

# CLINICAL FEATURES, DIAGNOSTIC AND THERAPEUTIC OPPURTUNITIES OF BRUCELLOSIS IN KOSOVA



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## Abstract

### Introduction:

Brucellosis, also known as “Undulant Fever,” is a zoonosis primarily transmitted through the consumption of unpasteurized milk and dairy products, direct contact with infected animals, and inhalation of contaminated aerosols [1,7,10]. It is also possible through interhuman and intrauterine transmission [12]. While it has been eradicated in most developed countries, over 500,000 new cases of brucellosis are reported globally each year [9]. Although the incidence of the disease has recently decreased in Kosovo, brucellosis remains a public health and social issue [3,6,15].

The aim of this study was to analyze the clinical features, diagnostic possibilities, and therapeutic approaches of brucellosis cases treated at the Infectious Disease Clinic in the University Clinical Center of Kosovo.

### Methodology:

This paper presents a retrospective study of all patients hospitalized in the Infectious Disease Clinic from January 1, 2023, to April 30, 2024, and diagnosed with brucellosis. Data on the disease history, clinical presentations, diagnostic methods, and therapeutic approaches were collected from the medical histories of patients treated at the Infectious Disease Clinic in Prishtina.

### Results:

During the period from January 2023 to April 2024, nine patients with brucellosis were treated at the Infectious Disease Clinic. Male patients predominated, with six cases (67%), and the average age was 35.4 years (range 20–63). All patients came from rural areas, most frequently from the municipalities of Suhareka, Istog, and Peja [3,6].

The most frequently reported symptoms were fatigue (100%), fever (88%), joint pain (55%), sweating (44%), back pain (33%), abdominal pain (33%), right testicular pain and swelling (33%), leg pain, and vomiting (11%). The duration of symptoms before hospitalization ranged from 3 days to 3 months (range 3–90 days). The osteoarticular system was the most commonly affected system (33%), followed by orchiepididymitis (33%) [2,13,14].

The disease was confirmed by positive serology in all cases (100%) and positive blood cultures in 22% of cases [5,12]. In all cases, combined therapy with doxycycline and gentamycin was administered for the first 2–3 weeks, followed by rifampicin and doxycycline for 6 weeks [1,5]. Most patients, 8 (89%), experienced acute disease progression. No pediatric cases or disease relapses were observed.

### Conclusion:

The most common complications of brucellosis in our cases were osteoarticular involvement and orchiepididymitis [2,13]. Initial therapy combining doxycycline and gentamycin, followed by doxycycline and rifampicin, was effective, with no relapses observed [1,5]. Early diagnosis and appropriate treatment were associated with favorable outcomes for patients.

### Keywords:

Brucellosis, therapy, complications, doxycycline, gentamycin.

### Introduction

Brucellosis, also known as “Undulant Fever,” “Mediterranean Fever,” or “Malta Fever,” is a zoonotic disease affecting domestic and wild animals [1,7,10]. This infectious disease has significant public health implications and presents considerable economic challenges, particularly in regions with weak food industry standards, hygiene practices, and veterinary care [7,8,10].

Historically, brucellosis has been recognized in the Mediterranean region, particularly among sheep and goats, dating back to ancient times [1]. In 1887, microbiologist David Bruce isolated the gram-negative coccobacillus from the spleen of fatal cases, later named *Brucella melitensis* [1].

There are six recognized *Brucella* species, of which four are pathogenic to humans: *B. melitensis*, *B. abortus*, *B. suis*, and *B. canis* [1,12]. In the majority of human cases, the causative agent is *B. melitensis* [1,3].

Brucellosis can be transmitted through direct and indirect contact with animals and their products,



Figure 1. Brucellar spondylodiscitis in the lumbosacral region of the spine.

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and it can also be acquired in microbiology laboratories [1,12]. *Brucella* bacteria utilize the host's immune defense mechanisms to establish chronic infections, leading to a range of clinical manifestations from fever, fatigue, and joint pain to severe complications like endocarditis and neurological disorders [1,5,12].

The objective of this study is to analyze the clinical features and diagnostic and therapeutic approaches for brucellosis cases treated at the Infectious Diseases Clinic in the University Clinical Center of Kosovo [3,6].

#### Results

Between January 2023 and April 2024, nine patients with brucellosis were treated at the Infectious Diseases Clinic. Of these, six were male (67%) and three were female (33%). The mean age of patients was 35 years (ranging from 20 to 63). No pediatric cases were reported [3].

The most frequently reported symptoms among all patients included fatigue (100%), fever (88%), joint pain (55%), sweating (44%), back pain (33%), abdominal pain (33%), pain and swelling of the right testicle (33%), leg pain (11%), and vomiting (11%). The duration of symptoms prior to hospitalization ranged from 3 days to 3 months (range 3–90 days).

All patients were hospitalized during summer, spring, and winter, with all coming from rural areas. The route of disease transmission was identified for all patients except one. All except one reported direct or indirect contact with infected animals and consumption of raw milk or dairy products [3,6,15].

