Clinical Features and Laboratory Analysis of 391 Cases of Brucellosis with Positive Bacterial Cultures Based on SVM and Single-layer neural network

Liping Zhang[1*], Yinning Niu[2,3*]

1 Ningxia People's Hospital, Ningxia 750002, China
2 State Key Laboratory of Surface Physics, Fudan University, Shanghai 200433, China
3 Center for Field Theory and Particle Physics, Department of Physics, Fudan University, Shanghai 200433, China

Abstract

Objective: This study aimed to analyze the clinical features and laboratory characteristics of brucellosis, providing a basis for clinical diagnosis and treatment. Methods: A retrospective analysis was conducted on clinical and laboratory data from 391 patients with positive bacterial cultures for brucellosis admitted to four hospital campuses of Ningxia Hui Autonomous Region People's Hospital from 2019 to 2023. The epidemiological characteristics (including age, gender, and time distribution), clinical manifestations, symptoms, and laboratory examination results were analyzed. Results: Among the 391 patients, there were 286 males and 105 females, with an average age of 42 years (range: 1-83 years). The top five symptoms and signs before clinical manifestation of brucellosis were fever in 235 cases (60.1%), lumbosacral and joint pain in 212 cases (54.2%), abnormal liver function in 107 cases (27.4%), respiratory system symptoms in 91 cases (23.3%), and concomitant cholecystitis in 76 cases (19.4%). Laboratory examinations showed decreased white blood cell count in 18.9%), decreased red blood cell count in 29.0%), decreased platelet count in 23.6%), and elevated levels of high-sensitivity C-reactive protein in 88.5%). Elevated levels of procalcitonin were observed in 68.2%). Abnormal liver function tests showed elevated levels of serum alanine aminotransferase in 42.0%) and aspartate aminotransferase in 50.8%). Among the 391 cases with positive bacterial cultures, the top three departments with isolates were the Department of Infectious Diseases (52.4%), Emergency Department (9.5%), and Department of Orthopedics (8.4%). Blood cultures had the highest detection rate, and sterile body fluids such as joint fluid, cerebrospinal fluid, puncture fluid, purulent fluid, and pleural or abdominal fluid also showed positive results. The rate of positive bacterial cultures for brucellosis significantly increased from 2021, with the highest rate observed during the period from April to August. Conclusion: Brucellosis exhibits a complex and diverse range of clinical manifestations, often affecting multiple systems without specific characteristics. Laboratory examination results may vary. It is important for clinicians to understand the clinical and laboratory features of brucellosis to achieve early diagnosis and treatment. Keywords: Brucella; Brucellosis.

Introduction

Brucellosis is a common zoonotic infectious disease caused by the Brucella genus and is one of the most important zoonotic diseases in the world. In China, it is classified as a Class B infectious disease under the ”Law on the Prevention and Control of Infectious Diseases.” Brucellosis is primarily transmitted through direct contact with the skin and mucous membranes, but can also be transmitted through the digestive and respiratory tracts. The population is generally susceptible to the disease, but clinical symptoms and complications may vary due to factors such as age, occupation, lifestyle habits, and environment. This study retrospectively analyzed the clinical data of 391 patients with positive bacterial cultures for brucellosis from January 2019 to December 2023 at Ningxia Hui Autonomous Region People's Hospital. It summarizes the epidemiological characteristics, clinical symptoms, and laboratory findings of brucellosis in the local region, aiming to deepen the understanding of brucellosis and improve its accurate diagnosis in clinical practice.

1 Materials and Methods

1.1 Study Subjects

Clinical data from 391 patients with positive bacterial cultures for brucellosis admitted to four hospital campuses of Ningxia Hui Autonomous Region People's Hospital from 2019 to 2023 were collected. The data included gender, age, clinical symptoms, physical signs, laboratory examinations, etc. The patients were grouped into four age ranges (1-14 years, 15-35 years, 36-60 years, ¿60 years) to compare the clinical symptoms and laboratory examination results.

1.2 Reagents and Instruments

The following reagents and instruments were used: BacT/ALERT 3D and BACTEC™ FX automated blood culture systems (BD, USA); blood agar plates, chocolate agar plates with vancomycin, and China blue agar plates (Oxoid, UK); oxidase reagent (bioMérieux, France); urea micro-biochemical reaction tubes (Binhe Microbiology Reagent Co., Ltd., Hangzhou, China).

