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Original Article

Evaluation of risk factors for the development of bacteremia and complications in patients with brucellosis: Is it possible to predict the clinical course?

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Abstract

Introduction: Brucellosis is often confused with other diseases or accompanies the conditions it imitates. It causes treatment delays, failure, relapse, and complications. This study aimed to investigate bacteremia and complication predictors in Brucellosis patients. Early detection may help reduce relapse rates, length of hospital stay, and surgical intervention rates by providing appropriate treatment.

Methodology: We examined 220 adult patients diagnosed with Brucellosis in our tertiary care hospital in the Black Sea Region between January 01, 2010, and January 01, 2022. Patients with and without bacteremia and complications were compared regarding demographic characteristics, clinical features, and laboratory parameters.

Results: The mean age was 46.4 ± 15.8 years (18-96 years), and 61% were male. Low back pain and absence of muscle pain were independent risk factors for predicting bacteremia (p = 0.049, p = 0.043, respectively). Weakness /fatigue, weight loss, and 1/320 Standard Tube Agglutination Test (STAT) or Brucella Coombs Gel Test (BCGT) titers were independent risk factors that reduced the risk of complications; in contrast, low back pain and splenomegaly were independent risk factors for development of complications. (p = 0.025, p = 0.007, p = 0.008, p = 0.003, p = 0.021 respectively). Thrombocytopenia was related to complications. When the platelet cut-off value was taken as 160,000/µL in predicting complications, the sensitivity was 31.30%, and the specificity was 97.73% (p = 0.011).

Conclusions: The risk of clinical progression and complications could be predicted with symptoms and signs such as myalgia, low back pain, weakness/fatigue, weight loss, splenomegaly, and easily accessible laboratory parameters such as serum STAT/BCGT titer and platelet level.

Key words: Brucellosis; blood culture; bacteremia; complication; risk factors.

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Introduction

Brucellosis is one of the most common diseases in humans and animals. Although it is common, especially in developing countries, it is endemic in regions dealing with animal husbandry [1,2]. Brucellosis is transmitted especially from unpasteurized milk and dairy products or after close and frequent contact with sick animals [1,3]. Due to the ability of the disease to involve all organ systems, cases may present with different clinical presentations, which lead to misdiagnosis and treatment. Focal complications developing in many systems, especially musculoskeletal ones, cause increased morbidity [4]. Although brucellosis rarely causes death, its complications significantly impair the quality of life [5-8]. The number of studies investigating the development of complications is limited [9-11].

Clinically, it can be seen as acute, subacute, chronic, relapsed, or asymptomatic infection. Bacteremia may develop in brucellosis cases. Late diagnosis of the disease may increase the frequency of bacteremia [1-3,12]. In some cases, relapse may develop due to deficiencies in the treatment process. Close monitoring of bacteremia in these cases is essential in terms of prognosis [5,12].

This study aimed to investigate the factors affecting bacteremia and complication development in brucellosis cases.

Methodology

Demographic Data

This study is a single-center retrospective study conducted by Ondokuz Mayis University, Medical Faculty Hospital, Infectious Diseases and Clinical Microbiology Clinic. Our hospital is a large regional hospital with 110 tertiary intensive care beds and a total bed capacity of 1100 in the Black Sea Region of Turkey. Patients 18 years or older with Brucella

Standard Tube Agglutination Test (STAT) or Brucella Coombs Gel Test (BCGT) titer ≥ 1/160 and those with blood cultures which revealed *Brucella spp*. were included in the study. Among the cases, those with false positive result, those with insufficient data or who got treatment in another medical center, pregnant patients, and those with organ involvement that could not be distinguished from comorbid diseases were excluded.

Data on demographic characteristics, symptoms, physical examination findings, laboratory parameters, blood culture positivity, presence and type of complications, clinical classification, and drainage/surgical procedures applied to the patients included in the study were obtained from the electronic registry system of our hospital. Patients were divided into groups according to the development of *Brucella spp.* bacteremia and the development of complications.

This study was approved by the local ethics committee of our university with the decision number 306/2022.

Clinical Descriptions

Cases were classified as acute (0-2 months), subacute (2-12 months), and chronic (> 12 months) as the duration of clinical signs and symptoms. Relapse was defined as clinical cases with symptoms and signs occurring or culture growth within six months after the completion of treatment [4]. The asymptomatic cases were defined as patients who coincidentally accompanied different clinical diagnoses, and those confirmed in laboratory tests.

