

**RESEARCH  
ARTICLE**

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## Contribution to Diagnosis of Magnetic Resonance Imaging and Inflammatory Markers in Musculoskeletal Involvement of Brucellosis

### ABSTRACT

**Objective:** Musculoskeletal involvement in brucellosis is very important. This study aimed to evaluate the magnetic resonance imaging (MRI) findings and hematological parameters as a predictive value for the diagnosis of musculoskeletal brucellosis.

**Method:** This prospective case-control study was conducted between June 2011 and November 2019 in a university hospital. Ninety-nine patients with the confirmed diagnosis of brucellosis without musculoskeletal involvement and forty-three brucellosis patients with musculoskeletal involvement were examined. The hematological, biochemical parameters, and radiological imaging findings of both groups were recorded. These parameters were statistically compared between the two groups.

**Results:** The mean age of the patients (non-involvement group) and musculoskeletal involvement groups was  $44.04 \pm 23.11$  and  $37.92 \pm 24.80$  years, respectively ( $P = 0.062$ ). C-reactive protein (CRP) and alkaline phosphatase (ALP) levels were significantly higher in the musculoskeletal involvement group ( $P < 0.05$ ). The lower lymphocyte level was statistically significant in this group. Based on the receiver operating characteristic (ROC) analysis, the sensitivity and specificity were 70% and 65% for ALP, 77% and 58% for CRP, 83% and 45% for lymphopenia, respectively. There was no statistically significant difference between the two groups in terms of the other hematological and biochemical parameters. Spondylodiscitis (34.8%) was the most common MRI finding in patients with musculoskeletal involvement.

**Conclusion:** Our study results show that CRP, ALP, and lymphopenia can be used as valuable markers in the preliminary diagnosis of musculoskeletal brucellosis.

**Keywords:** Brucellosis, Magnetic Resonance Imaging, Spondylodiscitis, Infectious Diseases.

## Brusellozda Kas İskelet Tutulumunda Manyetik Rezonans Görüntüleme ve İnflamatuar Belirteçlerin Tanıya Katkısı

### ÖZET

**Amaç:** Brusellozda kas iskelet sistemi tutulumu çok önemlidir. Bu çalışmada, manyetik rezonans görüntüleme (MRG) bulgularının ve hematolojik parametrelerin kas-iskelet sistemi brusellozu tanısında prediktif değer olarak değerlendirilmesi amaçlandı.

**Gereç ve Yöntem:** Bu prospektif vaka-kontrol çalışması Haziran 2011 ile Kasım 2019 tarihleri arasında bir üniversite hastanesinde yapıldı. Kas-iskelet tutulumu olmayan bruselloz tanısı doğrulanmış 99 hasta ve kas-iskelet tutulumu olan kırk üç bruselloz hastası incelendi. Her iki grubun hematolojik, biyokimyasal parametreleri ve radyolojik görüntüleme bulguları kaydedildi. Bu parametreler istatistiksel olarak iki grup arasında karşılaştırıldı.

**Bulgular:** Hastaların (tutum olmayan grup) ve kas-iskelet tutulum gruplarının ortalama yaşı sırasıyla  $44.04 \pm 23.11$  ve  $37.92 \pm 24.80$  yıldır ( $P = 0.062$ ). C-reaktif protein (CRP) ve alkalın fosfataz (ALP) düzeyleri kas-iskelet tutulumu grubunda anlamlı olarak daha yüksekti ( $P < 0.05$ ). Lenfosit miktarının düşüklüğü bu grupta istatistiksel olarak anlamlıydı. Alıcı işletim özelliği (ROC) analizine göre, duyarlılık ve özgüllük ALP için sırasıyla %70 ve %65, CRP için %77 ve %58, lenfopeni için %83 ve %45 idi. Diğer hematolojik ve biyokimyasal parametreler açısından iki grup arasında istatistiksel olarak anlamlı fark yoktu. Spondilodiskit (%34.8) kas iskelet sistemi tutulumu olan hastalarda en sık MRG bulgusuydu.

**Sonuç:** Çalışma sonuçlarımız, kas-iskelet sistemi brusellozunun ön tanısında CRP, ALP ve lenfopeninin değerli belirteçler olarak kullanılabileceğini göstermektedir.

**Anahtar Kelimeler:** Bruselloz, Manyetik Rezonans Görüntüleme, Spondilodiskit, Bulaşıcı Hastalıklar.

## INTRODUCTION

Brucellosis is a zoonotic bacterial infection that affects numerous organs and systems and is caused by *Brucella* species, which are small, intracellular gram-negative coccobacillus. Although the infection can be transmitted to humans in various ways, the most common way of transmission is through the consumption of unpasteurized milk and dairy products from an infected animal. Furthermore, it can be transmitted directly through damaged skin, conjunctival instillation, and the inhalation of infectious aerosols (1, 2). The most common complication of brucellosis in humans is the infection of bones and joints. It has been reported in high-risk regions, such as the Middle East, Asia, South and Central America, and Africa. The prevalence of musculoskeletal involvement ranges from 27% in low-risk regions to 36% in high-risk areas (3).

Musculoskeletal involvement in brucellosis is often diagnosed due to pain in joints or the evidence of infection, such as pain, swelling, functional disability, heat, tenderness, and redness at any location of the musculoskeletal region (3,4). Musculoskeletal brucellosis can occur at any time and can present as sacroiliitis, peripheral arthritis, spondylitis, and osteomyelitis (3,5). In endemic regions, brucellosis must be considered in a differential diagnosis for back pain and septic arthritis. Physical examination and laboratory tests should be performed, and imaging findings should be evaluated to make a diagnosis. Direct roentgenography, computed tomography (CT), magnetic resonance imaging (MRI), and bone scintigraphy are imaging modalities for the diagnosis of musculoskeletal brucellosis (6). The early diagnosis and early treatment of complicated cases is crucial. Since human brucellosis has variable non-specific clinical manifestations, the disease tends to be overlooked. The inadequate diagnosis of brucellosis causes an increase in the rate of chronic and complicated cases. MRI findings and inflammatory markers may be useful in identifying complicated brucellosis (5). Therefore, we focused on MRI findings and inflammatory markers in patients with musculoskeletal brucellosis in this study. In patients who had MRI evidence of musculoskeletal brucellosis, CRP, ALP, and lymphocyte levels were evaluated as possible indirect inflammatory biomarkers of musculoskeletal involvement.

