# The Distribution of Clinical Features of Brucellosis Patients at Different Stages

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## Abstract

The purpose of this research is to study the factors affecting the progression of brucellosis and to provide scientific suggestions for the prevention and treatment of brucellosis. it is a quality research Data Collection by brucellosis patients (symptoms, signs, complications and examination indicators) and follow-up information (general characteristics, medication compliance, behavioral habits, contact with livestock and psychological conditions) were collected from two infectious disease hospitals. Chi-square test was used to find out the factors affecting the progression of brucellosis by orderly multiple classification logistic regression model. and Analytical by using descriptive analysis.

The research results found that in a study of 569 confirmed brucellosis cases, patients were found in different stages—47.10% in the acute stage, 27.42% in the subacute stage, and 25.48% in the chronic stage. These patients, with a mean age of 57.09 years, predominantly included males (69.95%) and individuals working as farmers or herdsmen (76.45%). Common symptoms observed were fever (79.79%), fatigue (61.69%), and loss of appetite (51.67%), with weight loss being a prominent sign (22.85%). Lab results showed elevated C-reactive protein (70.83%) and erythrocyte sedimentation rate (50.79%). Significant differences were noted in symptoms and lab findings across different stages, with acute cases showing distinct patterns compared to chronic cases. The study concluded that the diagnostic accuracy for brucellosis remains low and emphasized the importance of using specific differential indexes for different stages to improve clinical diagnosis in relevant medical institutions.

**Keywords:** Clinical Features; Brucellosis Patients; Different Stages

## Introduction

Brucellosis is a bacterial infection caused by various species of Brucella bacteria. It primarily infects animals but can be transmitted to humans through direct contact with infected animals or consumption of contaminated animal products like unpasteurized milk. In humans, brucellosis can cause symptoms such as fever, fatigue, joint pain, and muscle pain. Treatment typically involves antibiotics, and prevention includes proper hygiene and avoiding consumption of unpasteurized dairy products (Bosilkovski, Dimzova and Grozdanovski, 2009: 8-11).

Brucella can infect human blood, musculoskeletal, urogenital and central nervous systems. Therefore, brucellosis can present with a variety of symptoms and signs clinically. According to the course of disease, brucellosis can be divided into acute stage, subacute stage and chronic stage. Patients with different clinical stages of brucellosis show different

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symptoms and signs. Among patients in different clinical stages, patients with chronic brucellosis have a higher probability of complications such as spondylitis, chronic fatigue syndrome, musculoskeletal pain, depression or anxiety compared with patients in acute and subacute stages, and it is more difficult to treat. In the chronic phase, some patients will develop drug resistance, which further increases the difficulty of treatment and leads to poor prognosis. According to existing studies, chronic brucellosis accounts for about 20%-40% of all brucellosis patients. Relevant studies have begun to search for factors influencing the progression of brucellosis to the chronic phase, and recent studies have shown that medication compliance, use of different therapeutic drugs, and delayed diagnosis and treatment are important factors affecting the progression of brucellosis patients to the chronic phase (Jay, 2004).

By describing the epidemiological characteristics of human brucellosis and finding the influencing factors (including meteorological factors that affect the onset of human brucellosis and factors that affect the progression of disease) in human brucellosis, this study provides scientific basis for the prevention and control of human brucellosis and the formulation of policies and measures to reduce the adverse effects of human brucellosis (Li, 2013).

Conclusion Serum IL-17 may be involved in the infectious immune process of brucellosis; Endotoxin, as a bacterial lipopolysaccharide, is involved in the infection process of Brucella, providing a certain basis for judging the degree of inflammatory response in brucellosis; Serum CRP can be used as a monitoring indicator of the early inflammatory response of acute brucellosis; serum PCT can be used as a monitoring indicator of the inflammatory response of acute brucellosis; dynamic monitoring of serum CRP and serum PCT during treatment can reflect the changes in the condition of patients with acute brucellosis and evaluate the condition and treatment effect (Zhai, 2018).

Brucellosis is a bacterial infection that can be transmitted from animals to humans, causing symptoms like fever, fatigue, and joint pain. The disease can progress through acute, subacute, or chronic stages, with chronic cases posing more treatment challenges and potential complications. Factors influencing the development of chronic brucellosis include medication compliance and timely diagnosis. Research on human brucellosis aims to identify factors affecting disease onset and progression, aiding in the formulation of prevention strategies. Serum markers like IL-17, CRP, and PCT are used to monitor inflammatory responses in acute cases, guiding treatment decisions and assessing patient progress.