The presence of symptoms and signs of infection in any anatomical region in a patient diagnosed with brucellosis was considered a complication. Haematological, osteoarticular, gastrointestinal, cardiovascular, genitourinary, neurological, ocular, pulmonary, and dermatological involvements were recorded. Ultrasonography (USG) and magnetic resonance imaging (MRI) studies were scanned and recorded to identify complications and organomegaly.

As the hematological complications, anemia was defined as a hemoglobin level less than 12 g/dL in women and 14g/dL in men in complete blood count; leukopenia as a leukocyte level below 4000/μL, and thrombocytopenia was defined as platelet level below 150,000/μL. Thrombocytopenia levels were also graded as below 50,000/μL and between 50,000-150,000/μL. The study did not include patients with abnormal haematological parameters due to concomitant diseases and pregnancy.

Hepatic involvement was defined as an increase of more than 5-fold in the alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels that any other reason could not explain [4,9,19]. Isolation of *Brucella spp.* in cerebrospinal fluid (CSF) and/or STAT/BCGT positivity at any titer accompanied by symptoms defined as a neurological complication. Infective Endocarditis Diagnostic Criteria According to the European Society of Cardiology 2015, Modifications were used to diagnose endocarditis. Accordingly, the presence of two major or one major plus three minor or five minor criteria, considering major findings such as positive blood culture and endocardial involvement compatible with infective endocarditis, and minor evidence such as predisposing factor, fever, vascular event, immunological event, and microbiological tests, makes the diagnosis of endocarditis [13].

Microbiological Tests

A diagnosis of brucellosis was made with serology or culture positivity accompanying clinical findings. Serological test positivity was accepted as STA test titer ≥ 1/160 with specific antiserum (Pendik Veterinary Control and Research Institute, Istanbul, Turkey) or ≥ 4-fold increase in STA test titer repeated 2-3 weeks apart [14,15]. Blood, bone marrow and other sterile body fluids were incubated with the BacT/Alert (BioMérieux, France) automated system. *Brucella spp*. were detected by VITEK2 Compact (BioMérieux, France) and VITEK MS (BioMérieux, France) devices.

Statistical analysis

All statistical analyzes in the study were done using SPSS V23 software (IBM SPSS, Chicago, IL, USA). Descriptive data were given as numbers and percentages. Comparisons between groups regarding categorical variables were made with the Chi-square test and Fisher's Exact Test. The compatibility of continuous variables with normal distribution was verified with the Kolmogorov-Smirnov Test. Differences between groups in continuous variables were evaluated with the Student's t-Test. Risk factors affecting complication and bacteremia were analyzed with a binary logistic regression model. Pearson's chi-square test was used to compare laboratory results, symptoms, and complications according to clinical outcome, and multiple comparisons were analyzed with Bonferroni corrected Z test. Analysis results were presented as mean ± standard deviation for quantitative data and as frequency (percentage) for categorical data. The cut-off value of quantitative parameters in predicting complications and bacteremia was determined by ROC analysis.

Table 1. Comparison of laboratory results, symptoms and complications by clinical situation