## MATERIAL AND METHODS

**Study Population:** The data obtained from patients who were diagnosed with brucellosis by clinical and serological tests and referred to the Department of Radiology for detecting any musculoskeletal involvement among brucellosis outpatients and inpatients between June 2011 and November 2019 were analyzed retrospectively. The study was performed with the permission obtained

from the Medical Clinical Research Ethics Committee of our university (Date:05/22/2020 Number:156). The patients' demographic data, radiological imaging and clinical findings, and laboratory results were obtained from the hospital records retrospectively. The history, laboratory and radiological data of each patient were obtained. The data of patients with multiple admissions due to brucellosis at the time of their first admission were included in the study. Patients with the etiologically confirmed diagnosis of brucellosis and whose laboratory tests were confirmed were included in the study. Furthermore, other inflammatory diseases, autoimmune and malignant diseases represented the exclusion criteria from the study. Pregnant patients and patients under 18 years of age were excluded from the study. None of the patients participating in the study received steroid therapy or took any other anti-inflammatory medication. The patients were categorized into two groups: the brucella group and the group of brucella patients with musculoskeletal involvement. Patient serums with the positive Rose Bengal test were examined by the immunocapture-agglutination technique to eliminate the factors that caused false negativity/positivity. The brucella group consisted of patients without any complications. Brucella patients with musculoskeletal involvement were evaluated as a separate group.

**Diagnosis of Brucellosis:** The diagnosis of brucellosis was made based on clinical and bacteriological and/or serological findings. The patient's serums were first screened by the Rose Bengal slide agglutination test (Seromed, Istanbul, Turkey). Then, the Brucella test (capt test) (Vircell SL, Granada, Spain) was performed according to the manufacturer's instructions. Antibody titers of 1/160 and above were accepted as positive for brucellosis. However, those lower than 1/160 were accepted as negative. Blood cultures were studied using the BacT/ALERT 3D (bioMérieux, France) automated blood culture system.

The isolated bacterial strains were determined by conventional methods (Gram stain, oxidase, catalase, urease tests, etc.) and a Phoenix 100 (Becton Dickinson, USA) automated system.

**Diagnosis of Musculoskeletal Brucellosis:** Musculoskeletal brucellosis was diagnosed by positive serological tests or positive culture with the clinical inflammatory signs of the affected regions. We retrospectively examined patients who had undergone MRI with a pre-diagnosis of musculoskeletal involvement. In our study, MRI was performed in all patients with pain and positive serological tests. Patients with musculoskeletal involvement were identified as cases of sacroiliitis, spondylitis, spondylodiscitis, paravertebral/epidural or soft tissue abscess and osteomyelitis. Musculoskeletal presentations of brucellosis were diagnosed by physical examination and compatible

laboratory findings verified by MRI features of the affected region.

**Radiological Imaging:** In our study, if there was a suspicion of musculoskeletal involvement (sacroiliitis, peripheral arthritis, spondylitis, spondylodiscitis, epidural or paravertebral abscess and osteomyelitis), MRI was carried out. MRI was conducted in our Radiology Department using a Siemens Magnetom Avanto Tirm+DOT System 1.5 T MRI scanner (Siemens Healthcare, Erlangen, Germany) with an appropriate coil for each location. T1 and T2-weighted without fat saturation, fat-saturated T1 and T2-weighted, STIR (Short Tau Inversion Recovery), postcontrast fat-saturated T1-weighted MRI sequences (after the administration of 15 or 20 mL of 0.5 mmol/ml gadoteric acid or 10, 15, or 20 mL of 0.5 mmol/ml gadopentetate dimeglumine) were performed on the coronal, axial, and sagittal planes. The contrast agent was given to the patients with suspected active inflammation.

**Image Evaluation:** In the diagnosis of spondylitis and spondylodiscitis, vertebral endplates, bodies, intervertebral discs, paravertebral soft tissue, and epidural spaces were assessed. In patients with spinal brucellosis, paraspinal, focal or diffuse involvement, epidural spreading and cord compression were evaluated. We accepted as typical MRI findings for spondylitis a hypointense signal in T1-weighted images and hyperintense signal in T2-weighted images in the vertebral corpus. For MRI diagnosis of discitis, we searched the presence of a hyperintense signal in intervertebral discs in T2-weighted images and blurring in vertebral endplates in T1-weighted images. In post-contrast T1-weighted fat-suppressed MRI of patients with spondylodiscitis, we demonstrated contrast enhancement in the vertebral endplate, intervertebral disc, and paravertebral soft tissue. In the radiological examination for the sacroiliac joint, unilateral or bilateral joint involvement, bone marrow edema, joint enlargement or narrowing, intra-articular fluid, joint irregularity (irregularity in the joint surfaces), joint sclerosis, periarticular involvement, and contrast enhancement were evaluated. In the appendicular joint involvement, bone marrow edema, joint derangement, synovial fluid, the enhancement of synovium and periarticular soft tissues were observed after the gadolinium-based contrast agent injection on MRI like as the literature data (7).

**Laboratory Data:** The erythrocyte sedimentation rate (ESR), complete blood count, and blood biochemistry profile were examined. Hemoglobin (Hb), red blood cell (RBC), white blood cell (WBC), lymphocyte, neutrophil and platelet count, mean platelet volume (MPV), red blood cell distribution width (RDW), C-reactive protein (CRP), alkaline phosphatase (ALP), blood urea nitrogen (BUN), creatinine, liver enzymes, and

lipid profile were recorded for each group. MPV, neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) were calculated. Blood samples were collected in tubes containing standard ethylenediaminetetraacetic acid (EDTA). All blood samples in our study were tested for hematological parameters using the same regularly calibrated analyzer (Abbott CELL-DYN 3700, United States).

**Statistical Analysis:** Statistical analysis was conducted using the SPSS 18.0 version program. For the evaluation of the results, standard statistical methods were employed. The average, standard deviation, minimum and maximum values of the data were revealed. Student's t-test was used to compare independent quantitative parameters with normal distribution. The Mann-Whitney U test was used to compare independent quantitative parameters without normal distribution. The chi-square test and one-way variance analysis (ANOVA) were used to compare categorical and continuous variables between the groups. The correlation between the investigated variables was determined using Pearson's coefficient linear correlation analysis. The data were evaluated at the 95% confidence interval, and  $p < 0.05$  was considered significant. The receiver operating characteristic curves (ROC) analysis, area under the ROC curve (AUC), sensitivity and specificity values were evaluated.