## Research Objective

To study the factors affecting the progression of brucellosis and to provide scientific suggestions for the prevention and treatment of brucellosis.

## Literature Review

Brucellosis is an infectious disease caused by the bacteria of the genus Brucella. These bacteria primarily infect animals, such as cattle, dogs, pigs, sheep and goats. People who are occupationally exposed to infected animals or their tissues, such as slaughterhouse workers, meat-packing workers, veterinarians and laboratory workers, are relatively at high risk (Zhang, 2014).

Brucellosis is endemic in certain parts of the world. Musculoskeletal involvement is the most common complication of brucellosis, and the spine is most frequently affected. Between November 1985 and March 1993, 334 patients with radiologically proved musculoskeletal brucellosis were seen. Involvement of the spine was either focal or diffuse, with a predilection to the lumbar region. Erosions and sclerosis in vertebral end plates, changes of inflammation at scintigraphy or magnetic resonance (MR) imaging, and intact disks were hallmarks of the focal form. Osteomyelitis of neighboring vertebrae, involvement of the intervening disk, and moderate epidural extension were features of diffuse brucellar spondylitis. The great majority of joints with scintigraphy evidence of disease demonstrated normal radiographic findings. Evidence of osteomyelitis or destructive arthritis was encountered in only a few cases. Although radiography is sufficient for demonstrating focal brucellosis, MR imaging is better for assessing diffuse disease (Al-Shahed & Sharif, 1994).

Brucellosis is not uncommon in children in endemic areas. We described clinical and laboratory features and therapeutic regimens for brucellosis in children under 14 who admitted in the Pediatric Medical Center Hospital, Tehran, Iran from March 1988 until February 2001. The male: female ratio was 2:1. Family history of brucellosis and consumption of un-pasteurized milk and dairy products was positive in 20.4% and 65.9%, respectively. The common clinical findings were arthritis (79.5%), fever (77.4%), anorexia (61.4%), sweating (52.3%), splenomegaly (43.2%), hepatomegaly (34.1%) and lymphadenopathy (13.65). Anemia, leukopenia and thrombocytopenia were recorded in 56.8%, 31.8% and 9.1%, respectively. Out of all patients, seropositivity rate for brucellosis was found in 97.7% using serum agglutination test. Culture of blood and bone marrow specimen were positive in 30% and 50% of samples obtained, respectively. Rifampin and co-trimoxazole were the most commonly used combination in 68.1%. The overall relapse rate was 13.6% (Afsharpaiman & Mamishi,2008: 20-45).

The Brucella data in Xinjiang between year 2009 to 2010to explore and analyze the spatial clustering features of brucellosis in Xinjiang, and provided the basis for prevention and control on brucellosis in Xinjiang,China.The time and population distribution of brucellosis in Xinjiang was analyzed for statistical analysis with descriptive epidemiology.Meanwhile,we also used quartile classification methods to map the incidence of brucellosis in Xinjiang spatial distribution, and calculated the Global Moran's I index on the spatial clustering analysis. Results showed that brucellosis in Xinjiang had obvious seasonal differences (peaked in May-September), more cases for male than that for female (gender ratio--2.96∶1), and the total incidence of 74% were farmer and herdsman, mainly concentrated at the age of 40 to 60years old. Compared with the onset range of brucellosis in 2009, there were clear tendency to spread in 2010.The Global Moran's I index was 0.116 4(P=0.017), showing the spatial clustering on the incidence of brucellosis in Xinjiang. The incidence of hot spots concentrated in Teaching and Altay, and the incidence of cold spots concentrated in Kashi. The incidence level brucellosis has significant spatial aggregation in the area of Xinjiang, which should be strengthened the prevention and control of high-risk areas (Wang, Yin, and CAO, 2015).

## Research Methodology

**1. Scope of study:** Clinical cases of brucellosis from 2017 to 2021 were collected.

**2. Research design:** To study the relationship between the whether the patient's compliance and clinical treatment regimen during clinical treatment have a differential impact on the treatment of brucellosis patients.