n (%)	Acute 120 (54.5%)	Subacute 65 (29.5%)	Chronic 17 (7.7%)	Relaps 12 (5.4%)	Asymptomatic 3 (1.3%)	Test statistics	*p*
Fever							
None	25 (20.8)a	34 (52.3)b	13 (76.5)b	8 (66.7)b	3 (100)b	40.31	**< 0.001**
Present	95 (79.2)	31 (47.7)	4 (23.5)	4 (33.3)	0 (0)		
Back pain							
None	80 (66.7)a	22 (34.4)b	7 (41.2)ab	4 (33.3)ab	3 (100)ab	23.389	**< 0.001**
Present	40 (33.3)	42 (65.6)	10 (58.8)	8 (66.7)	0 (0)		
Splenomegaly							
None	113 (94.2)a	58 (89.2)ab	13 (76.5)ab	8 (66.7)b	3 (100)ab	13.241	**0.010**
Present	7 (5.8)	7 (10.8)	4 (23.5)	4 (33.3)	0 (0)		
Complication							
None	51 (42.5)ab	21 (32.3)ab	10 (58.8)ab	1 (8.3)b	3 (100)a	13.970	**0.007**
Present	69 (57.5)	44 (67.7)	7 (41.2)	11 (91.7)	0 (0)		
Osteoarticular complication							
None	98 (81.7)a	35 (53.8)b	13 (76.5)ab	7 (58.3)ab	3 (100)ab	18.589	**0.001**
Present	22 (18.3)	30 (46.2)	4 (23.5)	5 (41.7)	0 (0)		
Spondylodiscitis							
None	105 (87.5)a	39 (60)b	13 (76.5)ab	8 (66.7)ab	3 (100)ab	19.935	**0.001**
Present	15 (12.5)	26 (40)	4 (23.5)	4 (33.3)	0 (0)		
Growth in blood culture							
None	97 (80.8)	62 (95.4)	15 (88.2)	11 (91.7)	3 (100)	8.549	0.073
Present	23 (19.2)	3 (4.6)	2 (11.8)	1 (8.3)	0 (0)		
Thrombocytopenia							
< 50000	32 (26.7)a	4 (6.2)b	2 (11.8) ab	3 (25) ab	0 (0)ab	13.170	**0.010**
50000 ≤×< 150000	88 (73.3)	61 (93.8)	15 (88.2)	9 (75)	3 (100)		

Pearson's chi-square test was used, a-b: There is no difference between clinical results with the same letter.

Table 2. Comparison of clinical and laboratory findings affecting reproduction in blood culture and regression analysis.

n (%)	Growth in blood culture		Univariate		Multivariate	
	None 191 (86.8%)	Present 29 (13.2%)	OR (95% CI)	*p*	OR (95% CI)	*p*
Fever	107 (79.3)	28 (20.7)	21.98 (2.93 - 164.88)	**0.003**	---	---
Sweating/Chills	39 (76.5)	12 (23.5)	0.36 (0.16 - 0.82)	**0.015**	4.93 (0.72 - 33.72)	0.104
Myalgia	61 (91)	6 (9)	0.56 (0.22 - 1.44)	**0.225**	0.1 (0.01 - 0.93)	**0.043**
Back pain	89 (89)	11 (11)	0.69 (0.31 - 1.55)	**0.371**	6.7 (1.01 - 44.49)	**0.049**
Headache	18 (72)	7 (28)	3.06 (1.15 - 8.14)	**0.025**	1.23 (0.2 - 7.49)	0.823
Splenomegaly	16 (72.7)	6 (27.3)	2.84 (1.01 - 7.98)	**0.048**	2.79 (0.21 - 36.35)	0.434
Complication	108 (82.4)	23 (17.6)	2.95 (1.15 - 7.56)	**0.025**	0.68 (0.09 - 5.33)	0.713
STA titer						
1/320	147 (89.6)	17 (10.4)	0.28 (0.11 - 0.68)	**0.005**	1.44 (0.1 - 20.43)	0.790
1/640	19 (90.5)	2 (9.5)	0.25 (0.05 - 1.29)	**0.099**	1.6 (0 - 802.89)	0.882
Anemia	108 (80)	27 (20)	10.25 (2.37 - 44.35)	**0.002**	6.83 (0.91 - 51.1)	0.061
WBC (mean ± SD)	7221.74 ± 3435.75	5598.97 ± 3528.79	0.98 (0.97 - 1)	**0.016**	0.99 (0.95 - 1.04)	0.708
PLT (mean ± SD)	261857.89 ± 109445	162586.21 ± 107400.29	0.99 (0.99 - 1)	**< 0.001**	0.99 (0.98 - 1)	0.093
PLT						
< 50000	28 (68.3)	13 (31.7)		**Reference values**		
50000 ≤ x < 150000	162 (91)	16 (9)	0.21 (0.09 - 0.49)	**< 0.001**	0.49 (0.04 - 7)	0.602
AST (ort ± SS)	47.39 ± 77.14	116.63 ± 135.31	1.01 (1 - 1.01)	**0.007**	1.02 (0.99 - 1.05)	0.140
ALT (ort ± SS)	42.53 ± 64.57	79.7 ± 94.58	1.01 (1 - 1.01)	**0.039**	0.98 (0.95 - 1.02)	0.292
CRP (ort ± SS)	44.31 ± 50.42	78.68 ± 70.39	1.01 (1 - 1.02)	**0.006**	1.01 (0.99 - 1.02)	0.296

OR: Odds ratio; CI: Confidence interval; STA: Standard tube agglutination; WBC: White blood cells; SD: Standard deviation; PLT: Platelet; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; CRP: C-reactive protein.

