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Evaluation of Clinical and Laboratory Findings in Patients with Brucellosis

Brusellozlu Hastalarda Klinik ve Laboratuvar Bulgularının Değerlendirilmesi

Necati MUMCU[1] *Yusuf Emre OZDEMİR*[2] *Melike ÇIVAK*[3]

Nagehan DAMAR[4] *Meryem SAHİN OZDEMİR*[2]

ÖZ

Amaç: Bu çalışmanın amacı bruselloz tanısı konulan hastaların demografik verilerini, klinik ve laboratuvar bulgularını ve organ tutulumlarını değerlendirmektir.
Araçlar ve Yöntem: Hastalar cinsiyete (kadın/erkek) ve yaşa (≤40 yıl/>40 yıl ve ≤30 yıl, 31-44 yıl, 45-59 yıl ve ≥60 yıl) göre gruplara ayrıldı.
Bulgular: Toplam 238 hasta değerlendirildi. Bunların %57.5'i (n=137) erkekti ve yaş ortalaması 43.8±15.0 yıldı. En sık görülen klinik semptomlar artralji (%93.7, n=223), miyalji (%84.9, n=202) ve yorgunluk (%84.5, n=201) idi. Kadın hastalarda miyalji (%92.1'e karşı %79.6, p=0.008), yorgunluk (%92.1'e karşı %78.8, p=0.005), baş ağrısı (%38.6'ya karşı %25.5, p=0.031) ve bulantı (%32.7'ye karşı %13.9, p=0.001) daha yaygındı, iştahsızlık (%43.5'e karşı %59.9, p=0.013) ise daha az yaygındı. Daha genç hastalarda (≤40 yaş) kilo kaybı (%48.0'e karşı %34.3, p=0.034) ve sakroileit (%13.2'ye karşı %5.0, p=0.029) daha yaygındı, spondilodiskit (%2.0'ye karşı %9.3, p=0.039) ise daha az yaygındı. Kilo kaybı ≤30 yaş grubunda 31-44 yaş grubuna (55.8% - %32.8, p=0.013) ve 45-69 yaş grubuna (55.8% - %35.3, p=0.019) göre daha yaygındı. Ateş ≤30 yaş grubunda 45-59 yaş grubuna (32.7% - %54.1, p=0.015) göre daha az yaygındı.
Sonuç: Endemik bölgelerde, artralji, miyalji, yorgunluk, lökopeni veya lökositoz ve yüksek ESR ve CRP'li hastaların ayırıcı tanısında bruselloz düşünülmelidir. Brusellozlu ≤40 yaş hastalar sakroiliit açısından değerlendirilmeli ve >40 yaş hastalar spondilodiskit komplikasyonları açısından değerlendirilmelidir.

Anahtar Kelimeler: brusella; cinsiyet; sakroileit; spondilodiskit; yaş

ABSTRACT

Purpose: The purpose of this study is to evaluate the demographic data, laboratory and clinical findings and organ involvement of patients diagnosed with brucellosis.
Materials and Methods: The patients were divided into groups according to sex (female/male) and age (≤40 years/>40 years and ≤30 years, 31-44 years, 45-59 years, and ≥60 years).
Results: A total of 238 patients were assessed. Among those, 57.5% (n=137) were male, and the mean age was 43.8±15.0 years. Arthralgia (93.7%, n=223), myalgia (84.9%, n=202), and fatigue (84.5%, n=201) were the most common clinical symptoms. In female patients, myalgia (92.1% vs. 79.6%, p=0.008), fatigue (92.1% vs. 78.8%, p=0.005), headache (38.6% vs. 25.5%, p=0.031), and nausea (32.7% vs. 13.9%, p=0.001) were more common, whereas loss of appetite (43.5% vs. 59.9%, p=0.013) was less common. Weight loss (48.0% vs. 34.3%, p=0.034) and sacroiliitis (13.2% vs. 5.0%, p=0.029) were more common, whereas spondylodiscitis (2.0% vs. 9.3%, p=0.039) was less common in younger patients (≤40 years). Weight loss was more common in the ≤30 age group compared to the 31-44 age (55.8% vs. 32.8%, p=0.013) and 45-69 age groups (55.8% vs. 35.3%, p=0.019). Fever was less common in the ≤30 age group compared to the 45-59 age group (32.7% vs. 54.1%, p=0.015).
Conclusion: In endemic areas, brucellosis should be considered in the differential diagnosis of patients with arthralgia, myalgia, fatigue, leukopenia or leukocytosis, and elevated ESR and CRP. Patients ≤40 years with brucellosis should be evaluated for sacroiliitis, and patients >40 years should be evaluated for spondylodiscitis complications.

Keywords: age; brucella; gender; sacroiliitis; spondylodiscitis

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[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Kırşehir Ahi Evran University, Kırşehir, Türkiye
[2]Department of Infectious Diseases and Clinical Microbiology, Basaksehir Cam & Sakura City Hospital, İstanbul, Türkiye.
[3]Department of Infectious Diseases and Clinical Microbiology, Igdır State Hospital, Iğdır, Türkiye.
[4]Department of Infectious Diseases and Clinical Microbiology, Balıkesir Ataturk City Hospital, Balıkesir, Türkiye.

