



BRIEF COMMUNICATION

# Clinical and laboratory findings of 97 pediatric brucellosis patients in central Turkey



Tamer Yoldas<sup>a</sup>, Hasan Tezer<sup>b</sup>, Aslinur Ozkaya-Parlakay<sup>a,\*</sup>,  
Tulin Revide Sayli<sup>a</sup>

<sup>a</sup> Ankara Hematology Oncology Children's Training and Research Hospital, Ankara, Turkey

<sup>b</sup> Gazi University Faculty of Medicine Pediatric Infectious Diseases Unit, Ankara, Turkey

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## KEYWORDS

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Brucellosis is a disease transmitted to humans by consumption of unpasteurized animal milk, or through direct contact with infected animals. The aim of this study was to evaluate clinical, laboratory findings of pediatric patients with brucellosis. Data of 97 patients diagnosed with brucellosis between January 2000 and December 2010 were evaluated retrospectively. Copyright © 2014, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. All rights reserved.

## Introduction

Brucellosis, a primary disease of domestic animals, is caused by small, fastidious Gram-negative coccobacilli of the genus *Brucella*.<sup>1</sup> The incidence of brucellosis has shown a mild decrease in Turkey according to data from the Ministry of Health; 7703 cases were reported in 2010.<sup>2</sup> Humans are commonly infected through ingestion of raw milk, cheese, or meat, or through direct contact with infected animals, and through inhalation of infectious aerosols.<sup>3</sup>

Clinical symptoms may vary, and include undulant fever, abortion, orchitis, spondylitis, arthritis, endocarditis, encephalitis, and asthenia.<sup>4</sup> The aim of this study was to evaluate the prevalence of acute, subacute, and chronic brucellosis, and also to emphasize clinical and laboratory findings of pediatric patients with brucellosis by comparing with patients reported in the literature.

## Methods

In this study, 97 patients diagnosed with brucellosis at Ankara Hematology Oncology Research Hospital between January 2000 and December 2010 were evaluated retrospectively. Data analysis included demographic data, signs and symptoms, physical findings, laboratory findings,

\* Corresponding author. Ankara Hematology and Oncology Research Hospital, Pediatric Infectious Diseases Unit, Diskapı, 06110, Ankara, Turkey.

E-mail address: [Aslinur.o@gmail.com](mailto:Aslinur.o@gmail.com) (A. Ozkaya-Parlakay).

treatment regimens, and outcome. Patients were classified as having acute brucellosis (<3 months), subacute brucellosis (3–12 months), or chronic brucellosis (>12 months). The study was approved by a local ethical committee.

The blood culture samples were studied with BacTAlert systems (Organon Technica, Durham, NC, USA) for 21 days. The diagnosis of brucellosis was made based on positive *Brucella* STA test results (titer > 160) in the presence of clinical signs and symptoms suggestive of brucellosis or a 4-fold increase in the serum antibody concentration in a serum sample obtained at 2–3 week intervals and/or isolation of *Brucella spp.* from the blood, bone marrow, or any body fluid or tissue culture. For data analysis, SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) was used. A *p* value of 0.05 was considered statistically significant.

## Results

The characteristics and clinical findings of the 97 patients are reviewed in Table 1.

Consumption of unpasteurized milk or dairy products was significantly more common in patients with a family history of brucellosis (96.9%, whereas patients with no family history of brucellosis had consumption of raw milk in 72.3%, *p* = 0.004). Initiation of symptoms was most common in spring and summer (65%).

By means of clinical findings, serum agglutination titers (SAT) > 1/800 did not affect the presence of fever, weakness, and arthralgia all together. Of patients with SAT < 1/

800 43.9% had these three clinical findings, whereas 48.4% of patients with SAT >1/800 had fever, weakness, and arthralgia. The presence of arthralgia was not significantly different in acute and subacute brucellosis cases (72.6% and 87.5%, respectively). Arthralgia was most common in the knee joint (63.9%); arthralgia in the hip was present in 27.8% of our patients and in the sacroiliac joint was encountered in 13.4% of patients, whereas sacroiliitis was present only in one patient. The presence of fever, hepatomegaly, splenomegaly, or arthritis was not significantly different between patients with acute and subacute brucellosis.

Laboratory studies of the patients are summarized in Table 2. Laboratory evaluation, which included the presence of anemia, elevated C-reactive protein (CRP), and sedimentation rates, did not significantly differ between acute and subacute brucellosis patients.

