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Original Article

Predictive Significance of Laboratory Tests in Bacteremic Brucellosis

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Abstract

Background: Brucellosis is one of the most common zoonotic infections. Although culture is the gold standard diagnostic method, bacterial growth in blood cultures may not always occur due to various factors. We aimed to investigate demographic, clinical, and laboratory findings that may have predictive significance for bacteremia in brucellosis.

Methods: Patients older than 18 years of age followed up with a diagnosis of brucellosis between 2012 and 2022 were included in this retrospective multicenter study. They were divided into two main subgroups according to their *Brucella* species reproductive status as bacteremic and non-bacteremic.

Results: A total of 743 patients, 370 (49.80%) bacteremic and 373 (50.20%) non-bacteremic brucellosis patients, were enrolled. The mean age of the bacteremic group (36.74 years) was lower than the non-bacteremic group (43.18 yr). High fever, chills/cold, sweating, nausea, vomiting, and weight loss were more common in the bacteremic group. In the bacteremic group, white blood cell count, platelet count, hemoglobin level, mean platelet volume, eosinophil, and neutrophil counts were lower, and lymphocyte, erythrocyte sedimentation rate, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, and ferritin levels were higher. According to the receiver operating characteristic (ROC) analysis, when the cut-off value of ferritin was considered 67, it was the parameter with the strongest predictive significance in *Brucella* bacteremia.

Conclusion: High ferritin level, low eosinophil count, and increased erythrocyte sedimentation rate were determined as the most critical laboratory findings in predicting bacteremia in brucellosis.

Introduction

Brucellosis is one of the most common zoonotic infections worldwide caused by the genus *Brucella*, a facultative intracellular pathogen, and continues to be a vital health problem in developing countries (1,2). Mediterranean basin, Balkans, Persian Gulf, Middle East are the regions where the disease is endemic (3). It is mainly determined in Central Anatolia, Eastern and Southeastern Anatolia regions in Turkey (4). While approximately 500,000 human cases of brucellosis are reported each year, it is estimated that official figures do not fully reflect the actual numbers (5). Disease transmission occurs through consuming unpasteurized milk/milk products, inhaling infected aerosols, or mucosal/skin contact of secretions from sick animals (6).

Brucellosis can be mistaken for various diseases since it causes various clinical presentations, from non-specific symptoms to severe symptoms, and because it involves many organs, as the diagnosis of the disease can be challenging (7). The most commonly defined symptoms and signs are high fever, muscle-joint pain, weakness, and loss of appetite (8). Due to the presence of variable and non-specific symptoms, microbiological laboratory approaches are very crucial for the diagnosis and follow-up of their cases. Laboratory diagnosis can be performed using three different approaches and microbiological procedures: direct diagnosis by culture, indirect diagnosis by serological tests, and molecular polymerase chain reaction (PCR)-based methods (9). Culture is the "gold standard" method in the laboratory diagnosis of brucellosis. There is always an initial bacteremic phase in the pathogenesis of brucellosis, and blood cultures should always be performed in the presence of clinical suspicion. However, acquiring two or three different blood culture sets is essential due to the low bacterial load during this period. As the infection progresses, the organism is removed from the blood and enters the macrophages, the concentration of bacteria in the circulation decreases, and their isolation becomes even more challenging (9,10). Therefore, isolation of bacteria may not always be possible.

We aimed to investigate demographic, clinical, and laboratory findings that may have predictive significance for bacteremia in brucellosis.

Materials and Methods

Study protocol

This retrospectively designed study included patients over the age of 18 yr and diagnosed with brucellosis who were admitted to the Infectious Diseases and Clinical Microbiology departments of 12 hospitals in Turkey between 2012 and 2022. Information about the patients was obtained from the Hospital Information Management System. The patient's age, gender, occupation, history of animal husbandry, consumption of unpasteurized milk/dairy products, clinical symptoms, and general laboratory and diagnostic tests were analyzed.

Definition of brucellosis and classifications

The brucellosis was diagnosed in the presence of appropriate clinical signs and symptoms and at least one of the following criteria:

a) Standard tube agglutination test (STA) titer of ≥1/160

b) Coombs-STA titer of ≥1/160

c) *Brucella* species (spp.) isolation in sterile body fluids.

Clinical symptoms and signs for less than 2 months were defined as acute, between 2-12 months as subacute, and the presence of more than 12 months as chronic brucellosis (3). Relapse brucellosis was defined as the reappearance of clinical signs and symptoms within 12 months after brucellosis treatment (11).