1.3 Methods

1.3.1 Brucella Cultivation and Identification

Specimens including blood cultures (365 cases), joint fluid (10 cases), puncture fluid (5 cases), cerebrospinal fluid (3 cases), purulent fluid (4 cases), pleural or abdominal fluid (3 cases), and bone marrow (1 case) were collected, totaling 391 cases. Peripheral blood and sterile body fluid samples were inoculated into aerobic and anaerobic blood culture bottles and incubated in an automated blood culture system. After a positive signal from the instrument, the samples were subcultured onto blood agar plates, chocolate agar plates with vancomycin, and China blue agar plates. The plates were incubated at 35°C under aerobic or 5% CO2 conditions for 48 hours. Gram staining or Wright staining was performed on smears, and after 48-72 hours of incubation, colonies with a diameter of 1-2 mm, smooth, shiny, and showing refractive properties were observed. Microscopically, typical sand-like colonies of small Gram-negative coccobacilli were seen. Positive results for oxidase, catalase, and rapid urease tests indicated presumptive Brucella species. All procedures were performed in a biosafety cabinet.

1.3.2 Data Analysis

SPSS 23.0 software was used for data analysis. Descriptive statistics, including counts and percentages (%), were used for categorical data. Chi-square test or Fisher's exact test was used for comparing categorical data among the four age groups. A p-value ¡ 0.05 was considered statistically significant.

2 Results

2.1 General Characteristics of Brucellosis

There were 286 male patients and 105 female patients. The age distribution was as follows: 23 cases in the age group of 1-14 years, 60 cases in the age group of 15-35 years, 211 cases in the age group of 36-60 years, and 97 cases in the age group of 61-83 years. The average age was 42 years (range: 1-83 years).

2.2 Seasonal Distribution of Positive Brucella Cultures at Ningxia People's Hospital from 2019 to 2023

The months of April to August showed a higher incidence of brucellosis. Please refer to Figure 1.

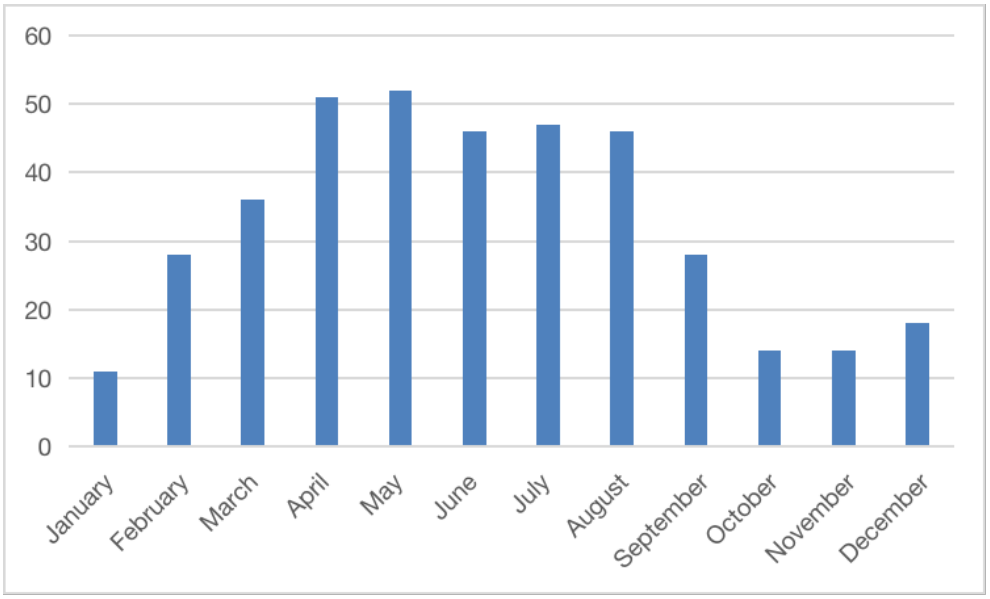

Figure 1. The Seasonal Distribution of Positive Brucella Cultures in Ningxia People's Hospital from 2019 to 2023

2.3 Distribution of Initial Departments for Brucellosis Diagnosis

The top five departments for initial diagnosis of brucellosis were the Department of Infectious Diseases (205 cases), Emergency Department (37 cases), Department of Orthopedics (33 cases), Department of Gastroenterology (23 cases), and Pediatrics (18 cases). Other departments included the Department of Respiratory Medicine, Department of Hematology, Department of Rheumatology and Immunology, Department of Neurology, Department of Cardiovascular and Vascular Surgery, Department of

Urology, and Department of Geriatrics, among others. A few patients were referred to different departments, and some critically ill patients were referred to the ICU.