## RESULTS

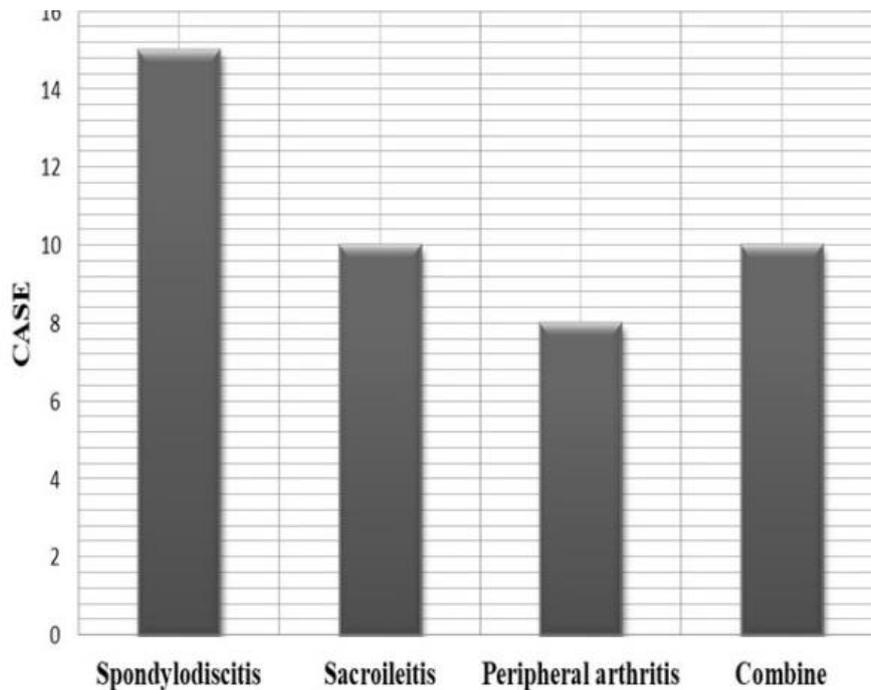
The study involved 142 patients (72 females and 70 males) with a mean age of  $49 \pm 17$  years and diagnosed with brucellosis. There were significant differences in the mean age of patients with and without musculoskeletal involvement ( $p < 0.05$ ). There were no significant differences in gender. There were no significant differences in the laboratory and serological findings between the groups, except for older age, high CRP and ALP levels, and lower lymphocyte level. These were found to be significant factors in predicting musculoskeletal involvement. The patients' demographic and laboratory characteristics are shown in Table 1. The distribution of brucellosis patients with musculoskeletal involvement is shown in Figure 1. MRI showed that 15 (34.8%) patients had spondylodiscitis (Figure 2), 10 (23.2%) patients had sacroiliitis (Figure 3), 8 (18.6%) patients had peripheral arthritis (Figure 4), and 10 (23.2%) patients had combined findings (soft tissue abscess and soft tissue inflammation) (Figure 5). The vertebral corpus morphology of patients with spondylodiscitis was preserved. In our study, two consecutive vertebrae were affected. And there was no cervical region involvement. In some of our cases, spondylodiscitis was accompanied by paraspinal soft tissue inflammation. The frequency of axial skeleton involvement was significantly higher than the appendicular skeleton ( $p < 0.05$ ). In patients with musculoskeletal involvement, the mean values of CRP and ALP were significantly higher than in patients without involvement (Table 1).

**Table 1.** Comparison of the demographic data and laboratory values according to the presence or absence of musculoskeletal involvement in brucellosis.

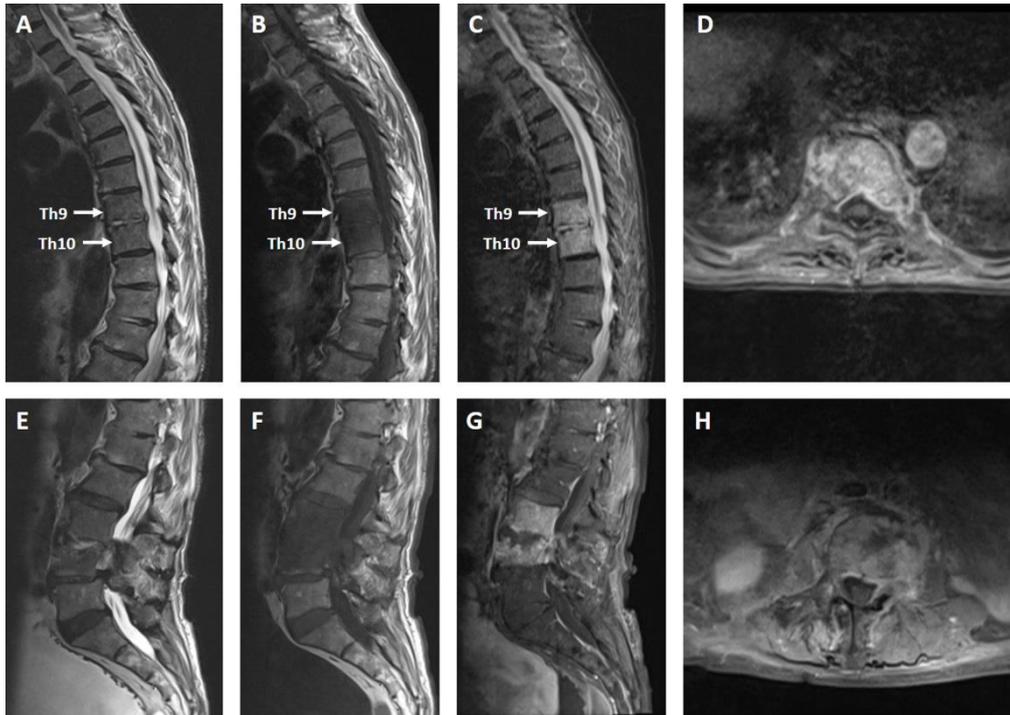
Parameters	All Brucella patients n=142	Patients without musculoskeletal involvement n=99	Patients with musculoskeletal involvement n=43	P-value
	Median ± IQR	Median ± IQR	Median ± IQR	
Age	49.15±17.50	48.00±20.00	50.50±19.25	<b>0.029*</b>
ESR	31.0338±38.00	23.0000±31.50	29.0000±38.75	0.262
CRP	26.2691±30.33	5.7000±24.56	15.2800±34.88	<b>0.049*</b>
WBC	7.544±3.15	7.3000±3.20	6.4500±3.25	0.142
Neutrophil	4.7752±2.90	4.6000±2.90	4.2000±3.33	0.416
Lymphocyte	1.9979±1.10	2.1000±1.20	1.6000±0.80	<b>0.042*</b>
NLR	2.9168±1.83	2.0909±1.75	2.5719±2.11	0.502
Monocyte	0.5773±0.30	0.5000±0.30	0.5000±0.30	0.960
Eosinophil	0.1397±0.20	0.1000±0.20	0.1000±0.20	0.759
Basophil	0.0348±0.10	0.0000±0.10	0.0000±0.10	0.866
Hemoglobin (Hb)	13.2979±2.35	13.5000±2.40	13.5000±2.65	0.896
RDW	14.6823±1.65	14.2000±1.70	14.0000±1.38	0.626
PC (Platelet count)	252.3972±115.50	238.0000±111.00	264.5000±134.25	0.499
MPV	8.3780±1.20	8.3000±1.10	8.1000±1.05	0.142
PLR	122.1053±81.75	120.000±77.45	135.200±93.18	0.103
BUN	15.6564±6.00	13.0000±6.50	15.0000±6.50	0.057
Creatinine	0.9545±0.28	0.8500±0.30	0.8200±0.25	0.348
HDL	41.3325±19.56	43.7300±20.46	38.1200±21.71	0.992
LDL	99.6194±45.74	87.0000±38.38	97.0000±60.38	0.204
AST	44.8087±15.00	22.0000±14.34	23.0850±14.54	0.324
ALT	38.3651±19.51	19.1700±19.45	21.5500±20.49	0.440
ALP	97.4400±39.05	83.1500±42.91	103.4500±45.36	<b>0.002*</b>