The patients were divided into two main subgroups, bacteremic and non-bacteremic brucellosis, according to the growth status of *Brucella* spp. in blood culture.

Hematological and biochemical examinations

From laboratory examinations; white blood cell (WBC), hemoglobin (HGB), hematocrit (HCT), platelet (PLT), neutrophil (NEUT), lymphocyte (LYMP), monocyte (MO), eosinophil (EOS), mean platelet volume (MPV), erythrocyte sedimentation ratio (ESR), prothrombin time (PT), international normalized ratio (INR), glucose, blood urea nitrogen (BUN), creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), albumin, total/direct bilirubin (T.bil/D.bil), lactate dehydrogenase (LDH), ferritin, procalcitonin (PCT), C-reactive protein (CRP) parameters were evaluated.

Serological analyzes

Patient blood sent to the laboratory was centrifuged at 3000 rpm for 10 minutes to obtain serum. Samples with positive Rose Bengal test results, used as a screening test, were examined with the STA test for further identification of Brucellosis. Dilutions of 1/40, 1/80, 1/160, 1/320, 1/640, 1/1280 were used in microplates using the Cromatest (Linear chemicals, S.L., Spain) kit, by the manufacturer's recommendations. Results of 1/160 and above were considered positive.

Blood culture analysis

5-10 ml of blood samples taken from the patients were inoculated into blood culture aerobe bottles (Aerob BACT/ALERT FA Plus bioMérieux, France). These vials were incubated in the incubator (BACT/ALERT 3D/60 bioMérieux, France) for 7 days. A few drops were taken from the samples giving a positive signal with the help of an injector, and inoculated into plates containing 5% sheep blood agar medium. Bacterial growth was achieved by keeping the plates in a bacteriological incubator at 37 °C for 48 hours. Oxidase and catalase tests were performed on the colonies that were determined to be Gram-negative coccobacillus by Gram staining, and the colonies with positive tests were evaluated as *Brucella* spp.

Statistical Analysis

Statistical analysis was carried out by utilizing SPSS 22 program (IBM Corp., Armonk, NY, USA). Categorical variables were presented as frequencies and percentages. Continuous variables were evaluated for parametricity using On-Sample Kolmogorov Simirnov test. Parametric (with normal distribution) continuous variables were expressed as mean± standard deviation and non-parametric (without normal distribution) continuous variables were expressed as median ±(third quartile-first quartile). The categorical variables such as sex, age group, occupation etc. of bacteremic and non-bacteremic patients were compared by using Pearson Chi-Square and Fisher exact test. Student T-test for parametric variables and Mann-Whitney U test for non-parametric variables were used to compare the laboratory results of bacteremic and non-bacteremic patients. One-way ANOVA and Kruskall-Wallis tests were applied to detect whether there were statistically significant differences between acute, subacute, chronic and relapse groups in terms of laboratory results. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnosing performance and determined cut-off values of the laboratory variables. The area under the ROC curve (AROC) were also calculated. AROC values higher than 0.9 were considered "outstanding", between 0.8 and 0.9 were considered "excellent", between 0.7 and 0.8 were considered "acceptable", between 0.5 and 0.7 were considered "not good", and lower than 0.5 were considered "no distinction". In all statistical analysis, P values<0.05 were considered as statistically significant.

Ethics committee approval

Approval was obtained from the Ethics Committee of the Faculty of Medicine of Harran University with the date of December 12, 2022, and the decision number of 2022/24/25.

Results

Of the patients, 408 (54.9%) were male. The mean age of all patients was 39.97±14.93 years, being

36.74±14.75 in bacteremic and 43.18±14.42 in non-bacteremic patients. The patients were mostly admitted during the winter season (n=602, 81.0%). The most diagnosed occupational groups were animal caretakers (n=130, 17.5%) and farmers (n=128, 17.2%), and the majority of the patients (n=503, 76%) were determined to live in rural areas. 450 (71.2%) patients described the consumption of unpasteurized fresh cheese. Of the patients, 480 (65.5%) were categorized as acute, 193 (26.3%) subacute, 13 (1.8%) chronic, and 47 (6.4%) relapsed brucellosis. Patients in both the bacteremic (n=301, 83.6%) and non-bacteremic (n=179, 48%) groups had higher admissions in the acute period, and this rate was more pronounced in the bacteremic group.