The Rose Bengal test was positive in 67/70 patients (95.7%), SAT was positive in 17/21 patients (80.9%), the agglutination test with 2-mercaptoethanol was positive in 23/27 patients (85.1%), and blood culture was positive in 29/81 patients (35.8%). In patients with SAT > 1/800, 48.4% had blood culture positivity, whereas in patients with SAT < 1/800, 48.3% of them had blood culture positivity. SAT titer did not affect blood culture positivity.

Neurobrucellosis was present in three patients, but cerebrospinal fluid cultures were negative in all. They were diagnosed with agglutination titer positivity in CSF.

When complications of brucellosis were evaluated, 23.7% had arthritis (19.6% monoarticular, 4.1% oligoarticular), 6.2% had pancytopenia, 3% had neurobrucellosis, 2.1% had hepatitis, 1% had osteomyelitis, 1% had pneumonia, and 1% had sacroiliitis.

Treatment regimens were composed of doxycycline and streptomycin in 29.9% of patients, doxycycline and rifampin in 24.7% of cases, and cotrimoxazole and rifampin in 27.8% of patients. The duration of therapy was 6 weeks in 94.9% of patients, 12 weeks in 3.1% of patients, and 24 weeks in 3.1% of patients. Relapse was observed in two patients who were treated with doxycycline and rifampin. No relapse was observed in these patients after 6 weeks of cotrimoxazole and rifampin.

## Discussion

Brucellosis is one of the most common zoonoses worldwide and remains endemic in the Mediterranean region, the Middle East, West Asian countries, and also in Turkey.<sup>5,6</sup> Studies from Turkey previously showed that a history of consumption of unpasteurized dairy products was present in 62.4–94.6% of patients with brucellosis.<sup>6–13</sup> Similar to the literature, consumption of unpasteurized dairy products was present in 80.4% of our patients. These results suggest that necessary precautions should still be taken to prevent consumption of such products. In pediatric brucellosis cases, family history has been reported between 15.6% and 47%.<sup>14,15</sup> In accordance with the literature, this rate was 33% in our study. So screening of family members when a patient with brucellosis is diagnosed is very important. In accordance with literature, our cases had

**Table 1** The characteristics and clinical findings of the patients

Characteristics	Mean
Mean age (y)	10 ± 3.8
Mean duration of symptoms before admission (d)	31.85 ± 44.3
	<i>n</i> (%)
Female	44.3
Living in a rural area	35.1
Consumption of unpasteurized milk or dairy products	80.4
Family history of brucellosis	33
Symptoms	
Fever	78.4
Arthralgia	76.3
Weakness	68
Clinical findings	
Hepatomegaly	30.9
Splenomegaly	20.6
Hepatosplenomegaly	14.4
Arthritis	23.7
Monoarticular	19.6
Oligoarticular	4.1
Clinical diagnosis	
Acute	75.3
Subacute	23.7
Chronic	1
Hospitalization	92.8

**Table 2** Laboratory studies of the cases

Laboratory findings	n	%
Anemia (<12 g/dL)	51	52.6
Leukopenia (<3.5 × 10 <sup>3</sup> /μL)	9	9.3
Thrombocytopenia (<150 × 10 <sup>3</sup> /μL)	14	14.4
Pancytopenia (Hgb < 12 g/dL, WBC < 3.5 × 10 <sup>3</sup> /μL, plt < 150 × 10 <sup>3</sup> /μL)	6	6.2
Leukocytosis (>10.5 × 10 <sup>3</sup> /μL)	17	17.5
Thrombocytosis (>450 × 10 <sup>3</sup> /μL)	10	10.3
Elevated ESR (mm/h)	71	73.2
<20	26	26.8
20–50	52	53.8
>50–100	16	16.3
>100	3	3.1
Elevated CRP (mg/dL)	44	45.4
<1	53	54.6
1–10	41	42.2
>10–50	3	3.1
Elevated AST (IU/L)	40	41.3
<40	57	58.7
40–200	39	40.3
>200	1	1
Elevated ALT (IU/L)	35	35.6
<40	62	64.4
40–200	34	34.6
>200	1	1
Elevated AST-ALT(IU/L)	28	28.9

ALT = alanine aminotransferase; AST = aspartate aminotransferase; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; Hgb = hemoglobin; WBC = white blood cell.

perennial accumulation in spring and summer due to raw milk and dairy product consumption.<sup>13,16</sup>

In adult patients with brucellosis, the acute form is reported to be observed in 25–77% of cases, the subacute form in 12.5–59% of cases, and the chronic form in 5–27.5% of cases.<sup>17</sup> In a study, the acute form was diagnosed in 61.6% of the pediatric patients, the subacute form in 21.6%, and the chronic form in 13.6% of the pediatric cases.<sup>13</sup> In our study, the acute form was present in 75.3% patients, whereas the subacute form was in 23.7%, and the chronic form was present in 1% of patients. This might be due to earlier admission in children.