\* p <0.05 was considered significant.

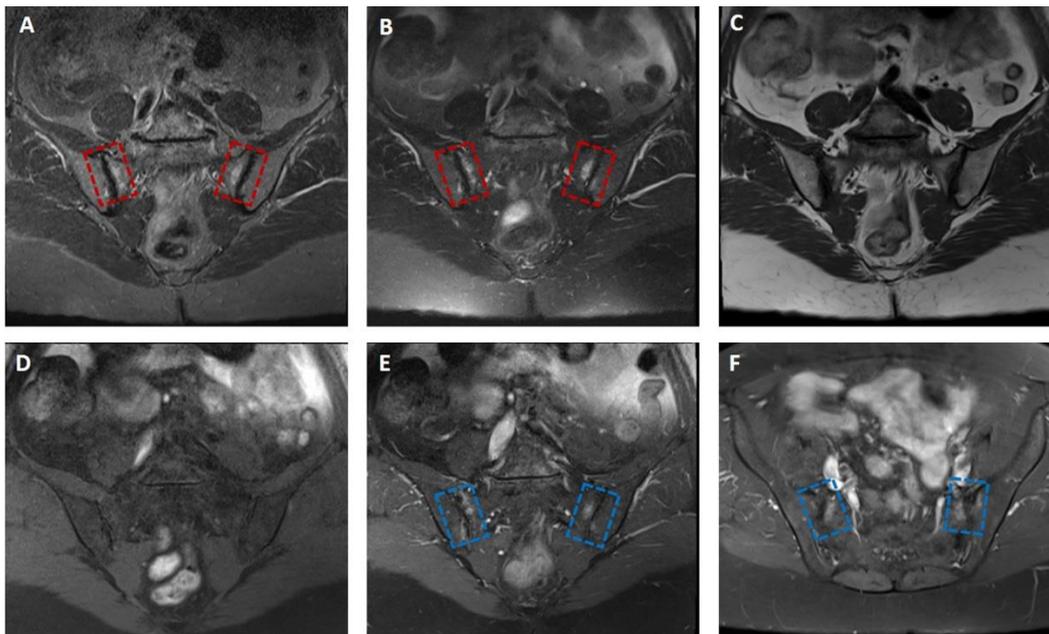
Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cell (WBC), neutrophil/lymphocyte ratio (NLR), hemoglobin (Hb), red blood cell distribution width (RDW), platelet count (PC), mean platelet volume (MPV), platelet/lymphocyte ratio (PLR), blood urea nitrogen (BUN), high-density lipoprotein (HDL), low-density lipoprotein (LDL), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP)



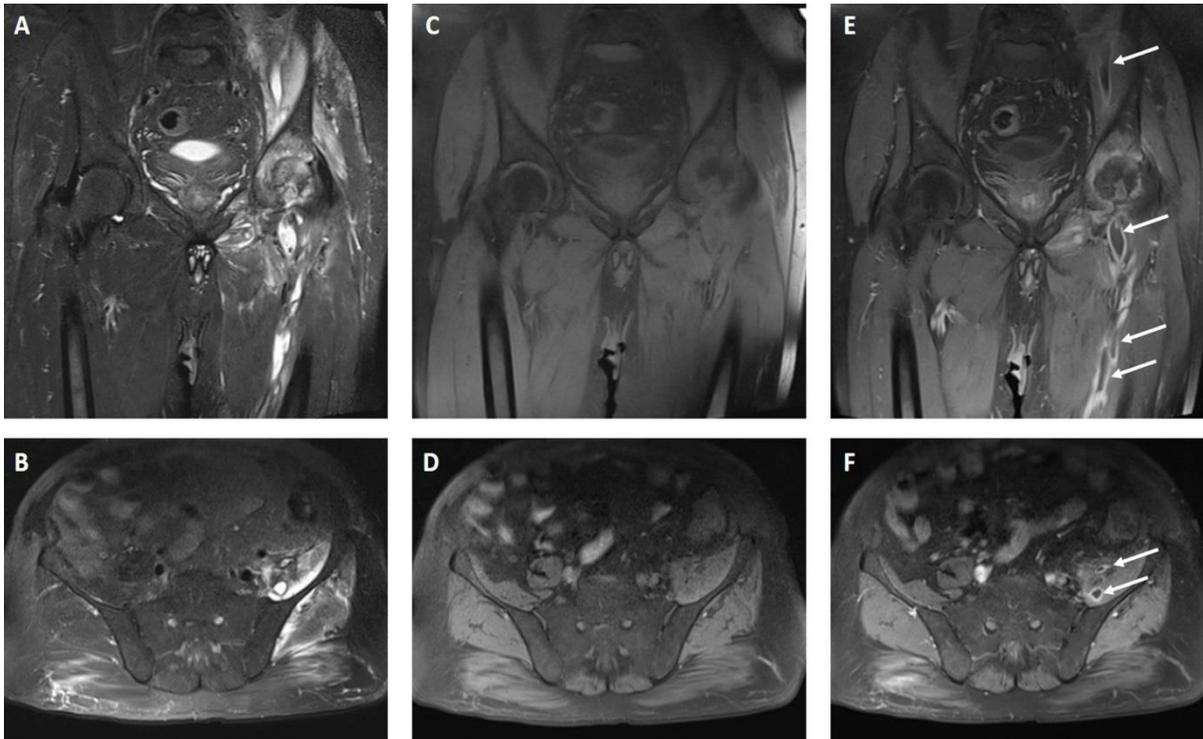
**Figure 1.** Distribution of brucellosis patients with musculoskeletal involvement according to clinical and radiological findings