The most frequently described symptoms by patients were muscle/joint pain (n=606, 84.5%), sweating (4%), high fever (63.4%), and chills (58.7%). The most commonly described symptoms were sweating (86.5%) and muscle/joint pain (84%) in the bacteremic group, while muscle/joint pain (85.3%) and sweating (84%) in the non-bacteremic group (61.93%). Symptoms with statistically significant differences between the bacteremic and non-bacteremic groups were high fever, chills, sweating, nausea, vomiting, and weight loss. It was observed that these symptoms were described at a higher rate in the bacteremic group (Table 1).

Table 1: Distribution of clinical symptoms

Variable	*Overall (n =743)*	*Bacteremic Group (n =370)*	*Nonbacteremic Group (n =373)*	*P*
High fever				
Yes	467 (63.4)	278 (76.4)	189 (50.7)	0.000
No	270 (36.6)	86 (23.6)	184 (49.3)	
Chills				
Yes	427 (58.7)	263 (74.1)	164 (44.0)	0.000
No	301 (41.3)	92 (25.9)	209 (56.0)	
Sweating				
Yes	545 (74.0)	314 (86.5)	231 (61.93)	0.000
No	191 (26.0)	49 (13.5)	142 (38.07)	
Muscle/ joint pain				
Yes	606 (84.6)	288 (84.0)	318 (85.3)	0.35
No	110 (15.4)	55 (16.0)	55 (14.7)	
Anorexia				
Yes	403 (61.7)	208 (61.7)	195 (61.7)	0.53
No	250 (38.3)	129(38.3)	121 (38.3)	
Nausea				
Yes	219 (33.5)	128 (38.0)	91 (28.8)	0.01
No	434 (66.5)	209 (62.0)	225 (71.2)	
Vomiting				
Yes	167 (25.6)	104 (30.8)	63 (20.1)	0.001
No	485 (74.4)	234 (69.2)	251 (79.9)	
Headache				
Yes	256 (39.1)	133 (39.3)	123 (38.9)	0.49
No	398 (60.9)	205 (60.7)	193 (61.1)	
Weight loss				
Yes	196 (34.0)	115 (41.7)	81 (26.9)	0.00
No	381 (66.0)	161 (58.3)	220 (73.1)	

Hepatomegaly was the most common pathological finding in patients who underwent abdominal or superficial tissue ultrasonography (USG). Statistically significant differences were demonstrated between the patient groups in terms of hepatomegaly, splenomegaly, lymphadenopathy, and normal USG findings (*P*=0.01). The rate of pathological USG findings was significantly higher in the bacteremic group (Table 2).

Table 2: Ultrasonography (USG) findings of the patients

USG findings	*Overall (n=273)*	*Bacteremic Group (n=150)*	*Non-bacteremic Group (n=123)*	*P*
Hepatomegaly	85	56	29	
Splenomegaly	68	51	17	
Lymphadenopathy	9	6	3	0.01
(LAP)	111	37	74	
Normal				

While the median or mean values in the laboratory parameters of WBC, HGB, HCT, NEUT, EOS, MPV, PLT, albumin, and glucose levels were statistically lower in the bacteremic group, the median or mean values of LYMP, ESR, PT, BUN, ALT, GGT, T.bil, D.bil, LDH and ferritin were significantly higher in the bacteremic group. There was no statistically significant difference between the bacteremic and non-bacteremic groups regarding MO, INR, creatinine, ALP, and CRP levels (Table 3).

ROC analysis was performed to evaluate the performance of laboratory parameters in diagnosing bacteremia (Table 4). Accordingly, the performances of only EOS (0.73), ESR (0.70), and ferritin (0.75) parameters in bacteremia were observed within acceptable limits. The diagnostic performances of other parameters were evaluated as "not good." The results from the ROC analysis can be summarized as follows:

- Patients with an EOS count below 64 mm^3 (cut-off value) were classified as "bacteremia." According to EOS, 63.96% of bacteremic patients, 71.66% of non-bacteremic patients, and 67.70% of all brucellosis patients were diagnosed correctly.
- Patients with an ESR value higher than 22/hours were classified as "bacteremia." According to ESR, 65.66% of bacteremic patients, 66.01% of non-bacteremic patients, and 65.84% of all brucellosis patients were diagnosed correctly.
- Patients with a ferritin value higher than 67 ng/ml were classified as "bacteremia." Ferritin correctly classified 87.43% of bacteremic patients, 54.26% of non-bacteremic patients, and 75.48% of all brucellosis patients.
- Ferritin was the parameter with the highest predictive significance in the bacteremia diagnosis.

