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# Clinical Manifestations and Laboratory Findings in Childhood Brucellosis, Ningxia Region, China: A Retrospective Study

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## Abstract

Background: This study aims to analyze the clinical manifestations and laboratory findings in pediatric brucellosis between May 2019 and September 2022. Methods: Demographic characteristics, clinical data, and laboratory test results of 126 cases were systematically evaluated. Results: Among the cases, 76 (60.32%) were male and 50 (39.68%) were female. A total of 96.03% had a history of close contact with sheep/goats, which increases the risk of infection in local children. The most common symptoms were fever (96/126; 76.19%), joint pain (95/126; 75.40%), and fatigue (61/126; 48.41%). The most common complications were knee joint effusion (51/126; 40.48%) and gastrointestinal disturbances (51/126; 40.48%). The present analysis highlights that *Brucella* infection causes significant health complications in children, primarily hematological abnormalities (e.g., White Blood Cell (WBC) and Platelet (PLT) disturbances), along with frequent elevations in liver enzymes (Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST)), cardiac markers (Lactate Dehydrogenase (LDH), Creatine Kinase-MB [CK-MB]), and inflammatory markers (C Reactive Protein (CRP)). Four indices measured were significantly elevated in *Brucella*-infected patients, including ALT ($p$ = 0.01), AST ($p$ = 0.001), LDH ($p < 0.001$), and CRP ($p = 0.027$). Following treatment, 89 patients (70.6%) demonstrated significant clinical improvement. Conclusions: This study's findings indicate that brucellosis can lead to severe complications in children, potentially impairing normal development. Timely diagnosis and immediate therapeutic intervention are crucial for reducing disease severity and complications.

**Keywords**

Brucellosis, Children, Clinical Manifestations, Complications, Laboratory Findings

## 1. Background

Brucellosis is a widespread zoonotic disease caused by infection with *Brucella* spp., a genus of bacteria commonly found in livestock that poses a significant threat to human health [1]. *Brucella* is a small, gram-negative bacterium with a high infective capacity and multiple routes of transmission [2], one of the most common of which involves direct and indirect contact between humans and infected animals [3]. Brucellosis in humans can lead to prolonged fever, arthralgia muscularis, fatigue, and sweating in the acute stage, followed by enlargement of the liver and spleen, as well as local infection and disability during the chronic course of the disease [4].

Brucellosis still predominantly affects middle-aged and elderly farmers who are frequently in indirect or direct contact with infected animals; however, owing to the geographic expansion of human brucellosis, its prevalence rate in nonoccupational populations has notably increased, including in children [5]. In familial clusters of brucellosis, children can become infected with *Brucella* strains through various routes, including the consumption of raw goat milk or transmission via breastfeeding [6]. Additionally, congenital brucellosis cases have also been reported in Türkiye, Saudi Arabia, and Kuwait, which are all areas in which the disease is severely endemic [7]. In humans, brucellosis is associated with a broad range of clinical manifestations, with multi-organ involvement. Consequently, it can easily be misdiagnosed as another multisystemic disease, which can lead to delays in treatment and an increased risk of complications [8]. The diagnosis of human brucellosis is challenging in children owing to its nonspecific symptoms and rare exposure history, which can lead to misdiagnosis and treatment delays [9] [10]. Therefore, timely and accurate diagnosis is essential for effective clinical management of brucellosis and for achieving favorable therapeutic outcomes [11].

Systematic epidemiological studies and proper analyses of laboratory findings in childhood brucellosis cases are vital steps in providing helpful clues to improve the diagnosis and management of the disease in children. Therefore, this study aimed to ascertain the epidemiological factors, clinical manifestations, complications, and laboratory findings associated with childhood brucellosis, and to provide novel insights that could be used to devise countermeasures to curb the spread of the disease and improve treatment outcomes.