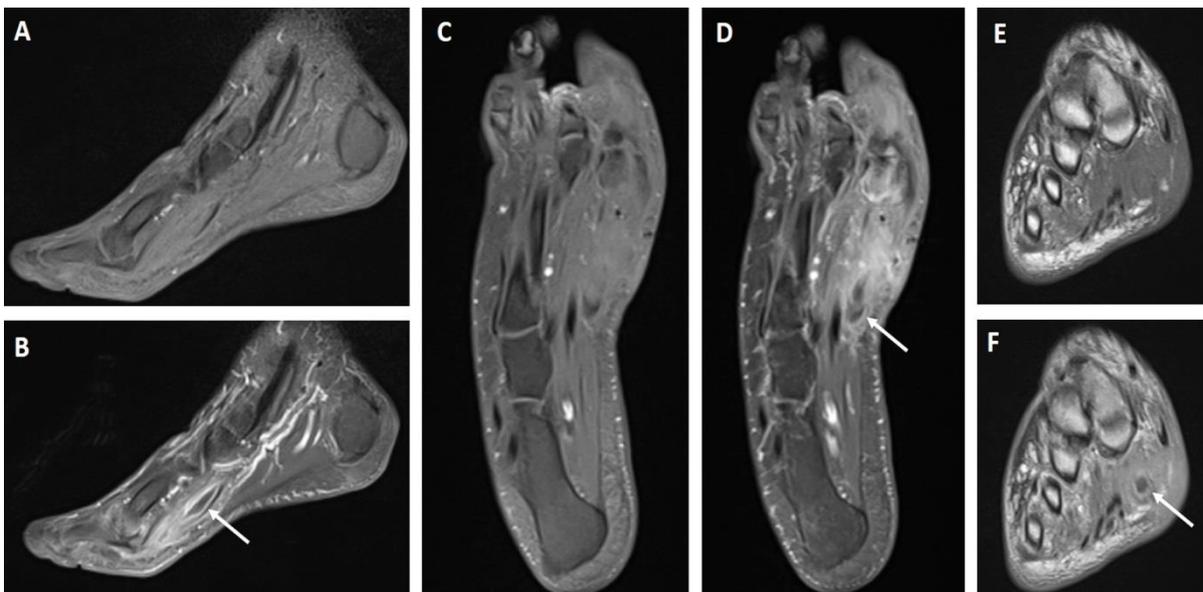
**Figure 2.** Thoracic spondylodiscitis: (A and B) The sagittal T2-weighted and sagittal T1-weighted images show a hypointense signals in the vertebral bodies and endplates (T9-10). (C) The sagittal STIR image shows a hyperintense signal in the vertebral bodies and endplates. (D) The contrast-enhanced T1-weighted fat-saturated axial image shows enhancement in the affected vertebra and paravertebral soft tissue. Lumbar spondylodiscitis: (E and F) The sagittal T2-weighted and sagittal T1-weighted images show a hypointense signals in the L3-L4 vertebral bodies and endplates. (G) The contrast-enhanced T1-weighted fat-saturated sagittal image shows the formation of spondylitis and the involvement of the intervertebral disc space between L3-L4 vertebral levels. (H) The contrast-enhanced T1-weighted fat-saturated axial image shows enhancement in the affected vertebra and paravertebral soft tissue.



**Figure 3.** Bilateral sacroiliitis: (A and B) Coronal STIR (Short tau inversion recovery) and fat-saturated TSE (Turbo spin echo) T2 weighted MR sequences show bilateral hyperintense signal changes (red frames) on both iliac wings and sacral surfaces. (C and D) Coronal T1 and fat-saturated precontrast T1 weighted MR images reveal narrowing of bilateral sacroiliac joint space, irregularity on the bony faces. (E and F) Coronal and axial postcontrast fat-saturated T1 weighted MR sequences show pathological enhancements (blue frames) in subarticular bone marrow



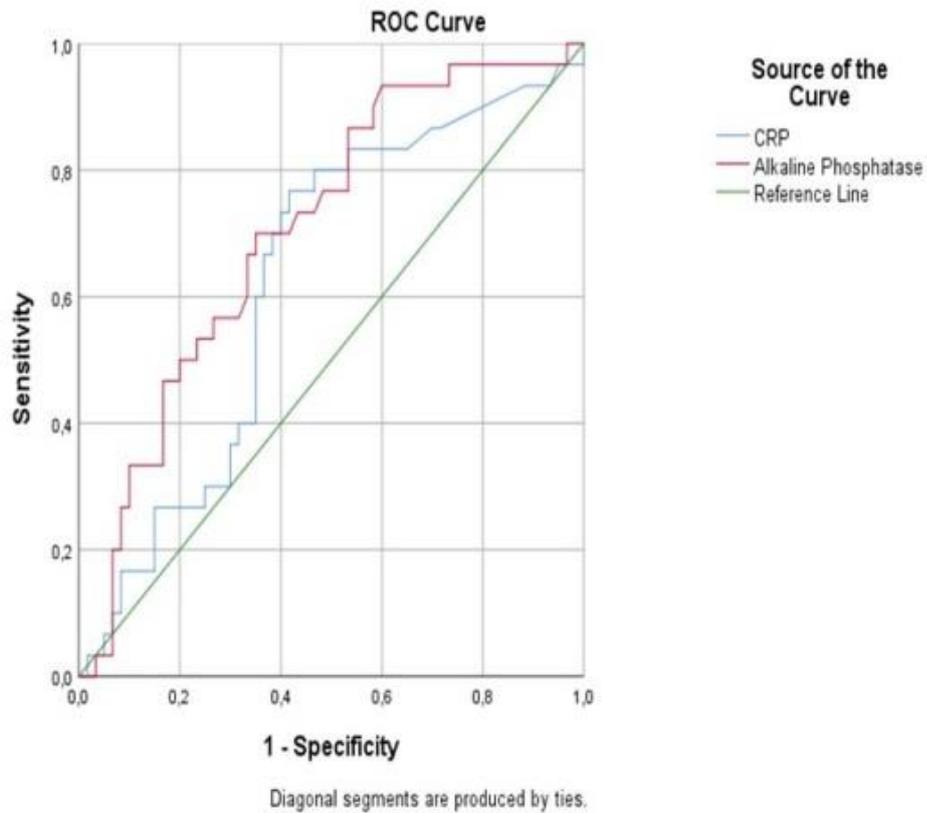
**Figure 4.** Left hip joint arthritis and accompanying left iliopsoas muscle abscess: (A and B) Coronal and axial fat-saturated T2 weighted MR images show diffuse hyperintense inflammatory signal changes in subarticular bone marrow of the left hip and periarticular soft tissues. (C-F) Pre- and post-contrast coronal and axial fat-saturated T1 weighted MR sequences reveal abscess formations (arrows) with peripheral enhancement in the left iliopsoas muscle and the adductor muscle planes of the left thigh.