Table 3: Laboratory results of brucellosis patients

Parameters	*Overall (n =743)*		*Bacteremic Group (n =370)*		*Nonbacteremic Group (n =373)*		*p*
	M	D	M	*D*	M	D	
WBC (mm3)	6895.00	8340-5500	6540.00	8065-5410	7210	8555-5595	0.01
HGB (g/dl)	13.30	14.50-12.20	13.10	1.69*	13.50	14.70-12.40	0.00
HCT (%)	39.67	4.61 *	39.16	4.70*	40	43-37	0.02
NEUT (mm3)	3500.00	4630-2640	3285	4400-2437.50	3750	4900-2885	0.00
LYMP (mm3)	2360.00	2932.50-1770	2430	3060-1790	2240	2800-1710	0.01
MO (mm3)	520.00	700.00-400.00	524	690-400	520	700-400	0.88
EOS (mm3)	80.00	170.00-20.00	40	100-10	110	210-57.50	0.00
MPV (f/L)	9.20	10.00-8.50	9	9.8-8.4	9.40	10.10-8.90	0.00
PLT (mm3)	247.00	293.50-201.00	232	281.50-189.00	260.00	311-218	0.00
ESR (saat)	22.00	40.00-12.00	29	51-17	16	29-8	0.00
PT (sec)	13.70	14.90-12.10	14	15-12.80	12.60	14.00-11.15	0.00
INR	1.10	1.20-1.00	1.10	1.2-1.00	1.08	1.20-0.99	0.16
Glucose (mg/dl)	96.00	109.75-89.00	94.50	106-88	97.50	112-90	0.01
BUN (mg/dl)	27.00	42.00-15.00	33	52-20	22	32-14	0.00
Creatinine (mg/dl)	0.77	0.89-0.66	0.75	0.87-0.65	0.80	0.90-0.67	0.37
AST (U/mL)	27.00	40.00-20.00	33.50	46.25-23.00	23	34-18	0.00
ALT (U/mL)	27.00	45.00-18.00	35.00	58-23	21	36-16	0.00
ALP (U/L)	88.00	116.00-70.00	94	125-69	84	110-71	0.09
GGT	36.50	54.75-23.00	41	62.50-27	31	46-20	0.00
Albumin (g/dl)	3.90	4.20-3.60	3.80	0.50*	3.90	4.20-3.65	0.01
T.bil (mg/dl)	0.60	0.90-0.40	0.68	1.04-0.46	0.52	0.80-0.36	0.00
D.bil (mg/dl)	0.20	0.34-0.10	0.25	0.46-0.15	0.18	0.24-0.10	0.00
LDH (U/L)	285.00	375-211.50	309.50	409.25-250.25	240	339-184.50	0.00
Ferritin (ng/ml)	158.00	287.50-57	203	320-120	60	172.75-13.75	0.00
PCT	0.45	1.77-0.12	0.50	1.87-0.14	0.12	1.00-0.10	0.05
CRP (g/dl)	10.00	29.68-3.00	11	31-3.6	9	24.15-2.90	0.16

M: Measures of central tendency (median), D: Distribution (mean), *: Standard deviation
WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, NEUT: Neutrophil, LYMP: Lymphocyte, MO: Monocytes, EOS: Eosinophil, MPV: Mean platelet volume, PLT: Platelet, ESR: Erythrocyte sedimentation rate, PT: Prothrombin time, INR: International normalized ratio, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, T.bil: Total bilirubin, D.bil: Direct bilirubin, LDH: Lactate dehydrogenase, PCT: Procalcitonin, CRP: C-reactive protein