Corresponding Author: Necati Mumcu, Department of Infectious Diseases and Clinical Microbiology, Kırşehir Ahi Evran University Faculty of Medicine, Kırşehir, Türkiye. e-mail: doktor_23mmcu@hotmail.com

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INTRODUCTION

Brucellosis is a zoonosis that can be transmitted to humans under certain conditions, affecting both farm animals and wildlife. Transmission to humans occurs through direct contact with infected animals, consumption of infected animal products, and inhalation of infected aerosols.[1,2] Recent studies estimate that the annual global incidence of brucellosis in humans is 1.6–2.1 million, which is 3-4 times higher than previously estimated.[3] The disease is endemic in regions such as the Middle East, the Mediterranean, and Central and South America.[4] Most patients with brucellosis present with nonspecific symptoms such as fever, sweating, fatigue, anorexia, nausea, weight loss, myalgia, and arthralgia. The lack of specific clinical findings may lead to misdiagnosis and delays in treatment. If the disease is not treated, it can progress to a chronic phase, and the risk of complications may increase.[1,5] Brucellosis is an infection that can affect almost any system. The most common systems involved are the musculoskeletal system, gastrointestinal system, central nervous system, hematological system, urogenital system, cardiovascular system, respiratory system and skin.[6] As a result of focal involvement, complications such as osteomyelitis, sacroiliitis, spondylodiscitis, septic arthritis, epidural abscesses and epididymo orchitis may occur. Focal involvement can be observed in more than half of patients, who sometimes require different and prolonged treatments.[1,2] In patients with focal brucellosis, delayed diagnosis and inadequate and ineffective treatment may lead to disease recurrence, organ damage and even death.[7] Brucellosis is diagnosed by the isolation of Brucella bacteria from blood or tissues or positive serology together with clinical findings suggestive of brucellosis. Among laboratory findings, the white blood cell count is usually low or normal, while erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) levels are variable.[5] Brucellosis is associated with a wide range of symptoms, ranging from mild to severe, and can affect many organs. Because the clinical symptoms of brucellosis vary widely, diagnosis is difficult.[1,5]

The purpose of this study is to evaluate the demographic data, laboratory and clinical findings and organ involvement of patients diagnosed with brucellosis. In addition, the clinical and laboratory findings of the patients were compared in terms of age and sex.

MATERIALS and METHODS

This study was approved by the Ethics Committee of Kafkas University protocol (dated 31.01.2024 and numbered 2024/01).

In this single-center, cross-sectional study, patients aged 18 years and over who were diagnosed with brucellosis and who applied to the Infectious Diseases and Clinical Microbiology outpatient clinic of Iğdır State Hospital, a secondary care hospital located in the Eastern Anatolia Region of Türkiye, between January 04, 2021, and December 29, 2023, were evaluated. The patients' age, sex, complaints, laboratory findings, and organ involvement were recorded on the prepared form. Patients were divided into groups according to sex (female/male) and age (≤40 years/>40 years and ≤30 years, 31-44 years, 45-59 years, and ≥60 years).

Diagnosis

Blood culture and standard tube agglutination (STA) test were used for diagnosis. In patients with clinical findings compatible with brucellosis, brucellosis was diagnosed with an STA ≥1/160, and/or *Brucella spp.* were isolated via blood culture. A BacT/Alert 3D automated system (bioMerieux) was used for blood culture. Routine laboratory tests, such as complete blood count, CRP, ESR, aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine were performed on all patients upon admission. Patients with hip and low back pain were assessed with magnetic resonance imaging (MRI) for sacroiliitis and spondylodiscitis. Patients with swelling and pain in the scrotum were evaluated with ultrasonography for genitourinary system involvement. Osteomyelitis, arthritis and bursitis were diagnosed via MRI in addition to findings such as joint pain, redness, swelling, and limited joint movement.

Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 25.0 was used for statistical analysis. Categorical variables are presented as numbers (n) and percentages (%), and

continuous variables are presented as the mean ± standard deviation (sd). The chi-square test was used to compare categorical variables. The Mann–Whitney U test was used to compare non normally distributed continuous parameters, whereas the t test was used to compare normally distributed continuous parameters. If the p value was < 0.05, the results were considered statistically significant.

RESULTS

A total of 238 patients were included. Among these patients, 57.5% (n=137/238) were male, and the mean age was 43.8±15.0 years. There was a family history of brucellosis in 121 (51.8%) patients. The mean duration of complaints was 58±79 days. The most common symptoms were arthralgia (93.7%, n=223), myalgia (84.9%, n=202), fatigue (84.5%, n=201), low back pain (62.6%, n=149), loss of appetite (52.9%, n=126), and fever (43.7%, n=104). STA titer was ≥1/640 in 52.1% of patients. The laboratory parameters of the patients are shown in Table 1. Brucella bacteraemia was detected in 33 (13.9%) patients, and focal involvement was detected in 47 (19.7%) patients. Among the patients with focal involvement, 42.5% (n=20/47) had sacroiliitis, 31.9% (n=15/47) had spondylodiscitis, 14.9% (n=7/47) had epididymoorchitis, 6.4% (n=3/47) had peripheral arthritis, and 4.3% (n=2/47) had bursitis (Table 1).

The mean duration of complaints was longer in female patients than in male patients (64±75 vs. 54±81, p=0.016). In female patients, myalgia (92.1% vs. 79.6%, p=0.008), fatigue (92.1% vs. 78.8%, p=0.005), headache (38.6% vs. 25.5%, p=0.031), and nausea (32.7% vs. 13.9%, p=0.001) were more common, whereas loss of appetite (43.5% vs. 59.9%, p=0.013) was less common. In addition, leukocyte count (6611±1806 vs. 7807±2456, p<0.001), neutrophil count (3519±1351 vs. 4402±2084, p<0.001), hemoglobulin (13.8±3.2 vs. 14.4±3.8, p<0.001), NLR (1.46±0.71 vs. 1.76±0.97, p=0.007), urea (26±8 vs. 32±10, p<0.001), creatinine (0.65±0.12 vs. 0.82±0.19, p<0.001), ALT (29±24 vs. 34±25, p=0.001), AST (26±19 vs. 26±19, p=0.007), total bilirubin (0.46±0.27 vs. 0.55±0.30, p=0.018), and CRP (10±15 vs. 20±26, p=0.009) were lower, and the platelet count (293±96 vs. 267±80, p=0.022), PLR (122±54 vs. 107±46, p=0.015), and ESR (27±20 vs. 23±20, p=0.030) were higher. The frequency of Brucella bacteremia was similar (13.9% vs. 13.9%, p=0.999) between the two groups, and focal involvement was less common (13.9% vs. 24.1%, p=0.050) in female patients (Table 1).