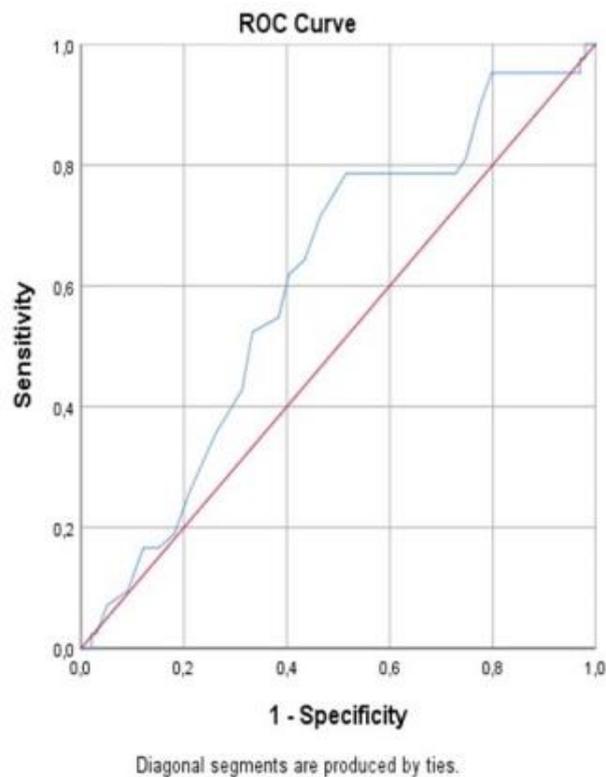
**Figure 5.** Right foot abscess: Pre- and post-contrast sagittal (A and B), axial (C and D), and coronal (E and F) fat-saturated T1 weighted MR images reveal inflammatory signal changes and peripherally enhancing abscess formation (arrows) on the plantar medial part of the right foot.

The frequency of lymphopenia was significantly lower in patients with musculoskeletal involvement. Among all patients, standard tube agglutination test (STA) titers ranged from 1/160 to > 1/1280. The differences in the distribution of the STA titers between patients with and without musculoskeletal involvement were statistically significant ( $p = 0.001$ ).

The majority of the patients with musculoskeletal involvement had a higher STA titer ( $\geq 1/640$ ) than patients without musculoskeletal involvement, and this difference was statistically significant ( $p = 0.001$ ). The ROC curves and AUC value for CRP, ALP, and lymphocytes are presented in Figures 6 and 7 and Table 2.



**Figure 6.** Receiver Operating Characteristic Curve (ROC) analysis for various cut-off levels of CRP and ALP in predicting musculoskeletal involvement in brucellosis.



**Figure 7.** Receiver Operating Characteristic Curve (ROC) analysis for various cut-off levels of lymphocyte in predicting musculoskeletal involvement in brucellosis.

**Table 2.** The area under the curve (AUC) of CRP (C- Reaktive Protein), ALP (Alkaline phosphatase) and Lymphocytes.

Variables	AUC (95% CI)	P-Value	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy
<b>CRP</b>	0.628 (0.505 – 0.749)	0.049	7.24	0.77	0.58	0.69	0.56	0.60
<b>ALP</b>	0.706 (0.595 – 0.817)	0.001	89.53	0.70	0.65	0.70	0.81	0.66
<b>Lymphocyte</b>	0.608 (0.509 – 0.707)	0.042	2.05	0.83	0.45	0.71	0.54	0.59

PPV: Positive predictive value

NPV: Negative Predictive Value

## DISCUSSION

Brucellosis is a serious infectious public health problem in many developing countries, including Turkey, where farming is still a notable means of subsistence (2). The musculoskeletal system is commonly affected. In our study, we compared the demographic, laboratory, and imaging findings of patients with and without musculoskeletal complications to investigate the effect of easily accessible parameters in determining musculoskeletal involvement in brucellosis.

In this study, there was a significant difference between the mean ages of the patients with and without musculoskeletal involvement. Older age ( $50.50 \pm 19.25$ ) was found to be a significant factor in predicting musculoskeletal involvement. While older age was found to be a risk factor for focal involvement (8), there was no significant difference between the mean ages of the patients with and without the osteoarticular affected region in some studies (9, 10).

In brucellosis, any region in the musculoskeletal system may be affected (11-13). The most important clinical presentations of musculoskeletal involvement are arthritis, spondylitis, bursitis, tenosynovitis, and osteomyelitis. Arthritis is usually observed in large joints and especially in the sacroiliac joint (14, 15). In this study, we found that spondylodiscitis was the most common site of involvement (23.2%). It was found that sacroiliitis was the most common involvement in other studies (16-18). Similar to our study, some other studies found that spondylodiscitis was more common (10, 19). There are studies indicating that peripheral arthritis is more common or spondylitis combined with sacroiliitis is more common (17, 20). Peripheral arthritis or sacroiliitis and spondylitis were more common radiological findings in some studies (16, 19, 21). As summarized in Figure 1, our results were similar to the studies.

Infectious spondylodiscitis is the involvement of anatomical structures such as the spine, intervertebral discs, paraspinal soft tissues, and epidural space by a specific organism, and it has been reported more frequently in adults over 50 years of age. Spondylodiscitis is a common and crucial musculoskeletal system complication of brucellosis infection and may cause spinal deformities and temporary or permanent neurological deficits if treatment is delayed (19, 22).