2.4 Major Clinical Manifestations and Diagnosis

2.4.1 Initial Clinical Symptoms

Brucellosis presents with a complex array of clinical manifestations, mainly including fever, fatigue, cough with sputum, headache, dizziness, and lumbar and leg pain. The primary initial clinical symptoms in this group of cases were fever (235 cases, 60.1%), lumbar and leg joint pain (212 cases, 54.2%), cough and sputum production (91 cases, 23.3%), headache and dizziness (45 cases, 11.5%), and abdominal pain and distension (44 cases, 11.3%). Other clinical symptoms included poor appetite, fatigue, rash, blurred vision, and hearing loss. There were statistically significant differences among the four age groups in terms of fever, abdominal pain and distension, headache and dizziness, and rash as initial clinical symptoms (P¡0.05). See Figure 2, 3 and table 1.

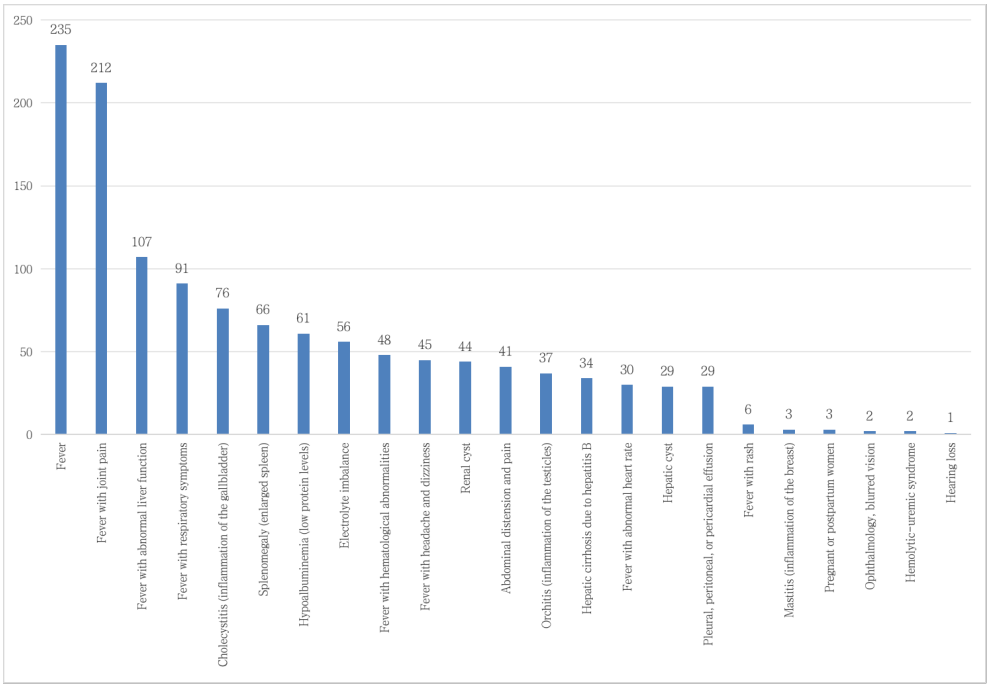

Figure 2. Clinical Manifestations, Affected Systems, and Complications in 391 Brucellosis Patients

2.4.2 Clinical Diagnosis and Systemic Complications

The main clinical symptoms and affected systems in this group of cases were abnormal liver function (107 cases, 27.4%), cholecystitis (76 cases, 19.4%), splenomegaly (66 cases, 16.9%), hypoalbuminemia (61 cases, 15.6%), electrolyte imbalances (56 cases, 14.3%), hematological disorders (48 cases, 12.3%), orchitis (37 cases, 9.5%), abnormal heart rate (30 cases, 7.47%), and severe conditions such as brucella meningitis, endocarditis, and hemophagocytic syndrome. There were statistically significant differences among the four age groups in terms of abnormal liver function, cholecystitis, hepatic cysts, renal cysts, splenomegaly, hypoalbuminemia, and complications of hepatitis B-related cirrhosis (P¡0.05). See Figure 3, 4 and Table 1.