## 2. Methods

### 2.1. Data Sources, Case Definition, and Diagnostic Metrics

This study included 126 pediatric patients (aged 11 months to 14 years) diagnosed

with brucellosis at the Fourth People's Hospital of Ningxia Hui Autonomous Region between January 2019 and December 2022. Human brucellosis was defined and diagnosed based on previously described criteria [12]. The case definition was based on serological test results, clinical manifestations, and epidemiological contact history. Screening was performed using the Rose Bengal Plate Test (RBPT) and confirmed through the Serum Agglutination Test (SAT) (Araj, 2010). A diagnosis of brucellosis was confirmed when the RBPT yielded positive results and the SAT showed a titer of ≥1:100, or when the duration of the disease course exceeded 1 year, with a titer of ≥1:50 [13]. Due to biosafety considerations, conventional bacterial biotyping is not routinely performed at our institution.

Following admission, all patients with brucellosis underwent a comprehensive clinical evaluation. Epidemiological exposure history, clinical manifestations, and physical examination findings were systematically extracted from electronic medical records. Routine laboratory analyses included complete blood count (Hemoglobin (Hb) levels, total leukocyte count, absolute neutrophil count, and Platelet (PLT) count), liver function tests (serum Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) levels, along with Total Bilirubin (TBIL)), myocardial enzyme profiling (Lactate Dehydrogenase (LDH) and Creatine Kinase-MB (CK-MB)), and C-Reactive Protein (CRP) quantification. The laboratory test results presented in this study were obtained from all patients upon hospital admission.

### 2.2. Group Allocations and Follow-Up

Based on established clinical classifications, patients were stratified according to disease duration into acute (<8 weeks), subacute (8 - 24 weeks), and chronic (>24 weeks) phases [14]. Furthermore, patients were stratified into *Brucella*-positive (n = 48) and *Brucella*-negative (n = 47) groups based on results of blood culture isolation of *Brucella* strains. The remaining 31 mildly symptomatic patients did not undergo blood culture, and were diagnosed serologically. All cultures were obtained during hospitalization prior to antimicrobial therapy. Treatment regimens consisted of at least two-drug combinations, tailored according to disease severity. Following hospitalization, patients were monitored throughout the 6-week oral therapy phase, with additional follow-up 6 months after completing the half-year treatment course.

### 2.3. Statistical Analysis

Microsoft Excel 2020 software was used to record and process the data. Data were analyzed using SPSS for Windows (version 20.0; SPSS, Chicago, IL, USA). Data with a non-normal distribution were evaluated using descriptive statistics, and percentages and median (Interquartile Range, IQR) values were recorded. Differences were considered statistically significant at $p < 0.05$. Inter-group comparisons were conducted using Mann-Whitney U tests, Analysis of Variance (ANOVA), or Welch's ANOVA based on the outcomes of Shapiro-Wilk's normality tests and

Bartlett's homogeneity of variance tests.

## 3. Results

### 3.1. Demographic and Exposure History of Brucellosis Cases

Among the 126 pediatric brucellosis cases, there were more males (n = 76, 60.3%) than females (n = 50, 39.7%) (Table 1). The median age was 7.5 years (range: 11 months–14 years), with the age distribution as follows: 0 - 3 years (n = 31, 24.6%), 4 - 9 years (n = 46, 36.5%), and 10 - 14 years (n = 49, 38.9%). All cases originated from rural areas, predominantly Ningxia (n = 122), with four from adjacent regions (Inner Mongolia: n = 3; Gansu: n = 1). Ethnically, most patients were Hui (62.7%, n = 79), followed by Han (36.5%, n = 46) and Mongolian (0.8%, n = 1).