MR imaging plays a crucial role in differentiating spondylodiscitis due to brucella from other spinal pathologies such as tuberculous spondylodiscitis, pyogenic spondylodiscitis, postoperative findings in the spinal region, spinal degenerative diseases that increase with age, and vertebral metastases (23, 24). Although conventional MRI has some difficulties in differentiating acute and chronic stages of spondylodiscitis, it should be considered as the first-choice imaging method for the diagnosis, treatment, and follow-up of brucellar spondylodiscitis (25).

Vertebral metastatic processes are not affect the intervertebral disc spaces (22). Moderate epidural spread associated with intradiscal gas, varying degrees of bone sclerosis, gibbus deformity, and subligamentous extension suggest tuberculosis-related involvement rather than brucellar involvement. The lumbar segment, especially the lower lumbar region, is more involved in brucellar spondylodiscitis (26-28). Therefore, when making the differential diagnosis of vertebral involvement, the patient's history, accompanying findings, results of clinical and serological tests, and imaging features should be evaluated.

In our study, the manifesting laboratory findings in patients with osteoarticular brucellosis are high CRP, ALP, PLR, STA levels and lower lymphocyte level. Some studies reported that the level of CRP was higher in osteoarticular brucellosis than in non-osteoarticular brucellosis (29, 30). Other studies have shown that leukopenia, elevated liver enzyme level, and high CRP levels are more frequently reported findings in patients with osteoarticular involvement (31, 32). However, there are studies that do not differ significantly in terms of the frequency of leukopenia between patients with and without osteoarticular involvement. The differences in the distribution of the STA titers between these two groups were statistically significant. As the results of our study have shown, the differences in the distribution of STA titers between these patients were statistically significant in the study conducted by Ciftdogan et al (33).

MRI is a powerful tool to diagnose brucellar spondylodiscitis, especially in its early period, and paraspinal or epidural abscess, chord or root compression secondary to brucellosis (10, 18). After the gadolinium injection, signal changes in

vertebral bodies without morphologic changes and the enhancement of facet joints have been identified as specific MRI findings of brucellar spondylitis (34). Vertebral corpus morphology is almost always preserved in spinal brucellosis. Vertebral corpus integrity was preserved in our study. The involved vertebrae are generally continuous, and non-continuous vertebral involvement is rare in spondylodiscitis due to brucella (35). In our study, two consecutive vertebrae were affected. Cervical region involvement is rare in brucellar spondylodiscitis, and a few cases have been reported in the literature (36, 37). In our study, there was no cervical region involvement, but rather the lower lumbar region was affected.

Various researchers have demonstrated that MRI can depict soft tissue lesions in 0-89% of the cases with brucellar spondylitis (11, 19). Paravertebral soft tissue involvement was present in the majority of our patients with lumbar spondylodiscitis (Figure 2). The paraspinal soft tissue involvement is larger in size than that due to tuberculosis. The thick and irregularly enhancing abscess wall and poorly circumscribed paraspinal pathological signal are more in favor of pyogenic spondylodiscitis (38, 39). The rim-shaped, thin, and smooth enhancement of the abscess wall and the presence of a well-defined paraspinal abnormal signal in MRI are in favor of tuberculous

spondylodiscitis, and narrowing of the disc distance is more frequently observed in tuberculosis-related spondylodiscitis (38-40).

Limitations of the research; The fact that it is retrospective, the number of patients is insufficient and the number of patients with and without musculoskeletal involvement due to brucellosis is not equal may cause these inflammatory markers to be insufficient in predicting the prognosis in terms of disease involvement. Another limitation is that this study focused only on MR imaging as a radiological evaluation and did not include other imaging findings (such as direct x-ray, computed tomography, and scintigraphy).

#### CONCLUSION

The laboratory results of this study and radiological imaging findings show that older age, high CRP, ALP, STA levels and lower lymphocyte level are significant factors in estimating musculoskeletal involvement. They can be used as precious markers in the preliminary diagnosis of musculoskeletal brucellosis. We believe that these variables can be considered fast, cheap, and easily measurable new inflammatory markers in musculoskeletal brucellosis patients. More comprehensive studies are still required to investigate the predictive value of these markers in complicated brucellosis with musculoskeletal involvement.

#### REFERENCES

1. Akpınar O. Historical perspective of brucellosis: a microbiological and epidemiological overview. *Le Infezioni in Medicina*. 2016;24(1):77-86.
2. Akpınar O, KILIÇ H. BRUCELOSIS: RETROSPECTIVE EVALUATION OF 382 PATIENTS. *Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi*.3(3):108-13.
3. Adetunji SA, Ramirez G, Foster MJ, Arenas-Gamboa AM. A systematic review and meta-analysis of the prevalence of osteoarticular brucellosis. *PLoS neglected tropical diseases*. 2019;13(1):e0007112.
4. Akpınar O, Guzel M. Spinal stenosis caused by epidural and paraspinal abscess due to brucella infection. *J Pak Med Assoc*. 2020;70(7):1275-8.
5. Duman A, Akpınar O. Brucellar spondylodiscitis in chronic low back pain patients. *Süleyman Demirel Üniversitesi Sağlık Bilimleri Dergisi*. 2016;7(3):63-5.
6. Esmailnejad-Ganji SM, Esmailnejad-Ganji SMR. Osteoarticular manifestations of human brucellosis: A review. *World journal of orthopedics*. 2019;10(2):54.
7. Bozgeyik Z, Aglamis S, Bozdogan PG, Denk A. Magnetic resonance imaging findings of musculoskeletal brucellosis. *Clinical Imaging*. 2014;38(5):719-23.
8. Demirdal T, Sen P. Risk factors for focal involvement in brucellosis. *Diagnostic Microbiology and Infectious Disease*. 2020;115003.
9. Özden H, Togan T. Osteoarticular Involvement among Brucellosis Cases in Konya City. *Cukurova Medical Journal*. 2015;40(3):483-94.
10. Turan H, Serefhanoglu K, Karadeli E, Togan T, Arslan H. Osteoarticular involvement among 202 brucellosis cases identified in Central Anatolia region of Turkey. *Internal Medicine*. 2011;50(5):421-8.
11. Taşova Y, Saltoğlu N, Şahin G, Aksu H. Osteoarthritic involvement of brucellosis in Turkey. *Clinical rheumatology*. 1999;18(3):214-9.
12. Gotuzzo E, Alarcón GS, Bocanegra TS, Carrillo C, Guerra JC, Rolando I, et al., editors. Articular involvement in human brucellosis: a retrospective analysis of 304 cases. *Seminars in arthritis and rheumatism*; 1982: Elsevier.
13. Colmenero J, Reguera J, Martos F, Sanchez-De-Mora D, Delgado M, Causse M, et al. Complications associated with *Brucella melitensis* infection: a study of 530 cases. *Medicine*. 1996;75(4):195-211.
14. Mousa ARM, Muhtaseb SA, Almudallal DS, Khodeir SM, Marafie AA. Osteoarticular complications of brucellosis: a study of 169 cases. *Reviews of infectious diseases*. 1987;9(3):531-43.