The results were evaluated within the 95% confidence interval, and $p < 0.05$ values were considered significant.

Results

Of the 232 patients included in the study, 12 were excluded, and 220 patients were analyzed. Clinical classification information could not be obtained in three patients. The mean age of the patients was 46.4 ± 15.8 (18-96) years, and 61% were male. Among the patients, 120 (54.5%) were classified as acute, 65 (29.5%) as subacute, and 17 (7.7%) as chronic. Twelve (5.4%) cases presented with relapse, and three (1.3%) cases resulted in death.

The fever was significantly higher in patients with the acute clinical picture ($p < 0.001$). Low back pain was significantly higher in patients in the subacute clinical group ($p < 0.001$). The presence of splenomegaly was found to be significantly higher in patients with relapse compared to patients with the acute clinical picture ($p = 0.01$). The rate of thrombocyte levels below 50,000/μL was significantly higher in patients in the acute group compared to those in the subacute clinical picture ($p = 0.01$). The rate of osteoarticular complications and spondylodiscitis classified in this group were significantly higher in patients in the subacute group ($p = 0.001$ for both) (Table 1).

Brucella spp. were detected in the blood culture of 29 (13.2%) patients, and 69% of *Brucella spp*. isolates were identified as *Brucella melitensis.* The rate of blood culture positivity was significantly higher in those with fever, headache, splenomegaly and complications ($p = 0.003$, $p = 0.025$, $p = 0.048$ and $p = 0.025$ respectively). Blood culture positivity was significantly lower in patients with sweating/chills and serum STAT/BCGT titer of 1/320 ($p = 0.015$, $p = 0.005$, respectively). The presence of anemia was significant in those with bacteremia, and serum leukocyte and thrombocyte levels were significantly lower ($p = 0.002$, $p = 0.016$, $p < 0.001$, respectively). In addition, those with platelet levels below 50,000/μL were more associated with bacteremia than those between 50,000-150,000/μL ($p < 0.001$). Serum AST, ALT, and C-reactive protein (CRP) levels were significantly higher in those with bacteremia ($p = 0.007$, $p = 0.039$ and $p = 0.006$, respectively). In the regression analysis, the presence of muscle pain decreased bacteremia risk by 0.1 times [95% Cl; (0.01 - 0.93) $p = 0.043$], the presence of low back pain increased the risk by 6.7 times [95% Cl; (1.01 - 44.49), $p = 0.049$], and both were determined as independent risk factors (Table 2).

It was determined that there was no difference between the groups in terms of gender, age, duration of symptoms, clinical classification, transmission route, reinfection and invasive intervention/surgical procedures, other symptoms, and laboratory parameters in terms of bacteremia ($p > 0.05$ for each).

Complications developed in 131 (59.5%) of the patients. Complications determined in order of frequency were haematological (56.4%), osteoarticular (27.7%), gastrointestinal (26.6%), neurological (4.09%), genitourinary (4.09%), and pulmonary (2.07%), dermatological (1.36%), cardiac (0.9%), and ocular (0.9%). The complication development rate was 91.7% in relapsing brucellosis, 67.7% in subacute, 57.5% in acute, and 41.2% in chronic clinical picture. No complications developed in asymptomatic patients. Complications were significantly higher in recurrent cases compared to asymptomatic cases, but there was no difference between other clinical classifications ($p = 0.007$) (Table 1).