When patients were evaluated according to age group, weight loss (48.0% vs. 34.3%, p=0.034) was more common in younger patients (≤40 years) than in older patients (>40 years). In addition, urea (25±7 vs. 32±10, p<0.001) and creatinine (0.72±0.15 vs. 0.77±0.20, p=0.014) values were lower and STA titers were higher (61.2% vs. 45.7%, p=0.018) in younger patients. Moreover, sacroiliitis was detected more frequently in younger patients (13.2% vs. 5.0%, p=0.029), whereas spondylodiscitis was detected more frequently in older patients (2.0% vs. 9.3%, p=0.039) (Table 2). The distribution of symptom frequencies according to age group in brucellosis patients is shown in Table 3. Weight loss was more common in the ≤30 years age group than in the 31–44 years (55.8% vs. 32.3%, p=0.013) and 45–69 years age groups (55.8% vs. 35.3%, p=0.019). Fever was less common in the ≤30 years age group than in the 45-59 years age group (32.7% vs. 54.1%, p=0.015). Headache was more common in the 31-44 year age group than in the 45–59 year age group (41.8% vs. 23.5%, p=0.017). There was no statistically significant difference in the distribution of other symptoms between age groups (Figures 1, 2).

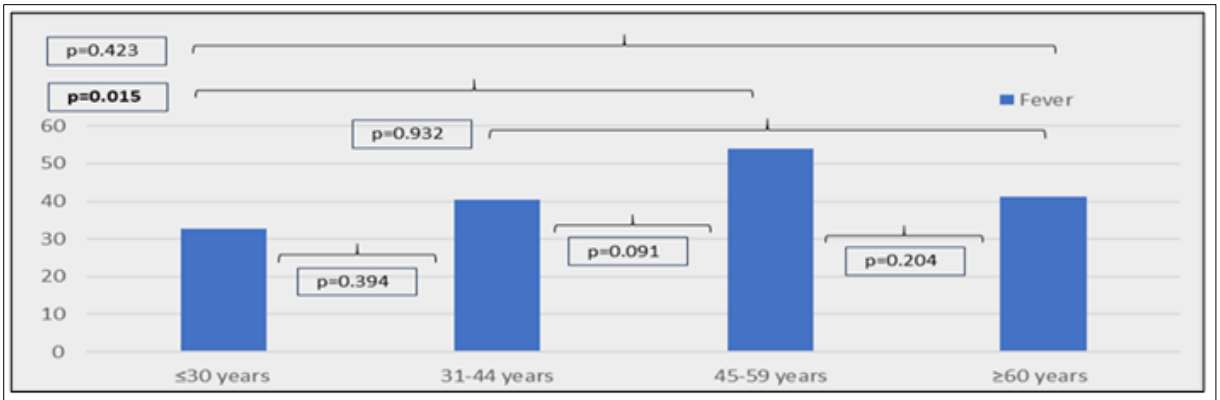

Figure A

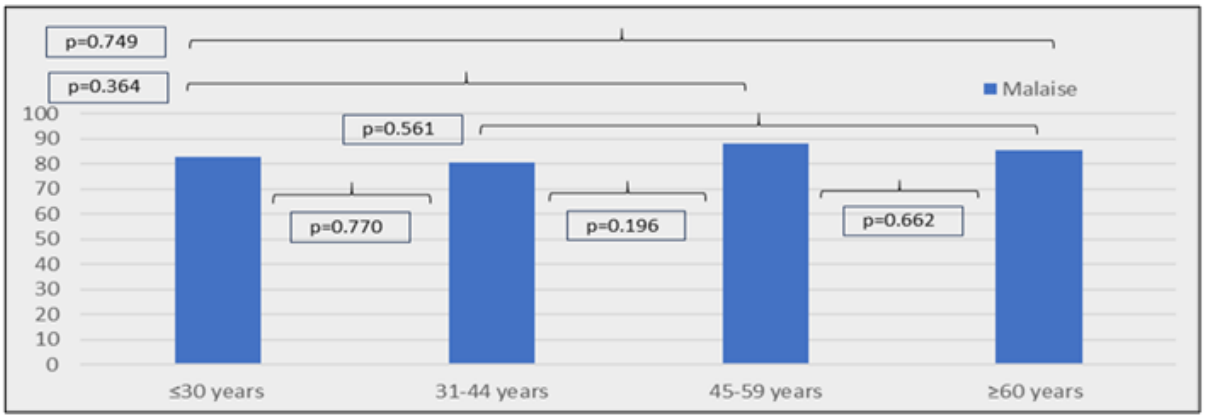

Figure B

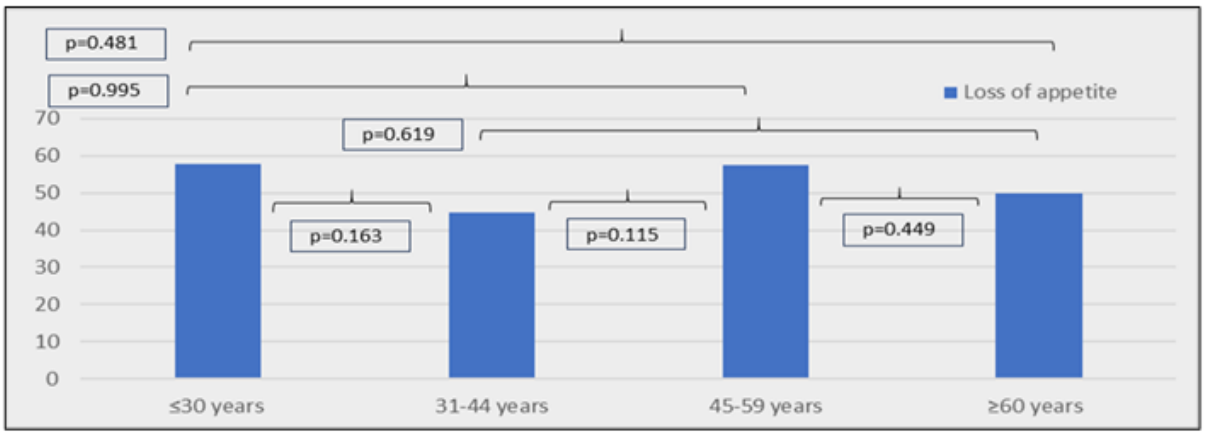

Figure C

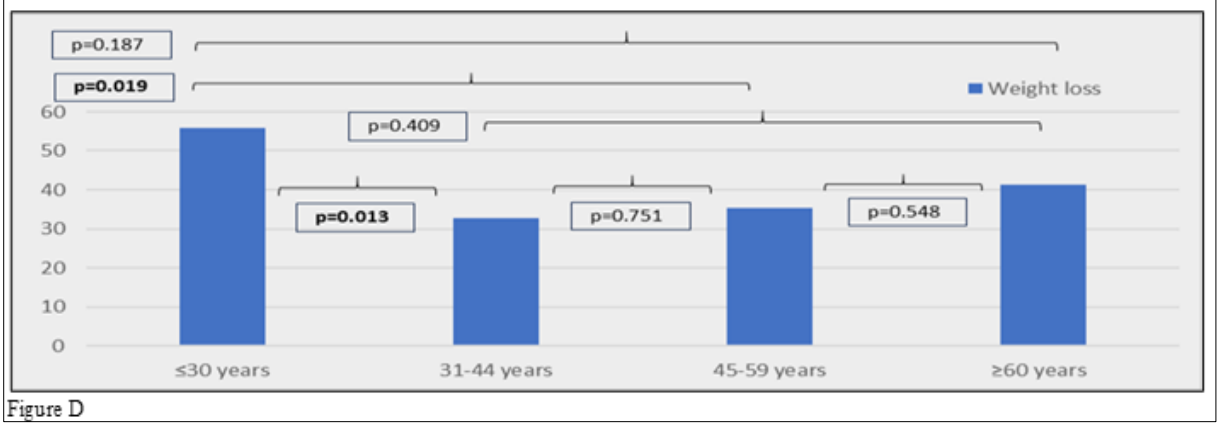

Figure D

Figure 1. Comparison of complaints of fever, fatigue, loss of appetite, and weight loss according to age groups.