Table 1. Demographic and epidemiological overview of child patients with brucellosis.

| Variable | | Overall (n = 126) | | *Brucella*-positive group (n = 48) | | *Brucella*-negative group (n = 47) | | Undetected (n = 31) | |
|---|---|---|---|---|---|---|---|---|---|
| Staging | Acute | 37 | 29.37% | 8 | 16.67% | 14 | 29.79% | 15 | 48.39% |
| | Sub-acute | 44 | 34.92% | 20 | 41.67% | 18 | 38.30% | 6 | 19.35% |
| | Chronic | 45 | 35.71% | 20 | 41.67% | 15 | 31.91% | 10 | 32.26% |
| Sex | Man | 76 | 60.32% | 27 | 56.25% | 30 | 63.83% | 19 | 61.29% |
| | Female | 50 | 39.68% | 22 | 45.83% | 17 | 36.17% | 11 | 35.48% |
| Age | 0 - 3 | 31 | 24.60% | 15 | 31.25% | 10 | 21.28% | 6 | 19.35% |
| | 4 - 9 | 46 | 36.51% | 17 | 35.42% | 18 | 38.30% | 11 | 35.48% |
| | 10 - 14 | 49 | 38.89% | 16 | 33.33% | 19 | 40.43% | 14 | 45.16% |
| Nation | Han | 46 | 36.51% | 19 | 39.58% | 16 | 34.04% | 11 | 35.48% |
| | Hui | 79 | 62.70% | 28 | 58.33% | 31 | 65.96% | 20 | 64.52% |
| | Mongolia | 1 | 0.79% | 1 | 2.08% | 0 | 0.00% | 0 | 0.00% |
| Contact history | Sheep | 121 | 96.03% | 47 | 97.92% | 45 | 95.74% | 29 | 93.55% |
| | Cattle | 4 | 3.17% | 1 | 2.08% | 2 | 4.26% | 1 | 3.23% |
| | Unknown | 1 | 0.79% | 0 | 0.00% | 0 | 0.00% | 1 | 3.23% |
| Place of residence | Ningxia | 122 | 96.83% | 45 | 93.75% | 46 | 97.87% | 31 | 100.00% |
| | Inner Mongolia | 3 | 2.38% | 2 | 4.17% | 1 | 2.13% | 0 | 0.00% |
| | Gansu | 1 | 0.79% | 1 | 2.08% | 0 | 0.00% | 0 | 0.00% |
| Hospitalization days | ~10 | 32 | 25.40% | 15 | 31.25% | 16 | 34.04% | 1 | 3.23% |
| | ~20 | 86 | 68.25% | 28 | 58.33% | 28 | 59.57% | 30 | 96.77% |
| | 20 - 41 | 8 | 6.35% | 5 | 10.42% | 3 | 6.38% | 0 | 0.00% |
| Follow up | Cured | 89 | 70.63% | 34 | 70.83% | 36 | 76.60% | 19 | 61.29% |
| | Treatmenting | 13 | 10.32% | 7 | 14.58% | 3 | 6.38% | 3 | 9.68% |
| | Occasional discomfort | 4 | 3.17% | 2 | 4.17% | 1 | 2.13% | 1 | 3.23% |
| | Missing | 20 | 15.87% | 5 | 10.42% | 7 | 14.89% | 8 | 25.81% |

Epidemiological investigation revealed that 96.0% of patients (n = 121) had exposure to sheep/goats, while 3.2% (n = 4) reported contact with cattle (Table 1). The mean hospitalization duration was 13.3 days (range: 3 - 41 days), categorized as <10 days (25.4%, n = 32), 10 - 20 days (68.3%, n = 86), and >20 days (6.4%, n = 8). Treatment outcomes showed 89 patients achieved cure (clinical symptoms disappeared and laboratory examination turned negative), 13 remained in treatment, 4 reported residual symptoms, and 20 were lost to follow-up.

### 3.2. Clinical Manifestations and Complications of Brucellosis Cases

In this study, 37 cases were of acute brucellosis (29.36%), followed by subacute (34.92%, n = 44) and chronic (35.71%, n = 45) forms. The most prevalent clinical manifestations included fever (76.2%, n = 96), arthralgia (75.4%, n = 95), and fatigue (48.4%, n = 61). Less common symptoms included headache (4.8%, n = 6), with additional reports of weight loss and night sweats.