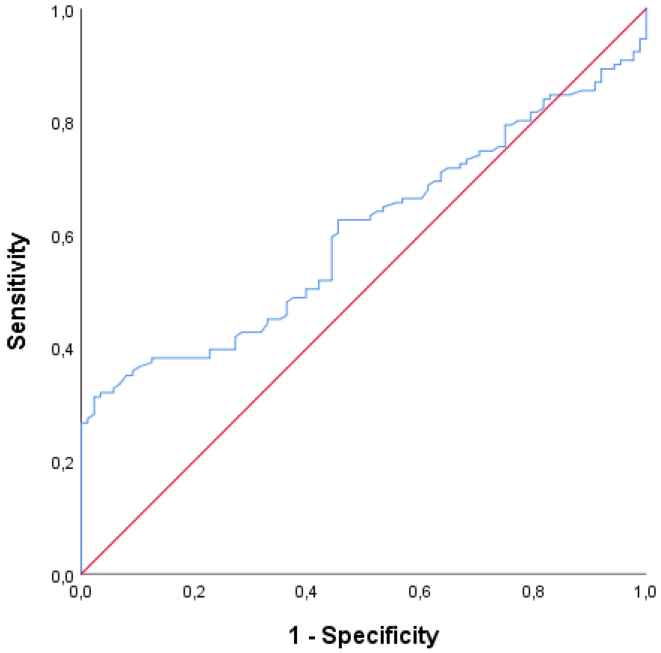
Table 3. Comparison of clinical and laboratory findings affecting the complication and regression analysis

n (%)	Complication		Univariate		Multivariate	
	None 89 (40.5%)	Present 131 (59.5%)	OR (95% CI)	*p*	OR (95% CI)	*p*
Age (mean ± SD)	43.75 ± 15.1	48.27 ± 16.12	1.02 (1 - 1.04)	**0.039**	1.01 (0.983 - 1.045)	0.390
Arthralgia	43 (49.4)	44 (50.6)	0.54 (0.31 - 0.94)	**0.029**	0.41 (0.15 - 1.13)	0.086
Weakness/fatigue	41 (47.1)	46 (52.9)	0.63 (0.37 - 1.1)	0.104	0.35 (0.14 - 0.87)	**0.025**
Weight loss	26 (51)	25 (49)	0.57 (0.3 - 1.07)	0.082	0.21 (0.07 - 0.65)	**0.007**
Back pain	32 (32)	68 (68)	1.95 (1.12 - 3.4)	**0.018**	4.16 (1.622 - 10.667)	**0.003**
Splenomegaly	5 (22.7)	17 (77.3)	2.475 (0.878 - 6.979)	0.087	13.54 (1.47 - 124.62)	**0.021**
Titer category						
1/160	4 (11.8)	30 (88.2)				
1/320	72 (43.9)	92 (56.1)	0.17 (0.06 - 0.51)	**0.001**	0.1 (0.02 - 0.56)	**0.008**
1/640	12 (57.1)	9 (42.9)	0.1 (0.03 - 0.39)	**0.001**	0.06 (0 - 1.07)	0.055
Growth in blood culture	6 (20.7)	23 (79.3)	2.95 (1.15 - 7.56)	**0.025**	1.3 (0.24 - 6.89)	0.760
Anemia	42 (31.1)	93 (68.9)	2.68 (1.53 - 4.71)	**0.001**	1.82 (0.72 - 4.61)	0.204
WBC (mean ± SD)	7479.32 ± 2704.98	6689.47 ± 3899.24	0.99 (0.99 - 1)	0.106	1.01 (0.99 - 1.03)	0.426
PLT (mean ± SD)	267715.91 ± 74214.96	235946.56 ± 133084.43	1 (0.995 - 1)	**0.046**	1 (1 - 1.01)	0.654

OR: Odds ratio; CI: Confidence interval; WBC: White blood cells; SD: Standard deviation; PLT: Platelet.

The older age and low back pain rates were significantly higher in patients with complications, but the arthralgia rate was significantly lower (p = 0.039, p = 0.018, p = 0.029, respectively). Gender, duration of symptoms, transmission route, reinfection status, other symptoms, and laboratory parameters were similar in terms of complication development rate (p > 0.05 for each). Complication risk was significantly lower in patients with serum STAT/BCGT titer of 1/320 and 1/640 (p = 0.001). The presence of anemia and low platelet levels were significant in cases with complications (p = 0.001, p = 0.046, respectively). In the regression analysis, weakness/fatigue decreased the complication risk by 0.35 times [Odds Ratio (OR); 95% Cl; (0.14 - 0.87), p = 0.025], the presence of weight loss by 0.21 times [OR; 95% Cl; (0.07 - 0.65), p = 0.007], 1/320 STAT/BCGT titer level by 0.1 times [OR; 95% Cl; (0.02 - 0.56), p = 0.008]. However, the presence of low back pain increased the complication risk by 4.16 times [OR; 95% Cl; (1,622 - 10,667), p = 0.003], and splenomegaly by 13.54 times [OR; 95% CI; (1.47 - 124.62), p = 0.021], and both were determined as independent risk factors (Table 3). The AUC value of the platelet value in predicting complications was found to be statistically significant with 0.601 (p = 0.011). When the cut-off value was taken as 160,000, the sensitivity was 31.30%, and the specificity was 97.73% (Table 4) (Figure 1).