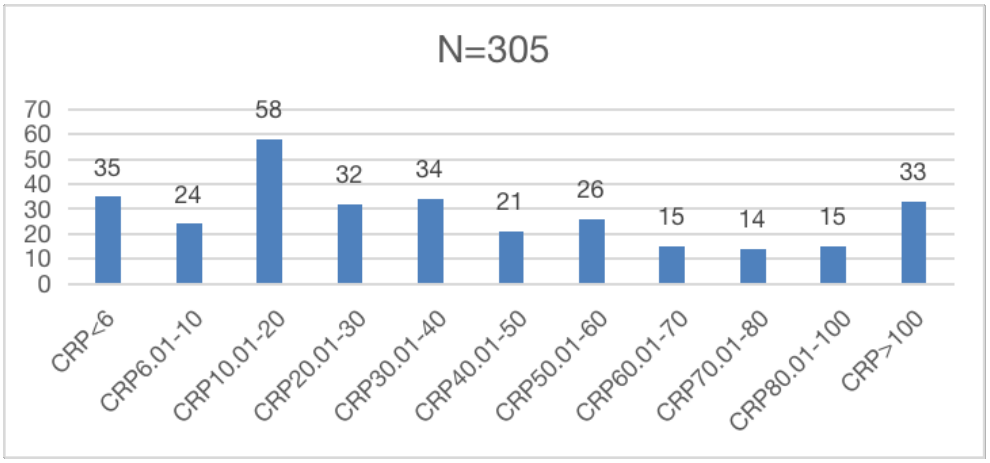

Figure 3. Distribution of CRP Levels in 305 Patients

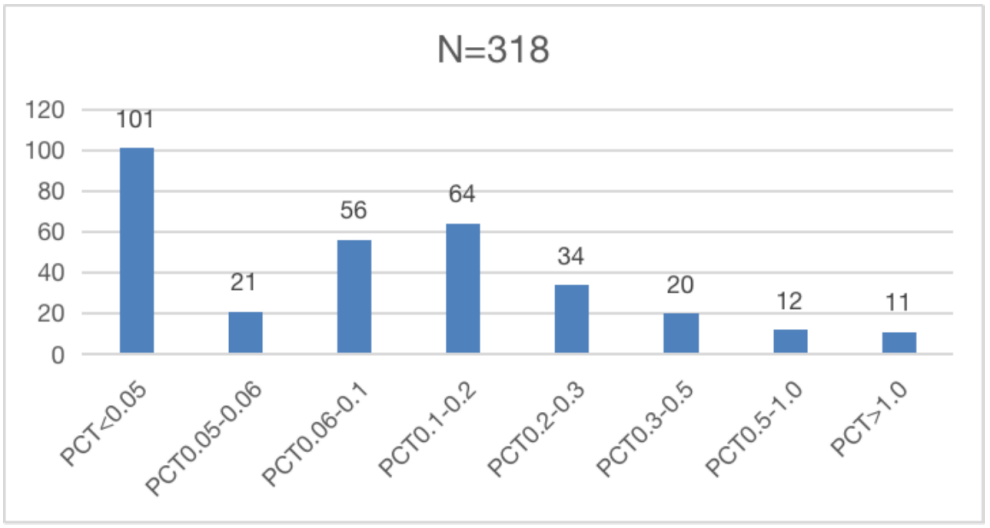

Figure 4. Distribution of PCT Levels in 318 Patients

2.4.3 Laboratory Examinations

Abnormal white blood cell (WBC) count was observed in 25.1% of cases, with 18.9% showing a decrease and 6.2% showing an increase. Abnormal red blood cell (RBC) count was observed in 31.9% of cases, with 29.0% showing a decrease and 2.9% showing an increase. Abnormal platelet (PLT) count was observed in 28.2% of cases, with 23.6% showing a decrease and 4.7% showing an increase. Elevated high-sensitivity C-reactive protein (hs-CRP) was found in 88.5% of cases, elevated alanine aminotransferase (ALT) in 42.0%, elevated aspartate aminotransferase (AST) in 50.8%, elevated total bile acid (TBA) in 24.1%, elevated adenosine deaminase (ADA) in 75.9%, elevated alkaline phosphatase (ALP) in 21.3%, and elevated gamma-glutamyltransferase (GGT) in 38.5%. Elevated procalcitonin (PCT) was found in 68.6% of cases, with 31.4% having a normal PCT level and 64.8% having a PCT value between 0.05 and 1.0. Only 11 cases (3.4%) had a PCT value greater than 1.0. Statistically significant differences among the four age groups were observed in CRP¿60, elevated ADA, elevated ALP, elevated GGT, and elevated PCT (P¡0.05).

3 Discussion

Brucella can enter the human body through pathways such as the skin, respiratory tract, and digestive tract, and after infecting the body, it can cause hematogenous dissemination, leading to bacteremia or septicemia. The gold standard for diagnosing brucellosis is the identification of Brucella in blood, bone marrow, or sterile body fluids through cultivation [6-7]. In this study, we retrospectively analyzed the clinical characteristics of 391 patients with positive bacterial cultures for Brucella infection admitted to our hospital from January 2019 to December 2023. Among the 391 patients, 365 had positive blood cultures for Brucella, and other specimens including joint fluid, cerebrospinal fluid, pleural or abdominal fluid, and puncture fluid were all inoculated into blood culture bottles for automated bacterial growth culture. The alarm time for positive Brucella culture was greater than 48 hours, which is similar to the results reported by Ma et al. [14]. Therefore, it is recommended that clinical suspected brucellosis patients collect blood cultures and sterile body fluid specimens for automated growth culture, and extend the culture time if necessary. Brucellosis is the most common zoonotic disease worldwide, and its incidence is closely related to occupation and lifestyle habits [6]. Ningxia Hui Autonomous Region is located in the northwest agricultural and pastoral area of China, and the local habits and close contact between patients and infected animals, their