Febrile cases typically demonstrated low-to-moderate elevations, with 74.6% (n = 94) showing temperatures between 37.2˚C - 39.0˚C (equally distributed between 37.2˚C - 38.0˚C and 38.1˚C - 39.0˚C). Only 1.6% (n = 2) developed high-grade fever (>41.0˚C). Major complications included: knee joint effusion (40.5%, n = 51), gastrointestinal disturbances (40.5%, n = 51), respiratory symptoms (23.8%, n = 30), splenomegaly (12.7%, n = 16), lumbar pain (10.3%, n = 13), testicular involvement (8.7%, n = 11). In addition, imaging studies identified joint abnormalities in 17.5% (n = 22) of cases.

### 3.3. Routine Laboratory Characteristics of Brucellosis Cases

We analyzed 14 laboratory parameters in this cohort of 126 patients with brucellosis. Hematological abnormalities: the overall mean white blood cell (WBC) count was 6.55 × $10^9$/L (range: 3.34 - 13.66 × $10^9$/L) (Table 2). Notably, 15.08% of patients (n = 19) had leukopenia with a mean WBC count of 3.34 × $10^9$/L, while 9.52% (n = 12) exhibited leukocytosis with a mean count of 13.66 × $10^9$/L. Granulocyte counts averaged 2.45 × $10^9$/L (range: 0.54 - 8.97 × $10^9$/L), and lymphocyte (LV) counts showed a mean of 3.53 × $10^9$/L (range: 1.01 - 12.12 × $10^9$/L). Among these, 38 patients (30.16%) demonstrated abnormal LV counts, including 29 cases (23.02%) of lymphopenia (mean: 1.69 × $10^9$/L; range: 0.01 - 1.99 × $10^9$/L) and 9 cases (7.14%) of lymphocytosis (mean: 9.29 × $10^9$/L; range: 7.12 - 12.12 × $10^9$/L).

Regarding biochemical markers, PLT counts averaged 280 × $10^9$/L (range: 71 - 525 × $10^9$/L), with 49 patients showing thrombocytosis (mean: 377 × $10^9$/L; range: 306 - 525 × $10^9$/L). The mean Hb level was 119.13 g/L (range: 79 - 168 g/L), with 63 patients (50%) presenting with anemia (mean: 108 g/L; range: 79 - 119 g/L).

Liver function tests revealed elevated transaminase levels in many patients. The mean ALT concentration was 57.18 U/L (range: 6.10 - 998.60 U/L), with 35 patients (27.78%) showing significant elevation (mean: 153.34 U/L; range: 40.9 - 998.6 U/L). Similarly, the median AST level was 62.0 U/L (range: 10.3 - 776.3 U/L), with 55 patients (43.65%) demonstrating elevated values (mean: 107.2 U/L; range:

40.5 - 776.3 U/L). TBIL levels remained within normal limits (mean: 7.5 μmol/L; range: 0.8 - 21.2 μmol/L). However, 21 patients (16.67%) showed hypoalbuminemia with a mean albumin (ALB) level of 32.25 g/L (range: 17.3 - 34.9 g/L) compared with the overall mean of 38.94 g/L (range: 17.3 - 48.7 g/L).

Cardiac and inflammatory markers were frequently elevated. The mean LDH concentration was 323.75 U/L (range: 122.5 - 915.6 U/L), with 82 patients (65.08%) showing values above the reference range (mean: 383.7 U/L; range: 246 - 915.6 U/L). CK-MB levels averaged 20.56 U/L (range: 6.5 - 77 U/L) in 121 patients, with 59 cases (48.76%) demonstrating elevated levels (mean: 26.95 U/L; range: 18.4 - 77 U/L). Among 114 patients tested, CRP levels averaged 8.57 mg/L (range: 0.07 - 61.67 mg/L), with 49 patients (42.98%) showing elevated concentrations (mean: 16.45 mg/L; range: 8.98 - 61.67 mg/L) (Table 2).