The most frequently reported clinical manifestation among treated cases was hepatosplenomegaly, present in all cases upon admission and later confirmed by ultrasonography [3]. Additionally, 33% of patients manifested brucellar spondylodiscitis



Figure 2. Grey scale ultrasound - the testis is shown with normal echostructure and a small amount of free fluid in the scrotum in one of the patients with Brucellosis.

in the lumbosacral region [2,6]. No cases of neurobrucellosis, respiratory, or cardiovascular involvement were observed [3,6].

Three male patients (33%) developed localized infection of the testis and epididymis (orchiepididymitis), all affecting the right side [2,13,14]. According to anamnesis data, 33% had family members with brucellosis, indicating a familial epidemic [3,6].

The disease was confirmed with positive serology in all cases (100%) and with positive blood cultures in two cases (22%). For serological testing, a rapid slide agglutination test (RSAT), Wright's reaction, and ELISA were performed [1,5,12]. Wright's reaction was positive in all patients with titers ranging from 1/160 to 1/1280.

Patients were treated with doxycycline and gentamicin for 2–3 weeks, followed by doxycycline and rifampicin for at least 6 weeks [1,5]. Complicated cases with spondylodiscitis received an additional antibiotic, ciprofloxacin, for 3 weeks [6]. Symptomatic therapy and short-term corticosteroids were administered in cases of spondylodiscitis and orchiepididymitis.

The hospitalization period averaged 21 days, and all patients were discharged in improved condition, continuing follow-up as outpatients. No relapses were recorded [3,6].

#### Discussion

Brucellosis is a zoonosis that has been virtually eliminated in most developed countries; however, human cases still occur, primarily imported from endemic regions [1,4]. Recent studies estimate the global incidence of human brucellosis at 1.6–2.1 million new cases per year, which is three to four times higher than earlier estimates [9]. Although its incidence has decreased, brucellosis remains present in Kosovo [3,5]. Due to weak controls in the animal industry and food safety, brucellosis continues to pose a public health risk [7,11].

The first documented cases of brucellosis in Kosovo were reported in 1980 [3,15]. According to data from the National Institute of Public Health of Kosovo, the average morbidity rate between 2000–2004 was 2.97 per 100,000 inhabitants, with the highest incidence recorded in 2010 at 4.9 per 100,000 [3]. Brucellosis is considered an occupational disease that primarily affects shepherds, farmers, veterinarians, slaughterhouse workers, and laboratory staff [7,8]. In our study, all patients were rural residents involved in agriculture and livestock farming, consistent with reports from similar endemic regions [5,13].

The predominance of male patients (67%) is also in line with findings from previous studies, which suggest that occupational exposure accounts for higher male prevalence [3,8]. The mean age of 35 years reflects an economically active population at greater risk for exposure through farming activities. No pediatric cases were observed during this period. However, in a previous study conducted in Kosovo (2006–2011), children accounted for 34% of all brucellosis cases, especially school-aged groups [3].

One-third (33%) of patients in our study reported other family members affected by brucellosis, suggesting familial outbreaks due to shared exposure or consumption of contaminated dairy products [13]. This finding aligns with several international studies showing intrafamilial clustering in endemic areas [5,7].

Brucellosis is known as a multisystemic infection with a wide clinical spectrum, from mild fever to severe organ complications [1,6,10]. The most frequently observed symptoms in our cases—fatigue, fever, joint

pain, and sweating—are typical for acute brucellosis [2,4]. Hepatosplenomegaly was present in all patients, consistent with prior studies indicating liver and spleen enlargement as common findings [3,6].

Spondylodiscitis was present in 33% of cases, predominantly affecting the lumbosacral region, in accordance with global data reporting spinal involvement in 2–54% of cases [10,12]. In a previous study from Kosovo (2006–2011), the hip joint was the most commonly affected site (20%), and meningitis occurred in 1.6% of cases [3]. In our series, no neurobrucellosis was observed.

Orchepididymitis was another significant complication, present in 33% of cases (50% of male patients). This is higher than the 0.8% incidence reported in earlier Kosovo data (2006–2011) [3]. Other studies have found orchepididymitis in 2–14% of cases due to hematogenous spread or excretion of *Brucella* in urine [2,13,14]. Clinicians, especially infectious disease specialists and urologists, should therefore consider brucellar orchepididymitis in

the differential diagnosis of nonspecific testicular inflammation in endemic regions.

No respiratory or cardiovascular involvement was observed, despite previous studies reporting up to 11% involvement of these systems [3,12]. Diagnosis in all patients was confirmed serologically, and 22% had positive blood cultures [6]. This diagnostic rate aligns with other regional studies, where culture positivity remains below 30% [9,12].