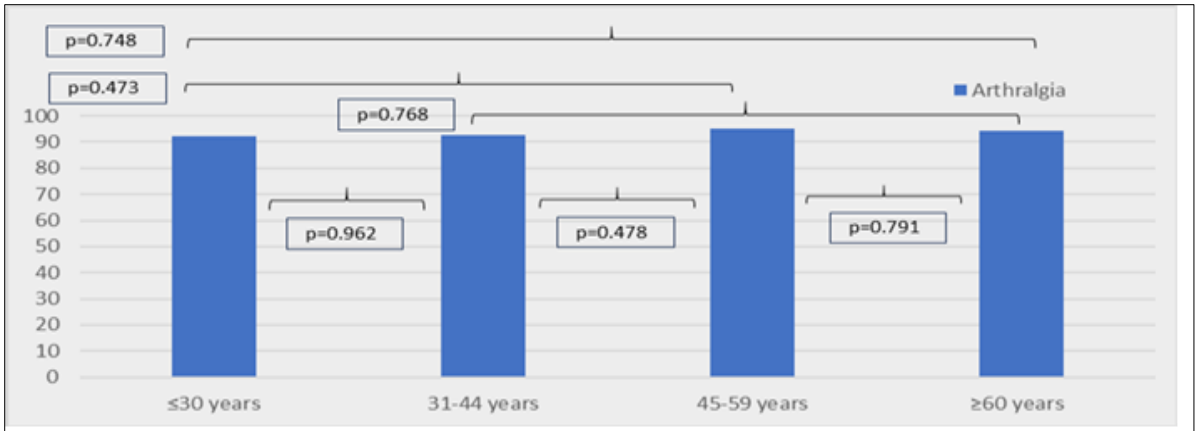

Figure A

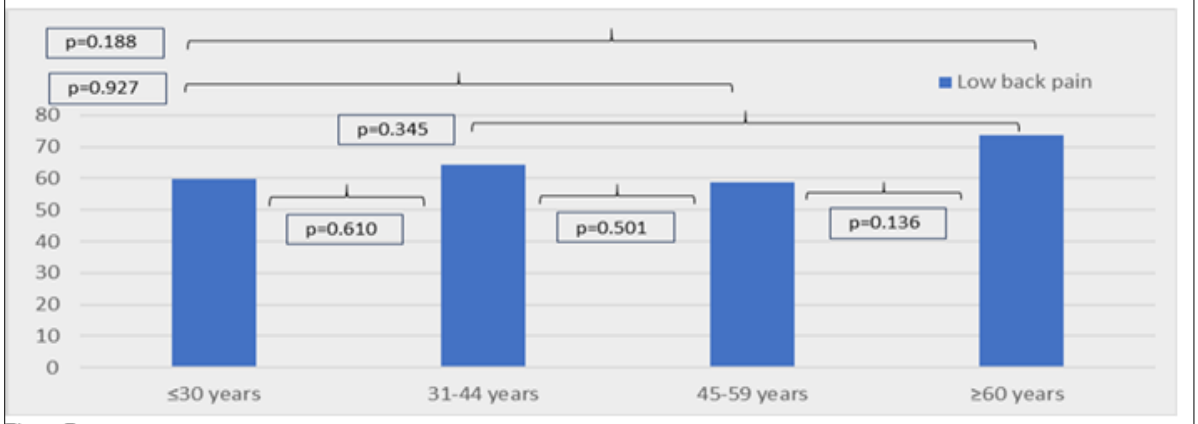

Figure B

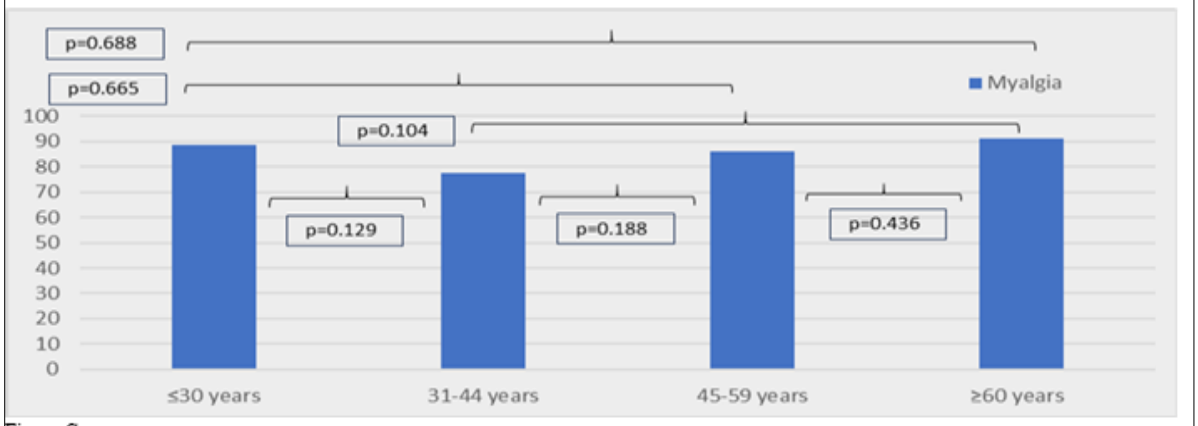

Figure C

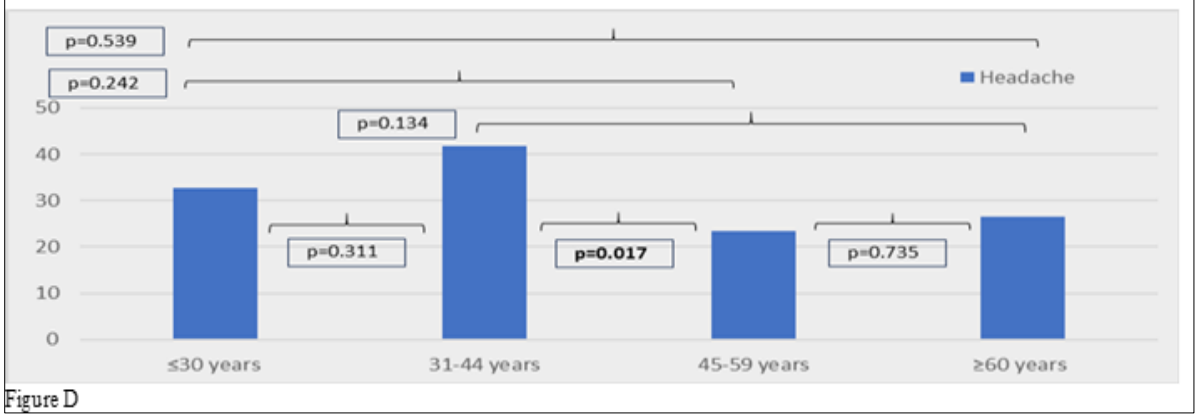

Figure D

Figure 2. Comparison of complaints of arthralgia, myalgia, headache and low back pain ac-cording to age groups.

Table 1. Comparison of demographic characteristics, clinical findings and laboratory parameters of patients diagnosed with brucellosis according to sex.