**Table 2.** Laboratory findings of child patients with brucellosis.

| Variable | Reference | No. of cases | Medium | Range |
|---|---|---|---|---|
| WBC ($10^9$/L) | | 126 | 6.55 | 2.43 - 18.6 |
| <4 | | 19 | 3.34 | 2.42 - 3.98 |
| >10 | | 12 | 13.66 | 10.52 - 19.6 |
| GRAN ($10^9$/L) | 0.8 - 8 | 126 | 2.45 | 0.54 - 8.97 |
| LV ($10^9$/L) | 2 - 7 | 126 | 3.53 | 1.01 - 12.12 |
| <2 | | 29 | 1.69 | 0.01 - 1.99 |
| >7 | | 9 | 9.29 | 7.12 - 12.12 |
| PLT ($10^9$/L) | 100 - 300 | 126 | 280 | 71 - 525 |
| | >300 | 49 | 377 | 306 - 525 |
| HB (g/L) | 120 - 220 | 126 | 119.13 | 79 - 168 |
| | <120 | 63 | 108 | 79 - 119 |
| ALT (U/L) | 0 - 40 | 126 | 57.18 | 6.1 - 998.6 |
| | >40 | 35 | 153.34 | 40.9 - 998.6 |
| AST (U/L) | 0 - 40 | 126 | 62 | 10.3 - 776.3 |
| | >40 | 55 | 107.2 | 40.5 - 776.3 |
| TBIL (umol/L) | 3.4 - 17.1 | 126 | 7.5 | 0.8 - 21.2 |
| ALB (g/L) | 35 - 50 | 126 | 38.94 | 17.3 - 48.7 |
| | <35 | 21 | 32.25 | 17.3 - 34.9 |
| LDH (U/L) | 109 - 245 | 121 | 323.75 | 122.5 - 915.6 |
| | >245 | 82 | 383.7 | 246 - 915.6 |
| CKMB | 0 - 18 | 121 | 20.56 | 6.5 - 77 |
| | >18 | 59 | 26.95 | 18.4 - 77 |
| CRP (mg/L) | 0.68 - 8.2 | 114 | 8.57 | 0.07 - 61.67 |
| | >8.2 | 49 | 16.45 | 8.98 - 61.67 |
| IL-6 ng/L | 0.373 - 0.463 | 7 | 35 | 0.97 - 160 |
| PCT | | 25 | 0.27 | 0.037 - 1.32 |

Serial laboratory evaluations across three distinct time points revealed a consistent downward trend in both the number of patients requiring testing and their corresponding biochemical values. With continued antimicrobial therapy, most patients (82/126, 65.1%) achieved normalization of their laboratory parameters. However, persistent abnormalities were noted in a clinically significant subset. Hepatic transaminases remained elevated at discharge in 21.6% of cases (26/120): ALT: mean 91.58 U/L (41.6 - 273.2), representing a 2.3-fold increase above the upper limit of normal (ULN); AST: mean 87.58 U/L (40.6 - 323.6), 2.1-fold above ULN. Inflammatory markers persisted in 18.4% of cases (22/120): CRP: mean 12.34 mg/L (8.2 - 25.6). These persistent abnormalities, particularly hepatic enzyme elevations exceeding twice the ULN, strongly indicate the necessity for extended therapeutic monitoring and consideration of adjunct hepatoprotective agents. Thus, scheduled follow-up testing at 4 - 6 weeks intervals post-discharge. The findings substantiate current guidelines recommending a minimum 6-week treatment course for pediatric brucellosis, with vigilance for patients demonstrating delayed biochemical normalization.