Figure 1. PLT value in predicting complications.



Discussion

The rate of bacteremia in brucellosis varies between 15-90% [1,16]. Complications ranging from focal involvement to mortality can be encountered in cases with *Brucella spp*. bacteremia. Therefore, it is crucial to determine the risk by looking at the patient's clinical findings to prevent complications [3,5,6,12]. In studies, the rate of fever was reported as significantly higher than in non-bacteremic patients [1,17,18]. In our study, the presence of fever increased the rate of bacteremia by 21.9 times. Copur *et al.* showed the presence of headache and muscle pain as independent risk factors for bacteremia [19]. However, Shi *et al.* reported a significantly lower rate of bacteremia in patients with muscle pain [20]. In our study, the headache increased the risk, while muscle pain and sweating decreased the risk. These conflicting results can be associated with the characteristics of the patients in the samples and the differences in sample size. In addition, low back pain and splenomegaly rates were significantly higher in bacteremic cases, and low back pain was an independent risk factor for bacteremia. The involvement of the spleen, which is a part of the reticuloendothelial system, by *Brucella spp*., an intracellular facultative aerobic bacterium, may explain splenomegaly. This result is consistent with the findings of Apa *et al.* [21].

In this study, hemoglobin, leukocyte, and thrombocyte levels were significantly lower in patients with bacteremia. However, these were insignificant in the multivariate model. All these findings can be explained by bone marrow involvement during bacteremia or sepsis. Thrombocytopenia may be found in 3-26% of brucellosis cases [3-6,12,22]. In our study, the rate of the ones with a platelet level below 50,000/μL was significantly higher in those with acute clinical picture or bacteremia. Studies also report that ALT and AST levels are similar between bacteremic and non-bacteremic groups [17,20]. However, in our study, serum CRP, ALT and AST levels were significantly higher in patients with bacteremia. The involvement of the liver, a member of the reticuloendothelial system, may explain these findings. The data in the literature reveal that the serum

Table 4. Investigation of cut-off value for PLT by ROC analysis in predicting complications.

	Break point	AUC (95% CI)	*p*	Sensitivity	Specificity	PPV	NPV
Thrombocyte	≤ 160000 /mL	0.601 (0.527 - 0.675)	**0.011**	31.30%	97.73%	95.35%	48.86%

AUC: Area under curve; CI: Confidence interval; PPV: Positive predictive value; NPV: negative predictive value.

STAT/BCGT titer is successful in diagnosing rather than evaluating the success of patient follow-up and treatment [23]. However, in our study, bacteremia was significantly lower than 1/160 in patients with a STAT/BCGT titer of 1/320. This finding suggested that the risk of bacteremia may be high due to the low antibody titer in the early period. However, the lack of significant results at higher titers may be attributed to insufficient cases with higher titers.

It has been reported that the rate of complication development in brucellosis cases varies between 36-90%, and the most common complications are skeletal-muscular, gastrointestinal, haematological, and genitourinary involvement. The relationship between the clinical classification of the disease and the development of complications is not clear in the literature [4,9,10,19,24]. In our study, the incidence of complications was 59.5%, and the most common ones were haematological, osteoarticular, and gastrointestinal complications. In our study, the rate of complication development was highest in patients who presented with relapse. The rate of osteoarticular complications was significantly higher in patients with subacute clinics. Accordingly, patients with subacute clinics should be evaluated more thoroughly regarding osteoarticular complications, especially spondylodiscitis. This finding could play an essential role in reducing the rate of surgical intervention, hospitalization day and cost, and preventing morbidity and loss of workforce.