Parameters	Total (n=238) n (%) / mean ± sd		Male (n=137) n (%) / mean ± sd		Female (n=101) n (%) / mean ± sd		p	OR
Demographic characteristics								
Age	43.8±15.0		44.2 ± 14.9		43.3 ± 15.1		0.540	
Height	168±9		173±7		162 6		<0.001	
Weight	73±12		75±11		69±13		0.029	
BMI (kg/m²)	27.7±24.3		25±3		31±38		0.089	
Smoking	71	29.8	54	39.4	17	16.8	<0.001	3.21
Family History	121	51.8	64	46.7	57	56.4	0.138	0.67
Clinical findings								
Arthralgia	223	93.7	128	93.4	95	94.1	0.844	0.89
Myalgia	202	84.9	109	79.6	93	92.1	0.008	0.33
Fatigue	201	84.5	108	78.8	93	92.1	0.005	0.32
Low back pain	149	62.6	82	59.9	67	66.3	0.307	0.75
Loss of appetite	126	52.9	82	59.9	44	43.5	0.013	1.93
Fever	104	43.7	62	45.3	42	41.6	0.573	1.16
Weight loss	95	39.9	58	42.3	37	36.6	0.375	1.27
Headache	74	31.1	35	25.5	39	38.6	0.031	0.54
Nausea	52	21.8	19	13.9	33	32.7	0.001	0.33
Cough	16	6.7	8	5.8	8	7.9	0.526	0.72
Vomitting	15	6.3	7	5.1	8	7.9	0.378	0.62
Diarrhea	5	2.1	2	1.5	3	3.0	0.422	0.48
Rash	3	1.3	2	1.5	1	1.0	0.748	1.48
Duration of complaint (day)	58±79		54±81		64±75		0.016	
Laboratory parameters								
White blood cells (/µl)	7297±2277		7807±2456		6611±1806		<0.001	
Leukocytosis	15	6.3	13	9.6	2	2.0	0.018	5.23
Leukopenia	5	2.1	0	0.0	5	5.0	0.009	1.05
Neutrophil count (/µl)	4026±1857		4402±2084		3519±1351		<0.001	
Lymphocyte count (/µl)	2715±1187		2807±1411		2591±782		0.377	
Lymphocytosis	50	21.0	33	24.1	17	16.8	0.174	1.56
NLR	1.63±0.88		1.76±0.97		1.46±0.71		0.007	
Hemoglobin (g/dL)	14.2±6.1		14.4±3.8		13.8±3.2		<0.001	
Anemia	30	12.6	13	9.6	17	16.8	0.096	0.52
Platelet count (103/µl)	278±88		267±80		293±96		0.022	
Thrombocytopenia	4	1.7	3	2.2	1	1.0	0.472	2.25
PLR	113±50		107±46		122±54		0.015	
Urea (mg/dl)	29±10		32±10		26±8		<0.001	
Creatinine (mg/dl)	0.75±0.18		0.82±0.19		0.65±0.12		<0.001	
ALT (IU/L)	32±25		34±25		29±24		0.001	
ALT >40 (IU/L)	58	24.4	39	28.7	19	18.8	0.081	1.73
AST (IU/L)	28±18		28±16		26±19		0.007	
AST >40 (IU/L)	33	13.9	21	15.4	12	11.9	0.434	1.35
Total bilirubin (mg/dl)	0.51±0.28		0.55±0.30		0.46±0.27		0.018	
CRP (mg/L)	16±232		20±26		10±15		0.009	
CRP >5 (mg/L)	127	53.4	83	60.6	45	44.5	0.013	1.92
ESR (mm/hour)	25±20		23±20		27±20		0.030	
ESR > 20 (mm/hour)	115	48.3	59	43.1	56	55.4	0.059	0.61
STA titer ≥ 1/320	199	83.6	115	83.9	84	83.2	0.873	1.5
STA titer ≥ 1/640	124	52.1	73	53.3	51	50.5	0.670	1.11
Focus of İnfection								
Bacteremia	33	13.9	19	13.9	14	13.9	0.999	1.00
Focal involvement	47	19.7	33	24.1	14	13.9	0.050	1.97
Sacroiliitis	20	8.4	14	10.2	6	5.9	0.245	1.80
Spondylodiscitis	15	6.3	9	6.6	6	5.9	0.843	1.11
Epididymoorchitis	7	2.9	7	5.1	0	0.0	0.093	11.6
Peripheral arthritis	3	1.3	2	1.5	1	1.0	0.749	1.48