### 3.4. Comparison Analysis of Laboratory Parameters at Different Groups

The variant analysis revealed statistically significant differences ($p < 0.05$) in four key laboratory parameters across patient subgroups, including LV counts ($p = 0.013$), ALT ($p = 0.032$), AST ($p = 0.042$), and CRP concentrations ($p = 0.005$) (Table 3). These findings suggest distinct pathophysiological patterns among clinical subgroups, with implications for immune response modulation (LV variation), inflammatory activity (CRP elevation), and hepatic involvement (ALT and AST abnormalities). Based on the bacteriology groups, four indices, including ALT ($p = 0.01$), AST ($p = 0.001$), LDH ($p < 0.001$), and CRP ($p = 0.027$), showed statistically significant differences in two groups (Table 4). In addition, fever showed a statistically significant difference in the *Brucella*-positive groups ($\chi^2$, $p < 0.001$).

**Table 3.** Statistical analysis of laboratory parameters in acute and chronic groups.

| Variants | Acute | Subacute | Chronic | F value | *P* |
|---|---|---|---|---|---|
| White Blood Cells (WBCs) | 7.185 ± 3.482 | 6.854 ± 3.181 | 5.744 ± 2.304 | 2.683 | 0.072 |
| Neutrophils | 2.530 ± 1.448 | 2.475 ± 1.378 | 2.360 ± 1.235 | 1.172 | 0.842 |
| Lymphocytes | 4.06 ± 2.380 | 3.742 ± 2.473 | 2.868 ± 1.388 | 4.643 | **0.013*** |
| Hemoglobin (Hb) | 115.65 ± 12.327 | 120.59 ± 15.977 | 119.64 ± 14.351 | 1.303 | 0.275 |
| Platelets (PLT) | 281.24 ± 104.539 | 295.25 ± 105.753 | 263.76 ± 76.264 | 1.206 | 0.303 |
| Alanine Aminotransferase (ALT) | 74.914 ± 170.298 | 68.111 ± 98.325 | 32.100 ± 29.368 | 3.666 | **0.032*** |
| Aspartate aminotransferase (AST) | 79.157 ± 136.260 | 68.441 ± 79.086 | 41.487 ± 29.594 | 3.352 | **0.042*** |
| Total Bilirubin (TBIL) | 7.605 ± 2.706 | 7.784 ± 3.509 | 7.169 ± 4.412 | 0.331 | 0.719 |
| Albumin (ALB) | 39.208 ± 3.631 | 39.498 ± 3.649 | 37.849 ± 5.235 | 1.862 | 0.16 |
| Lactate Dehydrogenase (LDH) | 337.364 ± 120.840 | 320.941 ± 126.860 | 319.093 ± 171.723 | 0.188 | 0.829 |
| Creatine Kinase (CK) | 21.292 ± 9.046 | 21.783 ± 11.250 | 18.633 ± 6.914 | 1.417 | 0.247 |
| C-Reactive Protein (CRP) | 3.574 ± 4.278 | 5.988 ± 7.217 | 10.682 ± 14.360 | 5.765 | **0.005*** |

**Table 4.** Comparison analysis of 12 variables in two bacteriology groups.

| Variable | *Brucella*-positive (n = 48) | *Brucella*-negative (n = 47) | U value | *P* |
|---|---|---|---|---|
| White Blood Cells (WBC) | 5.72 (4.723, 8.160) | 5.9 (4.49, 8.01) | 1146 | 0.893 |
| Neutrophils | 2.08 (1.5125, 2.765) | 2.52 (1.44, 3.16) | 1024.5 | 0.441 |
| Lymphocytes | 3.13 (2.2575, 4.5750) | 2.7 (1.93, 3.51) | 1371 | 0.07* |
| Hemoglobin (Hb) | 118.50 (109.00, 125.00) | 124 (111, 132) | 866 | 0.051 |
| Platelets (PLT) | 272.50 (190.0, 336.25) | 282 (227, 376) | 904 | 0.095 |
| Alanine aminotransferase (ALT) | 33.85 (16.375, 66.925) | 20 (12.7, 32) | 1474.5 | 0.01* |
| Aspartate aminotransferase (AST) | 45.250 (33.075, 70.050) | 31.6 (25, 44) | 1568 | 0.001* |
| Total Bilirubin (TBIL) | 6.25 (4.30, 8.650) | 7 (5.5, 8.5) | 1007 | 0.368 |
| Albumin (ALB) | 39.050 (36.775, 40.825) | 40 (37, 42.7) | 994 | 0.318 |
| Lactate Dehydrogenase (LDH) | 335.5 (270.6, 450.25) | 236.9 (199.5, 291.5) | 1661 | < 0.001 |
| Creatine Kinase (CK) | 18.95 (15.425, 25.025) | 17.8 (15, 22.5) | 1172 | 0.484 |
| C-Reactive Protein (CRP) | 5.4 (2.99, 12.51) | 2.4 (1.0, 8.1) | 1396 | 0.027* |