products, or contaminated materials make this region a high-prevalence area for brucellosis. The results of this study showed that the number of brucellosis patients admitted to our hospital has been increasing since 2019, and the positive rate of Brucella culture has significantly increased since 2021. Male patients were more than twice as common as female patients, and the disease mainly affected middle-aged and elderly individuals. Ningxia is a high-incidence area for brucellosis, and the disease occurs in all seasons, with the highest incidence in spring and summer. After invading the human body, Brucella can cause damage to multiple systems throughout the body, including the respiratory system, musculoskeletal system, circulatory system, blood system, central nervous system, digestive system, and immune system, leading to a variety of clinical symptoms and signs. In this study, the primary clinical symptoms were fever, fatigue, back pain, joint pain, and respiratory system involvement. Fever is the most common clinical manifestation of brucellosis, with 235 out of 391 patients (60.1%) presenting with fever as the initial symptom. However, 156 patients (39.9%) did not have fever symptoms, which should alert clinicians. Additionally, back pain and joint pain were the second most common initial clinical symptoms, accounting for 54.2%, which is consistent with several related studies on brucellosis patients [17-18]. Hepatic dysfunction (107 cases, 27.4%), cholecystitis (76 cases, 19.4%), splenomegaly (66 cases, 16.9%), hypoalbuminemia (61 cases, 15.6%), electrolyte imbalance (56 cases, 14.3%), hematological abnormalities (48 cases, 12.3%), and orchitis (37 cases, 9.5%) are the most common clinical symptoms and complications caused by Brucella infection. The incidence of abnormal liver function in brucellosis patients reported in foreign studies ranges from 2.5% to 43.6% [1, 19-20], which is consistent with the findings of this study. By comparing and analyzing the clinical symptoms, affected systems, and complications among different age groups, significant differences were found in fever, abdominal pain/distension, headache/dizziness, rash, abnormal liver function, cholecystitis, liver cysts, renal cysts, splenomegaly, hypoalbuminemia, and hepatitis B-related cirrhosis, with statistical significance observed among the four age groups (P¡0.05). Adolescents exhibit stronger immune responses, with higher proportions of fever and rash as clinical manifestations, while middle-aged and elderly individuals have a higher incidence of cholecystitis, liver cysts, renal cysts, hypoalbuminemia, and hepatitis B-related cirrhosis as underlying diseases. Brucella infection can induce systemic immune-inflammatory reactions, especially after Brucella bacteremia, which may be more intense and further contribute to the