**3.Population and Sample:** A total of 613 patient records (including 670 hospitalization records) were investigated. For patients who were hospitalized more than once between January 1, 2017, and December 31, 2020, only their first hospitalization record was evaluated. A total of 569 laboratory-confirmed cases meeting the case definition and inclusion criteria were included in the study. The clinical stage of the patient was determined according to the course of the disease at the end of follow-up.

**4. Data collection:** The first admission medical records of patients were included in this study, and the relevant data of patients were collected by telephone survey from January 1, 2020 to December 31, 2021, including:①General demographic data, including age, gender, ethnicity, occupation, address, etc.;②Past history, onset and treatment, including past history, epidemiological contact history, admission time, onset time, hospitalization days, discharge diagnosis, outcome, etc.;③ Clinical manifestations, including fever, hyperhidrosis, muscle pain, joint pain, fatigue, weight loss, enlargement of liver, spleen and lymph nodes, and cough; ④ Laboratory tests, including blood routine, liver function, blood lipids, biochemical tests, erythrocyte sedimentation rate, procalcitonin, etiology and serological tests; ⑤ Treatment after illness, including: medication type and medication adherence (Morisky medication adherence scale was used to evaluate the status of medication adherence. The full score of the scale was 8 points, and a score of <6 was defined as poor adherence, a score of 6-8 was defined as moderate adherence, and a score of 8 was defined as good adherence).

**5. Analytical statistics:** Epidata 3.1 software was used to input data, and the two-person dual-core input mechanism was adopted. Strict logic check was carried out on the data, the database was established, and statistical analysis was carried out with SPSS 25.0 statistical software. Categorical variables will be presented as frequency distributions, and continuity variables will be presented as mean, median, maximum, minimum, and standard deviation. For continuous variables, Wilcoxon rank sum test was used to compare the differences between groups. For categorical variables, the frequency of cases in each category was compared using Chi-square tests or Fisher precision tests. Adjusted P-values were used for comparison between groups. Variables with $P<0.05$ in univariate analysis or variables considered as potential risk factors associated with the results were included in the logistic regression model for analysis.

## Research Conceptual Framework

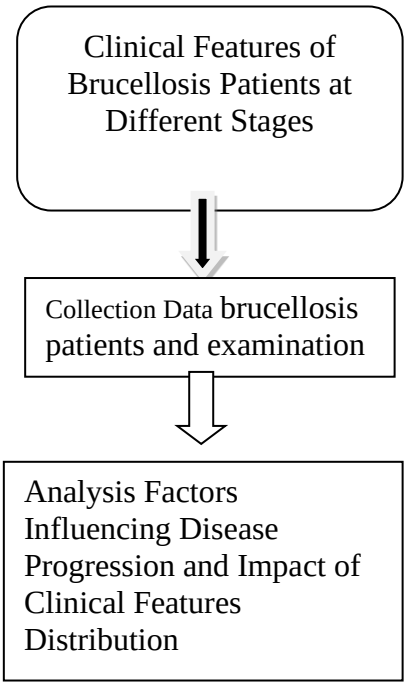


**Figure 1.** Research Conceptual Framework

## Research Results

### General characteristics of clinical patients with brucellosis

A total of 613 patient records (including 670 hospitalization records) were investigated. For patients who were hospitalized more than once between January 1, 2017, and December 31, 2020, only their first hospitalization record was evaluated. A total of 569 laboratory-confirmed cases meeting the case definition and inclusion criteria were included in the study. The clinical stage of the patient was determined according to the course of the disease at the end of follow-up. A total of 268 patients (47.10%) in the acute stage, 156 patients (27.42%) in the subacute stage, and 145 patients (25.48%) in the chronic stage were collected. The median age of the 569 patients was 57.09 (44.08, 70.10) years, of whom 69.95% were male, with a male-to-female ratio of 2.33:1. 434 patients (76.27%) were over 50 years old, 247 patients (43.41%) were between 50 and 64 years old, and 187 patients (32.86%) were over 60 years old. Among the 11 patients under 24 years old, 9 cases were acute, accounting for 81.82%. The occupation of patients was mainly farmers or herdsmen, with a total of 435 cases, accounting for 76.45%, as shown in Table 1.