15. Weil Y, Mattan Y, Liebergall M, Rahav G. Brucella prosthetic joint infection: a report of 3 cases and a review of the literature. *Clinical Infectious Diseases*. 2003;36(7):e81-e6.
16. Hashemi SH, Keramat F, Ranjbar M, Mamani M, Farzam A, Jamal-Omidi S. Osteoarticular complications of brucellosis in Hamedan, an endemic area in the west of Iran. *International journal of infectious diseases*. 2007;11(6):496-500.
17. Buchanan TM, Sulzer CR, Frix MK, Feldman RA. Brucellosis in the United States, 1960-1972: an abattoir-associated disease. *Medicine*. 1974;53(6):415-25.
18. Pourbagher A, Pourbagher MA, Savas L, Turunc T, Demiroglu YZ, Erol I, et al. Epidemiologic, clinical, and imaging findings in brucellosis patients with osteoarticular involvement. *American Journal of Roentgenology*. 2006;187(4):873-80.
19. Geyik MF, GüR A, Nas K, Cevik R, Saraç J, Dikici B, et al. Musculoskeletal involvement of brucellosis in different age groups: a study of 195 cases. *Swiss medical weekly*. 2002;132(7-8):98-105.
20. Bosilkovski M, Krteva L, Caparoska S, Dimzova M. Osteoarticular involvement in brucellosis: study of 196 cases in the Republic of Macedonia. *Croat Med J*. 2004;45(6):727-33.
21. Bodur H, Erbay A, Çolpan A, Akıncı E. Brucellar spondylitis. *Rheumatology international*. 2004;24(4):221-6.
22. Bozgeyik Z, Ozdemir H, Demirdag K, Ozden M, Sonmezgoz F, Ozgocmen S. Clinical and MRI findings of brucellar spondylodiscitis. *European journal of radiology*. 2008;67(1):153-8.
23. Arkun R, Mete BD, editors. *Musculoskeletal brucellosis*. Seminars in musculoskeletal radiology; 2011: © Thieme Medical Publishers.
24. Harman M, Unal Ö, Onbaşı K, Kıymaz N, Arslan H. Brucellar spondylodiscitis: MRI diagnosis. *Clinical imaging*. 2001;25(6):421-7.
25. Yang X, Zhang Q, Guo X. Value of magnetic resonance imaging in brucellar spondylodiscitis. *La radiologia medica*. 2014;119(12):928-33.
26. Solera J, Lozano E, Martínez-Alfaro E, Espinosa A, Castillejos ML, Abad L. Brucellar spondylitis: review of 35 cases and literature survey. *Clinical infectious diseases*. 1999;29(6):1440-9.
27. Gonzalez-Gay M, Garcia-Porrua C, Ibanez D, Garcia-Pais M. Osteoarticular complications of brucellosis in an Atlantic area of Spain. *The Journal of rheumatology*. 1999;26(1):141-5.
28. Namiduru M, Karaoglan I, Gursoy S, Bayazit N, Sirikci A. Brucellosis of the spine: evaluation of the clinical, laboratory, and radiological findings of 14 patients. *Rheumatology international*. 2004;24(3):125-9.
29. Bosilkovski M, Kirova-Urosevic V, Cekovska Z, Labacevski N, Cvetanovska M, Rangelov G, et al. Osteoarticular involvement in childhood brucellosis: experience with 133 cases in an endemic region. *The Pediatric infectious disease journal*. 2013;32(8):815-9.
30. Zamani A, Kooraki S, Mohazab RA, Zamani N, Matloob R, Hayatbakhsh MR, et al. Epidemiological and clinical features of Brucella arthritis in 24 children. *Annals of Saudi medicine*. 2011;31(3):270-3.
31. Al-Eissa YA, Kambal AM, Alrabeeh A, Abdullah A, Al-Jurayyan NA, Al-Jishi NM. Osteoarticular brucellosis in children. *Annals of the rheumatic diseases*. 1990;49(11):896-900.
32. Aktar F, Tekin R, Bektaş MS, Güneş A, Köşker M, Ertuğrul S, et al. Diagnostic role of inflammatory markers in pediatric Brucella arthritis. *Italian journal of pediatrics*. 2016;42(1):3.
33. Çiftdoğan DY, Aslan S. Osteoarticular involvement of brucellosis in pediatric patients: clinical and laboratory characteristics. *Turkish Journal of Pediatrics*. 2020;62(2).
34. Özaksoy D, Yücesoy K, Yücesoy M, Kovanlıkaya I, Yüce A, Naderi S. Brucellar spondylitis: MRI findings. *European Spine Journal*. 2001;10(6):529-33.
35. Mrabet D, Mizouni H, Khiari H, Rekik S, Chéour E, Meddeb N, et al. Brucellar spondylodiscitis affecting non-contiguous spine levels. *Case Reports*. 2011;2011.
36. Tekkök IH, Berker M, Özcan OE, Özgen T, Akalin E. Brucellosis of the spine. *Neurosurgery*. 1993;33(5):838-44.
37. de Divitiis O, Elefante A. Cervical spinal brucellosis: a diagnostic and surgical challenge. *World neurosurgery*. 2012;78(3-4):257.
38. Sharif HS, Aideyan OA, Clark DC, Madkour MM, Aabed MY, Mattsson TA, et al. Brucellar and tuberculous spondylitis: comparative imaging features. *Radiology*. 1989;171(2):419-25.
39. Jung N-Y, Jee W-H, Ha K-Y, Park C-K, Byun J-Y. Discrimination of tuberculous spondylitis from pyogenic spondylitis on MRI. *American Journal of Roentgenology*. 2004;182(6):1405-10.
40. Tali ET, Gültekin S. Spinal infections. *European radiology*. 2005;15(3):599-607.