Bursitis	2	0.8	1	0.7	1	1.0	0.735	0.82
Endocarditis	0	0	0	0.0	0	0.0	0.879	0.73
Meningitis	0	0	0	0.0	0	0.0	0.879	0.73

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, NLR: Neutrophil / lymphocyte ratio, PLR: Platelet / lymphocyte ratio, STA: Standard tube agglutination,

Table 2. Comparison of demographic characteristics, clinical findings and laboratory parameters of patients diagnosed with brucellosis according to age.

Parameters	Total (n=238)		≤40 years (n=98)		>40 years (n=140)		p	OR
	n (%) / mean±sd		n (%) / mean±sd		n (%) / mean±sd			
Demographic characteristics								
Sex (Female)	137	57.5	52	53.1	85	60.7	0.540	0.73
Height	168±9		169±9		168±9		0.738	
Weight	73±12		69±12		76±11		0.001	
BMI	27.7±24.3		24±4		31±332		<0.001	
Smoking	71	29.8	28	28.2	43	30.7	0.722	0.90
Family History	121	51.8	56	57.1	65	46.8	0.104	1.54
Clinical findings								
Arthralgia	223	93.7	89	90.8	134	95.7	0.126	0.44
Myalgia	202	84.9	80	81.6	122	87.1	0.243	0.65
Malaise	201	84.5	79	80.6	122	87.1	0.171	0.61
Low back pain	149	62.6	61	62.2	88	62.9	0.923	0.97
Loss of appetite	126	52.9	49	50.0	77	55.0	0.447	0.82
Fever	104	43.7	36	36.7	68	48.6	0.070	0.61
Weight loss	95	39.9	47	48.0	48	34.3	0.034	1.76
Headache	74	31.1	36	36.7	38	27.1	0.116	1.55
Nausea	52	21.8	25	25.5	27	19.3	0.253	1.43
Cough	16	6.7	6	6.1	10	7.1	0.757	0.85
Vomitting	15	6.3	7	7.1	8	5.7	0.655	1.26
Diarrhea	5	2.1	3	3.1	2	1.4	0.387	2.17
Rash	3	1.3	1	1.0	2	1.4	0.781	0.71
Duration of complaint (day)	58±79		54±81		64±75		0.016	
Laboratory parameters								
White blood cells	7297±2277		7510±2331		7150±2235		0.156	
Leukocytosis	15	6.3	7	7.2	8	5.7	0.640	1.28
Leukopenia	5	2.1	3	3.1	2	1.4	0.381	2.20
Neutrophil count	4026±1857		4201±1942		3904±1793		0.228	
Lymphocyte count	2715±1187		2692±798		2731±1394		0.487	
Lymphocytosis	50	21.0	19	19.4	31	22.1	0.608	0.84
NLR	1.63±0.88		1.68±0.97		1.56±0.82		0.374	
Hemoglobin	14.2±6.1		14.7±9.3		13.8±1.4		0.874	
Anemia	30	12.6	15	15.5	15	10.7	0.280	1.52
Platelet count	278±88		282±92		275±84		0.682	
Thrombocytopenia	4	1.7	0	0	4	2.9	0.093	0.15
PLR	113±50		112±43		114±55		0.940	
Urea	29±10		25±7		32±10		<0.001	
Creatinine	0.75±0.18		0.72±0.15		0.77±0.20		0.014	
ALT	32±25		35±27		30±23		0.110	
ALT >40	58	24.4	30	30.9	28	20.0	0.054	1.79
AST	28±18		29±18		27±17		0.199	
AST >40	33	13.9	16	16.5	17	12.1	0.341	1.42
Total bilirubin	0.51±0.28		0.51±0.28		0.52±0.28		0.458	
C-reactive protein	16±232		16±23		16±22		0.722	
CRP >5 mg/dL	128	53.8	57	58.1	71	50.7	0.435	1.25
ESR	25±20		24±19		25±202		0.611	
ESR >20	115	48.3	46	46.9	69	49.3	0.721	0.91
STA titer ≥ 1/320	199	83.6	84	85.7	115	82.1	0.464	1.30