Regarding treatment, all patients were treated according to WHO recommendations [1,8]. The combination of doxycycline and gentamicin for the first 2–3 weeks, followed by doxycycline and rifampicin for at least 6 weeks, yielded excellent outcomes. Patients with spondylodiscitis also received ciprofloxacin [9]. The combination therapy effectively prevented relapses in our cohort.

In comparison with earlier protocols used in Kosovo (2006–2011), where streptomycin was frequently used, gentamicin is now preferred due to concerns about *Mycobacterium tuberculosis* resistance in areas with high tuberculosis prevalence [3,9].

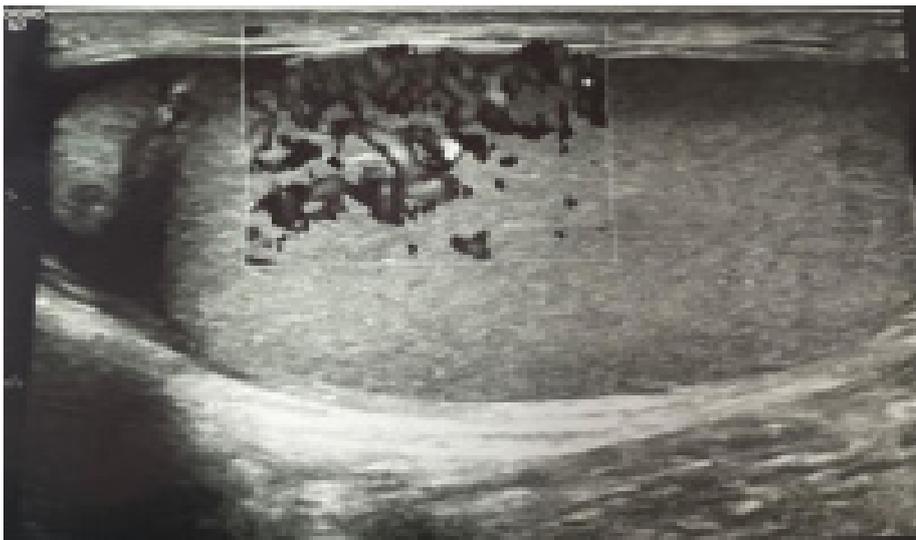


Figure 3. In Color-Doppler ultrasound images, increased vascularization of the testis is observed in a patient with Brucellosis.

Table 1. Symptoms and clinical presentation of patients with Brucellosis

Patient	The First	The Second	The third	The fourth
Age (years)	63 years old	36 years old	20 years old	52 years old
Gender	Male	Female	Female	Male
Duration of symptoms before hospitalization	4 weeks	3 months	1 month	3 days
Patient referral to the admission room	Back pain, difficulty in standing upright, fatigue, joint pain	Fever, back pain, fatigue, joint pain	Fever, sweating, fatigue	Fever, temperature, swelling and pain in the right testicle, fatigue, joint pain
Physical examination	Afebrile, hypertensive, eupneic, eucardiac, hepatosplenomegaly	Afebrile, normotensive, eupneic, eucardiac, hepatosplenomegaly	Afebrile, normotensive, eupneic, eucardiac, hepatosplenomegaly	Afebrile, eucardiac, normotensive, eupneic, swelling in the right testicle, hepatosplenomegaly

## Conclusion

The most common complications of brucellosis in our cases were osteoarticular involvement and orchiepididymitis. The therapeutic protocol consisting of doxycycline and gentamicin, followed by doxycycline and rifampicin, proved highly effective and relapse-free.

Brucellosis remains a significant zoonotic infection in Kosovo, predominantly affecting the rural population engaged in animal husbandry. Early detection, accurate diagnosis, and timely initiation of combination therapy are essential for preventing chronic complications and improving patient outcomes [9,10,12]. Strengthening veterinary control, food safety, and public awareness remain key strategies for brucellosis prevention.

Table 2. Symptoms and clinical presentation of patients with Brucellosis

Patient	The Fifth	The Sixth	The seventh	The Eighth	The Ninth
Age (years)	26 years old	23 years old	24 years old	53 years old	22 years old
Gender	Male	Male	Male	Female	Male
Duration of symptoms before hospitalization	1 month	3 months	4 weeks	3 days	3 days
Patient referral to the admission room	Fever, sweating, fatigue	Fever, temperature, pain in the right leg, pain and swelling in the right testicle, sweating, fatigue, joint pain	Fever, sweating, fatigue	Fatigue, fever, sweating, abdominal pain, vomitus, joint pain	Fever, temperature, abdominal pain, fatigue, pain and swelling in the right testicle
Physical examination	Afebrile, eupnoic, eucardiac, normotensive, hepatosplenomegaly	Afebrile, eupnoic, tahicardiac, normotenzive, hepatosplenomegaly	Afebrile, eupnoic, tahicardiac, normotenzive, hepatosplenomegaly	Afebrile, eupnoic, tahicardiac, normotenzive, hepatosplenomegaly	Afebrile, eupnoic, eucardiac, normotenzive, hepatosplenomegaly

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