Table 4: ROC Analysis for laboratory results

Parameters	*AROC*	*Cut-off Point*	*Sensitivity%*	*Specificity%*	*+PV%*	*-PV%*	*Accuracy%*
WBC	0.56	7360	64.77	47.99	55.2	57.9	56.33
HGB	0.57	12.8	44.17	68.10	57.8	55.2	56.19
HCT	0.55	35.8	25.47	87.13	66.2	54.2	56.47
NEUT	0.59	3080	46.17	72.12	61.9	57.7	59.26
LYMP	0.56	2910	31.44	80.43	61.4	54.2	56.07
EOS	0.73	64	63.96	71.66	70.5	65.2	67.70
MPV	0.59	8.9	47.46	74.11	66.5	56.5	60.25
PLT	0.61	216	42.28	75.81	63.4	57.0	59.11
ESR	0.70	22	65.66	66.01	65.4	66.2	65.84
PT	0.69	12	87.42	43.75	75.5	63.6	72.80
Glucose	0.57	94	50.00	61.30	55.3	56.1	55.78
BUN	0.66	32	52.08	75.24	64.5	64.5	64.51
AST	0.67	27	63.28	65.88	66.1	63.1	64.55
ALT	0.68	27	66.57	66.22	65.7	67.1	66.38
ALP	0.55	92	52.66	63.32	59.9	56.2	57.88
GGT	0.62	38	57.47	66.01	64.8	58.8	61.56
Albumin	0.57	3.98	63.37	49.34	52.5	60.4	55.92
T.bil	0.63	0.41	81.11	40.64	59.5	66.7	61.61
D.bil	0.67	0.26	49.24	78.88	71.0	59.6	63.69
LDH	0.66	243	76.56	52.85	61.8	69.4	64.67
Ferritin	0.75	67	87.43	54.26	77.2	70.8	75.48

WBC: White blood cell, HGB: Hemoglobin, HCT: Hematocrit, NEUT: Neutrophil, LYMP: Lymphocyte, EOS: Eosinophil, MPV: Mean platelet volume, PLT: Platelet, ESR: Erythrocyte sedimentation rate, PT: Prothrombin time, BUN: Blood urea nitrogen, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma glutamyl transferase, T.bil: Total bilirubin, D.bil: Direct bilirubin, LDH: Lactate dehydrogenase

Discussion

Due to the absence of characteristic symptoms and signs of brucellosis, its diagnosis can be easily overlooked (12). Because of the detection of consistently high antibody titers in people without active disease and repeated exposure to infected animals in countries where the disease is endemic, there are difficulties in interpreting STA results, so blood cultures are required for the definitive diagnosis of the disease (13). However, due to various reasons, it is not always possible to isolate the bacteria. Our main aim in this study was to investigate whether demographic, clinical, and some laboratory parameters had predictive significance in bacteremic brucellosis.

In countries where the disease is endemic, brucellosis has been revealed to affect people aged between 15-35 years more (14). In some studies, differences were determined in terms of the age distribution of bacteremic and non-bacteremic brucellosis patients. The mean age (34 years) of bacteremic patients with a diagnosis of brucellosis was lower than that of non-bacteremic patients (41.9 years) (15). The mean age of patients with bacteremia was lower (16). Moreover, the mean age of the patients was 30, and 71% of the patients included in the study were younger than 40 years of age (17). Our study observed that the mean age of bacteremic patients (36.74 years) was lower than non-bacteremic patients (43.18 years), and the results were similar to the literature.

The stage of the disease affects the blood culture results. For instance, 80-90% blood culture positivity is detected in acute brucellosis, while this rate decreases to 30-70% in chronic brucellosis (18). Acute brucellosis was generally associated with a high rate of bacteremia (16). Bacteremic patients were diagnosed more often in the acute brucellosis stage than non-bacteremic patients (19). While the majority of our patients (65.5%) included in the study were admitted in the acute stage, this rate was higher in patients with bacteremia (83.6%), and a statistically significant difference was determined in terms of brucellosis subgroups**.** Brucellosis is an endemic disease in our region and is well-known to the public. Therefore, in the presence of clinical symptoms, hospital admission is made in the early period, microbiological examinations are requested, and the diagnosis is achieved. Unsurprisingly, the diagnosis rate is higher in the acute period. The fact that this rate is higher in patients with bacteremia can be explained by the relationship between bacteremia and clinical symptoms. Symptoms such as fever, sweating, and chills/cold are described at a higher rate in patients with bacteremia. The earlier admission of patients describing these symptoms can be explained by the fact that it coincides with the period when the probability of bacteremia is high.

Brucellosis has a wide range of clinical manifestations, from asymptomatic to multi-organ involvement. In the acute period, non-specific symptoms and signs such as fever, sweating, chills, weight loss, weakness, arthralgia, and hearing loss are observed. The disease progresses to subacute and chronic stages during this period due to the lack of diagnosis and treatment (20). Some clinical symptoms, such as fever and chills, were determined to be associated with bacteremia (19). High fever was statistically higher in bacteremic patients (1, 21). Complaints of fever and chills were higher in bacteremic patients (15, 16). The most frequently described symptoms in all patients in our study were muscle/joint pain (84.5%), sweating (74%), high fever (63.4%), and chills/cold (58.7%). High fever, chills/cold, sweating, nausea, vomiting, and weight loss were higher in the bacteremic group, while a statistically significant difference was observed between the groups.