Note: Using Welch's ANOVA analysis.

## 4. Discussion

In recent years, the rapid economic development of agricultural and pastoral regions, along with economic challenges related to animal husbandry, quarantine, and immunization measures, has hindered the timely and effective implementation of positive changes. Additionally, the inability to promptly identify infected animals hinders effective control of transmission, contributing to the rapid spread of microorganisms and the establishment of epidemics among humans and animals [15]. Historically, farmers and herdsmen predominantly comprised infected populations; however, non-occupational individuals, such as children, are becoming increasingly affected [16] [17].

Brucellosis is concentrated in adults who are involved in the breeding and domestication of animals, which increases the likelihood of bacterial transmission through contact; therefore, many pediatricians may be unaware of the protean clinical manifestations of childhood brucellosis [18]. This unfamiliarity with the disease can delay diagnosis in children who are not occupationally exposed [19]. In the present study, 96.03% of the cases had a history of close contact with sheep/goats. The most common symptoms were fever (76.19%, 96/126), joint pain (75.40%, 95/126), and fatigue (48.41%, 61/126), and the most common complications were knee joint effusion (40.48%, 51/126) and gastrointestinal disturbances (40.48%, 51/126). In most cases, the children were from rural parts of the country, had direct contact with sick animals or sick family members, or had consumed unpasteurized dairy products from farms. These findings are generally consistent with

previous studies, which reported fever (78.86%) and joint pain (64.22%) as the most common clinical features in affected children [20].

The main source of infection was the consumption of raw milk in 80% (81.6/102) of the patients, and the predominant presenting symptoms and signs were fever, arthralgia, malaise, weight loss, arthritis, hepatosplenomegaly, and lymphadenopathy [21]. Brucellosis is a common childhood affliction in southwestern Saudi Arabia as well as in other parts of the country and the Middle East, with 92% (144/157) of children having either a history of contact with animals, usually with sheep or goats, or ingesting raw milk, milk products, or raw liver [22].

Children tend to seek medical advice earlier than adults do, or they exhibit more symptoms of infection and are, therefore, more likely to present to the hospital in a timely manner. The gold standard for the definitive diagnosis of brucellosis is the isolation and identification of *Brucella* spp. from blood or bone marrow cultures [23]. CRP, AST, and ALT were found to be significantly higher in the bacteremia group than in the non-bacteremia group [24]. In a study that included 43 patients diagnosed with brucellosis from May 2011 to December 2016 in Iran, anemia (65%), lymphocytosis (51%), an elevated erythrocyte sedimentation rate (86%), and increased CRP levels (67%) were the most prominent blood anomalies [25]. For the treatment of brucellosis, current guidelines recommend a combination of three antibiotics, such as rifampicin, ceftriaxone sodium, and cotrimoxazole [26]. The total course of treatment should be no less than 8 weeks, with discontinuation decisions made in real time based on each patient's clinical recovery. Because hepatic and renal functions and the immune system have yet to fully develop in infants, streptomycin, gentamicin, and other drugs that are excreted via the kidneys should not be used clinically. Norfloxacin, tetracycline, and other antibiotics that affect the bone development of children and can cause tooth discoloration should also be contraindicated in pediatric cases [27] [28]. During antibiotic treatment, it is important to closely monitor liver and kidney function, perform routine blood tests, be vigilant for symptoms of anaphylaxis in children, and adjust medications over time.