STA titer ≥ 1/640	124	52.1	60	61.2	64	45.7	0.018	1.87
Focus of İnfection								
Bacteremia	33	13.9	18	18.4	15	10.7	0.093	1.87
Focal involvement	47	19.7	23	23.5	24	17.1	0.228	1.48
Sacroiliitis	20	8.4	13	13.2	7	5.0	0.029	2.90
Spondylodiscitis	15	6.3	2	2.0	13	9.3	0.039	0.20
Epididymoorchitis	7	2.9	4	4.1	3	2.1	0.391	1.94
Peripheral arthritis	3	1.3	3	3.0	0	0.0	0.124	10.2
Bursitis	2	0.8	1	1.0	1	0.7	0.388	2.89
Endocarditis	0	0	0	0.0	0	0.0	0.859	1.42
Meningitis	0	0	0	0.0	0	0.0	0.859	1.42

ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, BMI: Body mass index, NLR: Neutrophil / lymphocyte ratio, PLR: Platelet / lymphocyte ratio, STA: Standard tube agglutination,

Table 3. Comparison of the clinical findings of patients diagnosed with brucellosis according to age group.

Parameters		**≤30 years (n=52)**		**31-44 years (n=67)**		**45-59 years (n=85)**		**≥60 years (n=34)**	
		n	%	n	%	n	%	n	%
Fever	Yes	17	32.7	27	40.3	46	54.1	14	41.2
	No	35	67.3	40	59.7	39	45.9	20	58.8
Malaise	Yes	43	82.7	54	80.6	75	88.2	29	85.3
	No	9	17.3	13	19.4	10	11.8	5	14.7
Loss of appetite	Yes	30	57.7	30	44.8	49	57.6	17	50.0
	No	22	42.3	37	55.2	36	42.4	17	50.0
Weight loss	Yes	29	55.8	22	32.8	30	35.3	14	41.2
	No	23	44.2	45	67.2	55	64.7	20	58.8
Arthralgia	Yes	48	92.3	62	92.5	81	95.3	32	94.1
	No	4	7.7	5	7.5	4	4.7	2	5.9
Low back pain	Yes	31	59.6	43	64.2	50	58.8	25	73.5
	No	21	40.4	24	35.8	35	41.2	9	26.5
Myalgia	Yes	46	88.5	52	77.6	73	85.9	31	91.2
	No	6	11.5	15	22.4	12	14.1	3	8.8
Headache	Yes	17	32.7	28	41.8	20	23.5	9	26.5
	No	35	67.3	39	58.2	65	76.5	25	73.5
Nausea	Yes	11	21.2	18	26.9	16	18.8	7	20.6
	No	41	78.8	49	73.1	69	81.2	27	79.4
Vomitting	Yes	5	9.6	3	4.5	5	5.9	2	5.9
	No	47	90.4	64	95.5	80	94.1	32	94.1
Diarrhea	Yes	1	1.9	2	3.0	1	1.2	1	2.9
	No	51	98.1	65	97.0	84	98.8	33	97.1
Cough	Yes	3	5.8	9	9.0	5	5.9	2	5.9
	No	49	94.2	58	91.0	80	94.1	32	94.1
Rash	Yes	0	0.0	1	1.5	2	2.4	0	0.0
	No	52	100	66	98.5	83	97.6	34	100

DISCUSSION

In this study, the demographic data, clinical and laboratory findings and organ involvement of brucellosis patients were evaluated according to the age and sex of the patients. Accordingly, the duration of complaints was significantly longer in women. Weakness, myalgia, headache and nausea were significantly more common in women, and loss of appetite was significantly more common in men. Re-

garding laboratory values, leukocytosis, NLR, hemoglobin, CRP elevation and mean CRP values were significantly higher in men, and leukopenia, PLR and mean ESR values were significantly higher in women. Weight loss and sacroiliitis were more common, and spondylodiscitis was less common in patients aged ≤40 years. Additionally, high STA titers (≥1/640) were higher in patients aged ≤40 years.

Brucellosis can be detected at any age, but the age group in which brucellosis is frequently detected varies from country to country and according to the studies conducted. It usually affects the productive age group. Buzgan et al.[8] reported the age range in which patients are frequently 13--34 years, whereas Jiang et al.[9] reported the age range of 41--65 years. In addition, in other studies, the average age of patients with brucellosis varies between 27 and 46 years.[10-12] A study conducted in California reported that the incidence of brucellosis was greater in individuals aged 65 and over than in other studies.[13] In this study, most of the infected individuals were middle-aged patients between the ages of 45 and 60, and the average age of all patients was 43.8 years. The reason why the age at which brucellosis is frequently observed varies according to studies may be related to differences in the age of animal husbandry from society to society.