occurrence of underlying diseases by affecting relevant organs. Furthermore, we also noted the occurrence of more severe complications in some patients, such as brucella meningitis and hemophagocytic syndrome. This study also analyzed the laboratory examination results of the 391 cases. Among them, 386 patients underwent complete blood count (CBC) tests, and these patients showed varying degrees of blood cell abnormalities, with 18.9% having decreased white blood cell (WBC) counts, and only 6.2% having increased WBC counts. Red blood cell (RBC) reduction was observed in 29.0% of the cases, and platelet (PLT) reduction was observed in 23.6% of the cases. Brucellosis can affect multiple organ systems, with the liver being the most severely affected. Among the 386 patients who underwent serum biochemical tests, 42.0% showed elevated alanine aminotransferase (ALT) levels, 50.8% showed elevated aspartate aminotransferase (AST) levels, and 24.1% showed elevated total bile acid (TBA) levels. These findings are due to liver cell damage, increased cell membrane permeability, and elevated ALT activity. Liver cell necrosis, reaching the level of organelles, leads to increased AST activity [11]. Additionally, 75.9% showed elevated adenosine deaminase (ADA) levels, and 21.3% showed elevated alkaline phosphatase (ALP) levels. There were significant differences in ALP and gamma-glutamyl transferase (GGT) biochemical reactions among different age groups, which may be attributed to the higher incidence of cholecystitis as an underlying disease in the middle-aged and elderly groups. The occurrence of brucella infection triggers inflammatory damage to liver cells, resulting in impaired bile excretion and bile reflux into the blood [12]. Elevated high-sensitivity C-reactive protein (hs-CRP) accounted for 88.5% of the infection markers, which is consistent with the results of Qie et al. [25]. Significant differences were observed among the four age groups when comparing CRP levels greater than 60, indicating that hs-CRP, as an inflammatory marker, lacks specificity. With increasing age, underlying diseases such as cholecystitis and hepatitis-related cirrhosis increase, leading to elevated hs-CRP levels. Procalcitonin (PCT), as a bacterial infection marker, did not show significant elevation in brucella bacteremia. In this study, 68.6% of the cases showed elevated PCT levels, while 31.4% did not, and the majority of elevated PCT values ranged from 0.05 to 1.0, accounting for 64.8%, with only 11 cases (3.4%) exceeding 1.0. During brucella bacteremia, procalcitonin levels were significantly lower than those observed in patients with bacteremia caused by Escherichia coli and Staphylococcus aureus, providing a basis for the preliminary diagnosis of brucella bacteremia by clinicians [26].

4 Summary

In conclusion, brucellosis is a significant public health issue in China, and its incidence has been increasing in recent years. Ningxia Hui Autonomous Region is a high-risk area for brucellosis. Due to its nonspecific and diverse clinical manifestations, the disease is often challenging to diagnose. Therefore, it is crucial for clinicians to have a thorough understanding of the clinical characteristics of the disease and the specificity of laboratory tests in order to achieve early diagnosis and treatment. Indeed, your summary is accurate. Brucellosis is a major public health problem in China, and its incidence has been increasing in recent years. Ningxia Hui Autonomous Region is one of the high-risk areas for this disease. The clinical manifestations of brucellosis are typically nonspecific and complex, making diagnosis challenging. Therefore, clinicians should have a comprehensive understanding of the clinical features of the disease and the specificity of laboratory tests to achieve early diagnosis and treatment. Early diagnosis is crucial for the treatment and prognosis of brucellosis. Common laboratory tests used in clinical practice include blood tests, serum biochemical markers, and inflammation indicators. These tests can help evaluate the patient's condition and the

extent of inflammation, providing diagnostic evidence. In summary, early diagnosis and treatment are essential for brucellosis. Clinicians need to have a thorough understanding of the clinical characteristics and specific laboratory tests of the disease to achieve timely and accurate diagnosis and initiate appropriate treatment measures.

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