**Table 1** Comparison of general characteristics of brucellosis patients[n(%)]

| Variable | acute stage (n=268) | Subacute stage (n=156) | Chronic period (n=145) | Total (n=569) | $\chi^2$ | *P* | group comparison& |
|---|---|---|---|---|---|---|---|
| Sex | | | | | 0.219 | 0.896 | no significant differences |
| Male | 190(70.90) | 108(69.23) | 100(68.97) | 398(69.95) | | | |
| Female | 78(29.10) | 48(30.77) | 45(31.03) | 171(30.05) | | | |
| Gender（years） | | | | | 7.060 | 0.530* | no significant differences |
| ≤ 14 | 6(2.24) | — | — | 6(1.05) | | | |
| 15–24 | 3(1.12) | 2(1.28) | — | 5(0.88) | | | |
| 25–49 | 70(26.12) | 32(20.51) | 22(15.17) | 124(21.79) | | | |
| 50–64 | 112(41.79) | 69(44.87) | 66(45.52) | 247(43.41) | | | |
| ≥ 65 | 77(28.73) | 53(33.97) | 57(39.31) | 187(32.86) | | | |
| occupation | | | | | | | |
| Farmers and herdsmen | 203(75.75) | 119(76.28) | 113(77.93) | 435(76.45) | 11.32 | 0.169* | no significant differences |
| stockman | 9(3.36) | 4(2.56) | 6(4.14) | 19(3.34) | 6 | | |
| Meat and dairy workers | 7(2.61) | 6(3.85) | 12(8.28) | 25(4.39) | | | |
| Pupil | 6(2.24) | 2(1.28) | 2(1.38) | 10(1.76) | | | |
| other | 43(16.04) | 25(16.03) | 12(8.28) | 80(14.06) | | | |

record：*：Fisher exact probability method was used to analyze the test method for the 2×2 cell table with theoretical frequency less than 5, and the test method for the 2×R cell table with theoretical frequency less than 5, and the rest were analyzed by Pearson2 test. & : Adjusted P values were used for comparison between groups.

**2、Comparison of clinical signs and symptoms of brucellosis patients in acute stage, subacute stage and chronic stage**

Table 5 lists the main signs and symptoms of the acute, subacute, and chronic phases of brucellosis. The most common symptoms were fever (398 cases, 69.95%), fatigue (377 cases, 66.26%), arthralgia (304 cases, 53.43%), loss of appetite (264 cases, 46.40%) and low back pain (238 cases, 41.83%). The most common signs were weight loss (124 cases, 21.79%), splenomegaly (24 cases, 4.22%), and lymph node enlargement (20 cases, 3.81%). Fever, anorexia and cough were higher in acute group (80.60%, 53.73% and 13.06%, respectively) than in chronic group (66.90%, 37.93% and 4.83%, respectively). 2=31.442, P<0.05; 2=9.408, P<0.05; 2=6.980, P<0.05). Acute cases with joint pain and low back pain (45.15%, 36.19%, respectively) were significantly lower than chronic cases (68.28%, 50.34%, respectively). 2=20.240, P<0.05; 2=8.018, P<0.05). There was a significant difference in arthralgia between subacute and chronic cases (2=6.565, P < 0.05)

**Table 2** Comparison of clinical signs and symptoms of brucellosis patients in acute, subacute and chronic stages [n (%)]