We observed different results in studies on the relationship between brucellosis incidence and sex. In contrast to studies reporting that sex is associated with the occurrence of brucellosis in humans,[14-16] other studies reporting that it is not associated with brucellosis.[17,18] In general, community-based studies report that brucellosis is detected at equal or very close rates in men and women and that it is more common in men in societies where occupational exposure is more common.[19-24] In this study, most of the brucellosis patients (57.5%) were men. This result was consistent with studies reporting that brucellosis is more common in males.[16,24-27] The change in brucellosis incidence according to sex may be related to occupational exposure and the mode of transmission of the disease.[23]

The clinical symptoms of brucellosis vary considerably.[8] Most patients with brucellosis have nonspecific symptoms such as fever, sweating, fatigue, anorexia, nausea, weight loss, myalgia, and arthralgia.[1,5] Although the most common symptoms vary from study to study and according to the stage of the disease, fever, sweating, fatigue, and arthralgia are generally the most frequently reported complaints.[8,9,28] In this study, consistent with the literature, arthralgia, myalgia, and fatigue were the most common clinical symptoms. When we evaluated the clinical symptoms of patients with brucellosis according to sex and age in this study, fatigue, myalgia, headache, and nausea were significantly more common in women, anorexia in men, and weight loss in individuals under the age of 40. Hasanjani et al.[23] reported that arthralgia was significantly more common in women, Zaks et al.[29] reported that myalgia was significantly more common in men and that the frequency of other clinical symptoms was the same in both genders. Another study reported that headache, arthralgia, myalgia, and fatigue were more common in women.[30] Fritz et al. reported that fever, sweating, and headache complaints were more common in patients under 65 years of age.[13] Another study reported that fever, headache, joint pain, and fatigue were more common in individuals aged 20-44 years and that myalgia, night sweats, and weight loss were more common in individuals aged 45 years and over.[30] In this study, weight loss was more common in individuals under 30 years of age, headache was more common in the 31-44 years age group, and fever was more common in the 45-69 years age group. However, the role of geographic region, age, sex, ethnicity, or other factors in the clinical symptoms of brucellosis has not yet been clarified.

Brucella infection can involve any organ or tissue in the body. Focal involvement can be observed in more than half of patients.[2] Osteoarticular involvement is the most common.[2,8,19] The prevalence of osteoarticular involvement has been reported to be between 10% and 85%, depending on the study, age, duration of the disease and infection with Brucella species.[5] In this study, 19.7% of the patients had focal involvement, and 85.1% of them had osteoarticular involvement. Among areas with osteoarticular involvement, peripheral arthritis, sacroiliitis and spondylitis are the most commonly affected areas.[5,8,19,23] Hasanjani et al.[23] reported that focal involvement and spondylitis were significantly more common in men than in women, whereas Zaks et al.[29] reported that osteoarticular involvement was similar in both sexes. In this study, focal involvement was

more common in men, but there was no significant difference in osteoarticular involvement. While spondylitis is usually observed in elderly men, sacroiliac joint involvement is observed in both sexes, young and old.[5] In this study, the most common osteoarticular involvements were sacroiliitis (50%) and spondylodiscitis (37.5%). Sacroiliitis was significantly more common in patients under 40 years of age, whereas spondylodiscitis was significantly more common in individuals over 40 years of age.

Among the laboratory findings of brucellosis, the white blood cell count is generally normal or low, whereas the levels of AST, ALT, ESR and CRP are variable.[5,8] Among the hematological findings, anemia, leukocytosis, leukopenia, thrombocytosis, thrombocytopenia and pancytopenia are relatively common. Hematological findings may be associated with hypercellularity, hemophagocytosis and granulomas, disseminated intravascular coagulation and hypersplenism in cases where the bone marrow is involved.[2] In previous studies, leukocytosis was reported as 5.6-15.2%, leukopenia as 3-37.1%, thrombocytopenia as 2-26%, anemia as 7-55%, CRP elevation as 36-66.2%, and ESR elevation as 38-77.8%.[8,19,23,31-33] In our study, when laboratory abnormalities were taken into consideration, 6.3% of our patients had leukocytosis, 2.1% had leukopenia, 12.6% had anemia, 1.7% had thrombocytopenia, 53.4% had CRP and 48.3% had ESR elevation. Leukocytosis, NLR, hemoglobin CRP elevation and mean CRP values (20±26) were significantly greater in male patients, and leukopenia, PLR and mean ESR values (27±20) were significantly greater in female patients. Demiraslan et al.[31] reported that leukopenia and anemia were more common in females and that leukocytosis was more common in males.

Brucellosis is diagnosed by the isolation of Brucella bacteria from blood or tissues or by positive serology together with clinical findings suggestive of brucellosis.[5] All patients in this study had STA titers of ≥1:160, and *Brucella spp.* were isolated from the blood cultures of 33 (13.9%) patients. A total of 52.1% of patients had STA tests of ≥1:640, which was significantly greater in individuals under 40 years of age than in individuals over 40 years of age.

Although the fact that the study was conducted in a region where mostly small livestock farms are performed and that it was a single center may limit the generalizability of the results, the fact that all brucellosis cases in the region were collected in this center contributes to the homogeneous distribution of the cases, which makes our results generalizable.

As a result, the clinical symptoms, laboratory values and complications of brucellosis vary significantly. Some of them were found to be related to age and sex. In regions where brucellosis is endemic, it should be considered in the differential diagnosis of patients with arthralgia, myalgia, weakness, leukopenia or leukocytosis, and elevated ESR and CRP. In particular, patients ≤40 years with brucellosis should be evaluated for sacroiliitis, and patients >40 years should be evaluated for spondylodiscitis complications.

Conflict of Interest

The authors declare that there is not any conflict of interest regarding the publication of this manuscript.

Ethics Committee Permission

This study was approved by the Ethics Committee of Kafkas University protocol (dated 31.01.2024 and numbered 2024/01).

Authors' Contributions

Concept/Design: NM, YEO, MÇ, ND, MSO. Data Collection and/or Processing: NM, YEO, MÇ, ND, MSO. Data analysis and interpretation: NM, YEO, MÇ, ND, MSO. Literature Search: NM, YEO. Drafting manuscript: NM, YEO. Critical revision of manuscript: NM, YEO

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