It has been reported that there is no significant clinical change with age in brucellosis cases [1-3,12]. However, in one of the studies no relationship was found between age and complications, while in another study, it was reported that the mean age was significantly higher in cases with complications [9,19]. In this study, the older age was significantly higher in patients with complications. This finding supports that elderly patients should be followed more closely for complications.

Copur *et al.* reported that the risk of developing complications in patients with low back pain increased 3.2 times [19]. In our study, the risk of complications was found to be 4.1 times higher in patients with low back pain. This result shows that low back pain can be used as a complication marker. Splenomegaly has been reported in 29-56.6% of brucellosis cases [25]. In the pathogenesis, 15-30% of *Brucella spp.* survive in the phagosome and cause localized or systemic infection in organs such as the kidney, liver, spleen, breast, and joints via the lymphatic system [26]. In this study, the rate of splenomegaly was significantly higher in patients with relapse clinics. Therefore, in our study, it was not surprising that splenomegaly was found as an independent risk factor in predicting complications.

The literature has reported that the rate of arthralgia in patients with complications is similar to those without complications [9,19]. In our study, the rate of complication development was significantly lower in patients with joint pain and weakness/fatigue. This finding can be explained by early admission to a health institution due to limited mobility and decreased quality of life. However, arthritis complications should be kept in mind in patients with arthralgia. Weight loss is one of the rare findings in some cases [2,3,12]. While some studies reported that the rates of weight loss were similar in cases with and without complications, it was reported as a factor increasing the risk of complications in some studies [9,10,19]. In our study, the complication rate was significantly lower in those with weight loss. However, not evaluating weight loss quantitatively can explain this inconsistency in results. More comprehensive studies are needed to use the weight loss finding as a complication marker.

It is controversial whether there is a direct relationship between the development of complications and bacteremia in brucellosis cases. Copur *et al.* and Demirdal *et al.* reported that blood culture positive was similar in groups with and without focal involvement [9-11,19]. In this study, bacteremia increased the risk of complications 2.9 times. This result can be explained by the fact that bacteremia causes focal abscess foci in the tissues.

The effect of anemia on the prognosis of brucellosis is not apparent [9,10,19]. Kerget et al. showed that platelet level is an easily accessible marker in the evaluation and follow-up of organ involvement in cases with brucellosis [27]. In our study, low hemoglobin and thrombocyte levels were found to be significantly related with complications. Thrombocytopenia can be explained by bone marrow suppression, hypersplenism, hemophagocytosis, diffuse intravascular coagulation and immune destruction of platelets in brucellosis [22]. The low sensitivity and high specificity of the platelet cut-off value determined in our study to predict complications suggest that it will be meaningful in supporting the diagnosis rather than screening, but more comprehensive studies are needed.

The literature has reported that there is no difference between cases with and without complications in terms of gender, serum STAT/BCGT titer levels and transmission routes. Copur *et al.* and Demirdal *et al.* reported that STAT positivity ≥ 1/160 was similar in groups with and without focal

involvement [9,19]. Alsubaie et al. also showed no correlation between antibody titer of brucellosis and clinical outcomes, and they reported no correlation between baseline serology and culture positivity [29]. Our results were different from the literature. The complication rate in our patients with STAT/BCGT titers of 1/320 and 1/640 was lower than those with 1/160. The 1/320 STAT/BCGT titer was a protective, independent marker for the development of complications. This finding can be explained by the inability to limit the infection with low antibody titer and the insufficient number of high titer cases. In addition, STAT mainly detects IgM positivity, which may be negative in complicated cases, but BCGT, Brucella Capt and ELISA detect higher levels of IgG positivity in complicated cases [28]. The use of STAT in diagnosing the cases included in our study until 2014 can be associated with this result.

The cross-sectional planning of the study, the need for regular and long-term follow-up because most of the patients live in rural areas, and the low number of cases with some data examined in case groups limited the study. However, this study's high number of cases, which was conducted in a low endemic region, strengthens the findings.

Conclusions

This study showed that clinical progression and complication risk could be predicted in brucellosis cases with easily accessible clinical and laboratory parameters such as myalgia, low back pain, weakness/fatigue, weight loss, splenomegaly, and serum STAT/BCGT titer and platelet level. In addition, we can prevent labor loss and reduce the rate of surgical intervention, length of hospital stay and cost with our findings.

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