Brucellosis in children remains challenging to diagnose, largely due to limited available information and the difficulty in determining accurate epidemiological contact histories. The disease is also diverse, lacks specificity, and the clinical symptoms are similar to those of a variety of diseases; this makes it challenging to identify, and it is easily misdiagnosed, making treatment difficult [29] [30]. For example, healthcare providers should conduct a detailed inquiry to ascertain a patient's place of residence, whether they have had contact with cattle and sheep, and whether they have consumed cattle and sheep products. Serological testing (RBPT and SAT) and etiological examinations, such as cerebrospinal fluid/blood culture, should be performed to detect the presence of *Brucella* in children. To facilitate the differential diagnosis of fevers related to brucellosis, screening of serum samples should be simplified and prioritized, especially in endemic regions.

Although this study provides important insights into brucellosis in the Ningxia region, there are several limitations to consider. First, the retrospective nature of

the study, which relies on existing data, is subject to potential incompleteness or bias in the data. For example, some cases may not have complete details recorded or may be missing data during the data collection process. Second, the fact that the study was conducted at a single center may affect the generalizability of the findings. Since the epidemiology of brucellosis may vary by region, the limitations of a single-center study may result in findings that cannot be generalized to other areas. In addition, the incomplete blood dataset in the study is also an important limitation. Blood culture is the gold standard for the diagnosis of brucellosis, providing direct evidence of the causative agent. However, due to the incompleteness of the data, the study was unable to fully assess the severity of the disease and the effectiveness of treatment. This may affect the accurate assessment of the epidemiology of brucellosis in the Ningxia region.

## 5. Conclusion

The findings of this study highlight two critical components for brucellosis prevention in endemic regions. First, targeted health education campaigns should be directed toward parents, particularly those involved in domestic animal breeding, to raise awareness of pediatric brucellosis risks and effective prevention strategies. Second, primary healthcare workers require enhanced training programs to boost their diagnostic capabilities and treatment proficiency. Key prevention strategies should focus on keeping children away from livestock rearing activities, preventing contact with farm animals and their waste, promoting proper meat cooking practices, and encouraging exclusive consumption of pasteurized dairy products. Through coordinated efforts among public health authorities, healthcare providers, and high-risk communities, these interventions could substantially decrease disease transmission and enhance health outcomes for children in brucellosis-endemic areas.

## Ethics Approval and Consent to Participate

This study was performed in accordance with the principles of the Declaration of Helsinki. Design of this study was reviewed and approved by the Ethics Committee of the Ningxia Fourth People's Hospital (Grant No. 202201). All samples were collected and tested for diagnostic and therapy purposes. All patients and their guardians, if applicable, provided informed consent. All patient data were anonymized, and their identifiable information, including names, identification numbers, home addresses, and telephone numbers, was discarded.

## Availability of Data and Materials

The datasets used and/or analyzed in the current study are available in the manuscript.

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## Author Contributions

J. X. F., L. B. F., and L. G. T. were responsible for data collection and curation. W. J. Y., Z. R. Q., and Z. P. performed data processing and statistical analysis. J. X. F. and L. Z. G. drafted the manuscript. L. B. F. and L. G. T. contributed to study design and provided critical revisions of the manuscript. All authors reviewed and approved the final manuscript for submission.

## Conflicts of Interest

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as conflicts of interest.

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## List of Abbreviations

ALT: Alanine aminotransferase

AST: Aspartate aminotransferase

LDH: Lactate Dehydrogenase

CK-MB: Creatine Kinase MB

CRP: C-Reactive Protein