| Variable | acute stage (n=268) | Subacute stage (n=156) | Chronic period (n=145) | Total (n=569) | $\chi^2$ | *P* |
|---|---|---|---|---|---|---|
| symptom | | | | | | |
| fever. | 216(80.60) | 103(66.0) | 79(54.48) | 398(69.95) | 32.097 | 0.000 |
| fatigue. | 177(66.04) | 104(66.6) | 96(66.21) | 377(66.26) | 0.017 | 0.991 |
| arthralgia | 121(45.15) | 84(53.85) | 99(68.28) | 304(53.43) | 20.240 | 0.000 |
| perspire | 65(24.25) | 30(19.23) | 45(31.03) | 140(24.60) | 5.678 | 0.058 |
| Loss of appetite | 144(53.73) | 65(41.67) | 55(37.93) | 264(46.40) | 11.379 | 0.003 |
| Nausea/vomiting | 19(7.09) | 13(8.33) | 18(12.41) | 50(8.79) | 3.383 | 0.184 |
| Lumbago and backache | 97(36.19) | 68(43.59) | 73(50.34) | 238(41.83) | 8.018 | 0.018 |
| thoracodynia | 15(5.60) | 8(5.13) | 8(5.52) | 31(5.45) | 0.044 | 0.978 |
| celialgia | 10(3.73) | 5(3.21) | 6(4.14) | 21(3.69) | 0.186 | 0.911 |
| headache | 24(8.96) | 15(9.62) | 18(12.41) | 57(10.02) | 1.287 | 0.525 |
| orchialgia | 8(2.99) | 3(1.92) | 6(4.14) | 17(2.99) | 1.272 | 0.529 |
| shiver | 28(10.45) | 19(12.18) | 18(12.41) | 65(11.42) | 0.481 | 0.786 |
| Out of mind | 85(31.72) | 57(36.54) | 48(33.10) | 190(15.82) | 1.038 | 0.595 |
| Muscle soreness | 47(17.54) | 30(19.23) | 31(21.38) | 108(18.98) | 0.912 | 0.634 |
| cough | 35(13.06) | 13(8.33) | 7(4.83) | 55(9.67) | 7.740 | 0.021 |
| sign | | | | | | |
| Joint enlargement | 9(3.36) | 4(2.56) | 4(2.76) | 17(2.99) | 0.229 | 0.950* |
| splenomegaly | 12(4.48) | 8(5.13) | 4(2.76) | 24(4.22) | 1.129 | 0.569 |
| hepatomegaly | 2(0.75) | 2(1.28) | 1(0.69) | 5(0.88) | 0.642 | 0.853* |
| Testicle enlargement | 7(2.61) | 3(1.92) | 3(2.07) | 13(2.28) | 0.237 | 0.937* |
| lymphadenopathy | 11(4.10) | 6(3.85) | 3(2.07) | 20(3.51) | 1.165 | 0.612* |
| Weight loss | 60(22.39) | 30(19.23) | 34(23.45) | 124(21.79) | 0.890 | 0.641 |
| rash | 6(2.24) | 5(3.21) | — | 11(1.93) | 4.733 | 0.084* |

record：*：Fisher exact probability method was used to analyze the test method for the 2×2 cell table with theoretical frequency less than 5, and the test method for the 2×R cell table with theoretical frequency less than 5, and the rest were analyzed by Pearson2 test. &: Adjusted P values were used for comparison between groups.

## Discussion

Research objectives was studying The Distribution of Clinical Features of Brucellosis Patients at Different Stages found that Brucellosis is closely related to occupation and living habits. Unprotected contact with livestock and consumption of raw animal products are high-risk behaviors for brucellosis infection. Of the patients in this survey, 84.18% were in occupations with a risk of brucella infection. 15.9% of patients reported exposure to livestock that had not been vaccinated, and 3.3% had a history of consumption of raw milk and dairy products. In addition, the survey found that the affected population showed family clustering, with 19.3% of patients having a family history of brucellosis, which may be related to the similar lifestyle of each family member compliant with (Zhang, 2014)

According to the duration of symptoms, brucellosis can be divided into three stages: acute, subacute and chronic. Among the 569 patients, 47.10% were acute, 27.42% were subacute, and 25.48% were chronic, which was consistent with the results of some previous studies. However, the proportion of chronic patients in our study was 25.48%, higher than some previous reports, which may be related to the differences in living habits and medical level of patients.

In this study, the most common symptoms of brucellosis patients on admission were fever, fatigue, loss of appetite, and joint pain. The most common signs were weight loss, lymph node enlargement, splenomegaly and testicular enlargement. The proportion is lower than that reported by WHO. We found that patients at different clinical stages showed different clinical characteristics. Compared with other stages, acute brucellosis patients have a higher proportion of fever, poor appetite and cough. Joint pain and low back pain are more common in chronic stage, and similar characteristics have been described in other studies. It has also been reported that enlargement of the liver and spleen is less common in chronic brucellosis than in acute and subacute brucellosis. No such difference was found in our study (Bosilkovski, Dimzova and Grozdanovski ,2009: 8-11).