The most common clinical findings were reported as fever and joint complaints, with prevalence of 41–85% and 73–91%, respectively.<sup>16–22</sup> Fever was present in 78.4% and arthralgia in 76.3% of our patients. In addition, arthritis was present in 23.7% of our patients (19.6% monoarticular, 4.1% oligoarticular). In adult patients with brucellosis, musculoskeletal involvement was the leading complication, spondylodiscitis was reported in the old age group, whereas sacroiliitis was reported in the young age group.<sup>6</sup> From the previous reports of 50 children who presented with arthritis, 36 (72%) had monoarthritis; knee (24 patients) and hip (23 cases) were the most commonly involved joints,<sup>16</sup> similar to our patients. In our patients, sacroiliitis was present only in one patient, highlighting

that brucellosis has different outcomes according to the age group.

Laboratory study is usually not helpful in differential diagnosis of pediatric brucellosis; leukocyte count, CRP, and erythrocyte sedimentation rate (ESR) are normal or mildly elevated in most cases.<sup>18,22</sup> Similarly, in our study ESR was >55 mm/hour in 19.4% of cases and CRP was negative in 54.6% of cases.

Diffuse hepatic involvement is usually reported during the course of brucellosis. Involvement of the liver varies; a slight increase in transaminase levels, mild hepatosplenomegaly, chronic suppurative disease, and more rarely, acute hepatitis could be encountered.<sup>23</sup> Elevated transaminases were reported in 18–66% of pediatric cases.<sup>8,24–26</sup> In our study, aspartate aminotransferase (AST) elevation was present in 41.3%, and alanine aminotransferase (ALT) elevation in 35.6% of our cases. In 28.9% of the patients both ALT and AST were elevated. These rates of elevated transaminases were similar to reported cases in the literature.

Hematological studies during the active course of brucellosis showed that leukopenia occurred in 33% of patients, anemia in 44%, thrombocytopenia in 5%, and pancytopenia in 14%.<sup>27,28</sup> Furthermore, pancytopenia was detected in 10% of children suffering brucellosis.<sup>29</sup> The frequency of pancytopenia with brucellosis varies from 3% to 21% in the previous studies, being relatively higher in adults than children.<sup>30,31</sup> The possible mechanisms suggested for pancytopenia include autoimmune process, hypersplenism, granuloma formation in the bone marrow, phagocytosis of formed elements by reticuloendothelial cells, or bone marrow depression due to the associated septicemia. In our study, anemia was present in 52.6%, thrombocytopenia in 14.4%, leukopenia in 9.3%, leukocytosis in 11.3%, and thrombocytosis in 6.2% of the patients.

Neurobrucellosis is a rare complication of brucellosis that could be diagnosed with the clinical picture of meningitis and meningoencephalitis in most cases.<sup>22</sup> Its prevalence has been reported to range between 1.7% and 17.8%<sup>17,32–36</sup> in various studies. The mortality due to neurobrucellosis ranges between 0% and 5.5%, depending on the use of appropriate antibiotics.<sup>37</sup> There was no mortality due to neurobrucellosis in our patients.

Depending on the type of antibiotic and duration of treatment, the relapse rate in pediatric brucellosis cases was reported between 0% and 85%.<sup>17,26,28,37</sup> In our study, only two patients who were treated with doxycycline and streptomycin (3 weeks; 2.1%) had relapse of the disease. The relapse rates of our patients were near to the lower limits compared to studies in the literature. As most of our patients received therapy for 6 weeks (94.9%), a lower relapse rate might be possibly related with longer duration of therapy compared to patients receiving 3 weeks of therapy.

In conclusion, as brucellosis is still endemic in Turkey, strict control of veterinary studies and precautions to prevent consumption of raw milk products is mandatory. In patients admitted with fever, arthralgia, fatigue, and sweating, brucellosis should be kept in mind. In addition, family of patients with brucellosis must be screened.

## Conflicts of interest

All authors declare no conflicts of interest.

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