Hematological complications due to brucellosis are frequent. Leukopenia, lymphomonocytosis, and mild anemia are common findings (22). The liver, the largest organ of the reticuloendothelial system, plays a vital role in defense against *Brucella* spp. related infection. However, liver functions are significantly affected due to bacteria infecting hepatocytes and their intracellular replication. In a study, liver functions such as ALT, AST, GGT, and LDH were demonstrated to be impaired in approximately half of the patients. In the same study, leukopenia, high LDH, low platelet count, high AST, hypoalbuminemia, and total and direct bilirubin levels were higher in patients in the bacteremic group compared to the non-bacteremic group (19). In a study (1), elevations of CRP, AST, and ALT, and in another study (21), elevations of AST, ALT, CRP, and low hemoglobin were statistically more significant in patients with bacteremia. Our study indicated that WBC, HGB, HCT, NEUT, PLT, albumin, and glucose were lower in bacteremic patients, LYMP, ESR, PT, BUN, AST, ALT, GGT, T.bil, D.bil, and LDH values were higher, and statistically significant differences were observed. Although the results reflect the general laboratory findings of brucellosis, the increase or decrease in these parameters is more pronounced in the bacteremic group. It is stated that eosinopenia, defined as a decrease in the number of eosinophils in the peripheral blood, might be a good diagnostic marker in some infections (23). The number of eosinophils in patients with brucellosis was significantly reduced compared to patients with general bacterial infection and healthy volunteers (24). The eosinophil count was statistically significantly lower in brucellosis patients (25). In our study, the eosinophil count was statistically lower in bacteremic patients. According to the ROC analysis, low eosinophils can be considered one of the parameters that can be used in predicting bacteremia, although it was not strong.

Pathogenic microorganisms compete with the host for iron to colonize, multiply, and cause

disease, while the host takes advantage of the toxicity of iron to kill pathogens in addition to their metabolic pathways. *Brucella* species also require iron to survive inside macrophages. They obtain this from the host in several ways and store it in the form of ferritin and/or bacterioferritin above intracellular iron to be released when necessary in cellular metabolisms. Generally, an increase in ferritin levels occurs due to the inflammatory response to infections (18,26). While Kara et al. (18) determined lower iron and higher ferritin levels in the bacteremic group in their study on pediatric patients with a diagnosis of brucellosis, ferritin is the strongest predictive indicator of bacteremia when the cut-off value is 122 ng/mL, with a sensitivity of 91% and a specificity of 78%. Serum iron levels decreased and CRP and ferritin levels increased significantly in patients with brucellosis (27). In our study, ferritin value was significantly higher in bacteremic patients. According to the ROC analysis, when the cut-off value of ferritin was taken as 67 ng/mL, it was the strongest predictive indicator of *Brucella* bacteremia.

Hepatomegaly and splenomegaly occur due to the spread of *Brucella* to reticuloendothelial tissues such as the liver and spleen during bacteremia (1). In some studies, hepatomegaly and splenomegaly were higher in bacteremic patients diagnosed with brucellosis (1,15,21). Shi et al. (19) found no significant difference between bacteremic and non-bacteremic patients regarding hepatomegaly and splenomegaly rates. In our study, the most common pathological finding in all patients was hepatomegaly. The incidence of hepatomegaly, splenomegaly, and lymphadenopathy was significantly higher in the bacteremic group.

There were some limitations in this retrospective design study, such as the fact that only one-third of the patients had USG results, *Brucella* subtypes were not determined, and serum iron level results were unavailable. Despite this, we consider that our study will make significant contributions to the literature in terms of its large case series and some predictive results.

Conclusion

Brucellosis continues to be common worldwide. Although blood culture is the gold standard for diagnosing the disease, bacterial growth is not always possible due to various factors. Therefore, clinical and some laboratory parameters of patients with brucellosis may be useful in predicting bacteremia. In this study, high ferritin levels, low eosinophil counts, and increased ESR were determined as the most important laboratory findings in predicting brucellosis bacteremia. In particular, high ferritin levels can be used to predict brucellosis bacteremia. Furthermore, the higher rate of USG findings, such as hepatomegaly and splenomegaly, along with symptoms of fever, chills/cold, and sweating, are other critical study results in bacteremic patients.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflicts of interest

The author(s) declare that there are no conflicts of interest.

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