The most common laboratory findings for brucellosis patients on admission are elevated C-reactive protein, elevated erythrocyte sedimentation rate, elevated alanine aminotransferase, anemia, and elevated Aspartate aminotransferase. The results of laboratory examination in acute stage, subacute stage and chronic stage patients were compared and analyzed. It was found that C-reactive protein, erythrocyte sedimentation rate, alanine aminotransferase and Aspartate aminotransferase were higher in acute stage patients. Related studies reported similar results. In addition, some studies have reported that anemia is more common in acute stage cases, and there is no significant difference in the proportion of anemia in each stage in this study (Zhai, 2018).

**The New Knowledge**

Of the surveyed patients, 84.18% were in high-risk occupations, while 15.9% reported exposure to unvaccinated livestock and 3.3% had consumed raw dairy. Family clustering was observed, with 19.3% having a history of brucellosis among relatives, likely due to shared lifestyles. The disease presented in three stages—acute (47.10%), subacute (27.42%), and chronic (25.48%), with a higher proportion of chronic cases possibly attributed to lifestyle and healthcare disparities. The study on brucellosis patients highlighted a male predominance possibly influenced by occupational gender distributions. Contrary to expectations, severe manifestations were not significantly different between genders. High-risk behaviors like unprotected livestock contact and raw animal product consumption were prevalent among patients. Family clustering of the disease was noted, likely due to shared lifestyles. Brucellosis presented in acute, subacute, and chronic stages, with a higher proportion of chronic cases observed. Clinical symptoms and laboratory findings varied across stages, emphasizing the importance of tailored management strategies for improved patient outcomes.

## Recommendation

The study revealed a higher prevalence of brucellosis among male patients, consistent with prior research, potentially influenced by the greater representation of females in livestock-related occupations in China. While previous studies suggested more severe manifestations in female patients, this study did not find such a correlation. Brucellosis incidence was closely linked to occupation and lifestyle habits, notably unprotected contact with livestock and consumption of raw animal products. A significant portion (84.18%) of surveyed patients were engaged in high-risk occupations, with notable percentages reporting exposure to unvaccinated livestock and consumption of raw dairy. Family clustering was observed, with 19.3% having a familial history of brucellosis, likely due to shared lifestyles.

Understanding these diverse clinical manifestations across brucellosis stages is crucial for tailored patient management strategies and improved outcomes. By delineating these patterns, healthcare providers can better diagnose, monitor, and treat individuals at different points in the disease progression, enhancing overall care efficacy and patient well-being.

## Recommendation further research.

Recommendation further research can study in those factor as Longitudinal studies tracking patients from acute onset to chronic stages to understand symptom evolution. Investigation into genetic factors influencing disease severity and clinical outcomes in brucellosis. Comparative analysis of clinical features in brucellosis patients from different geographical regions to evaluate potential variations. Exploration of novel biomarkers or imaging techniques for early diagnosis and monitoring of brucellosis progression. Interventional studies assessing the efficacy of targeted treatments based on stage-specific clinical features in brucellosis patients.

## Reference

Bosilkovski, M., Dimzova, M., & Grozdanovski, K. (2009). Natural history of brucellosis in an endemic region in different time periods. *Acta Clinica Croatica*. 3 (2), 8-11.

Li, F. (2013). *The clinical diagnostic value of PCT testing in infectious diseases*. The Fifth People's Hospital of Pingdu City, Shandong Province.

al-Shahed, M. S., Sharif, H. S., Haddad, M. C., Aabed, M. Y., Sammak, B. M., & Mutairi, M. A. (1994). *Imaging features of musculoskeletal brucellosis. Radiographics: A Review Publication of the Radiological Society of North America*, Inc.

Afsharpaiman, S., & Mamishi, S. (2008). Brucellosis: review of clinical and laboratory features and therapeutic regimens in 44 children. *Titanium Academic.* 3 (13), 20-45

Wang, W., Yin, F., & Cao, M. (2015). *Spatial clustering analysis of brucellosis in Xinjiang, China*. Sichuan University.

Zhai, X. (2018). *Changes in serum interleukin-17, endotoxin, high-sensitivity C-reactive protein, and procalcitonin during the treatment of acute brucellosis*. Ningxia Medical University.

Zhang, M. (2014). *Analysis of 1187 cases of brucellosis in outpatient population*. Jilin University.