioned studies can also be considered helpful in supporting this fundamental principle.

Despite the detailed analyses in our study, the retrospective design, the lack of interobserver and intraobserver reliability, and absence of the total mSASSS are significant limitations of our study. Because of the retrospective design, disease duration may reflect cumulative structural damage rather than a direct aetiological effect. Therefore, the observed association may be mediated by unmeasured structural progression rather than time exposure alone. Moreover, the degree of CSI was not measured in millimetres and was assessed only dichotomously; therefore, the relationship between the severity of instability and clinical findings could not be analysed. The sensitivity of conventional radiography in detecting CSI lesions is lower compared to CT and MRI, which may have led to a spuriously lower frequency of CSI (27). Therefore, the true prevalence of CSI in our cohort may be higher than that detected in our study. Consequently, the prevalence reported in this study may underestimate the true burden of cervical instability. This limitation should be considered when interpreting the findings. Another limitation of this study is the potential for multicollinearity between age and disease duration. Given their intrinsic correlation, this issue may have affected the stability and interpretability of the multivariable model, and thus the results should be

interpreted with caution. The fact that the study was conducted at a tertiary-level rheumatology unit inherently introduces a selection bias in patient recruitment, even if unintended. Potential for overfitting and limited statistical power due to the low events-per-variable ratio is the another limitation of this study; with only 31 events, the multivariable model may be underpowered, and the findings should therefore be interpreted with caution.

Conclusion

In our study investigating the frequency of radiographic CSI and associated factors in axSpA patients with a disease duration of more than 10 years and receiving b/tsDMARD treatment (and thus having high disease activity) in a tertiary rheumatology unit, we detected CSI in approximately one-fifth of the patients. While studies conducted on this topic generally examine only aAAS as CSI, in this study, in which we examined all CSI lesions, 54.5% of the CSI lesions were aAAS and 45.5% consisted of non-aAAS lesions.

These results highlight the need for increased clinical awareness of cervical spine involvement in axSpA and support the consideration of cervical imaging in patients with prolonged disease duration, severe sacroiliitis, or uveitis. Further prospective studies with more sensitive imaging techniques are warranted to clarify the potential causal association.

Disclosure statement

No potential conflict of interest was reported by the authors.

Author contributions

CRediT: **S Ketenci:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **H Oğuzman:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing; **M Pekdiker:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

Ethical approval

The study was conducted in accordance with the principles of the Declaration of Helsinki and was ethically approved by the Hatay Mustafa Kemal University Non-Interventional Clinical Research Ethics Committee at its meeting on 19 February 2025 (meeting number 03, decision number 36).

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