ORIGINAL RESEARCH

Epidemiological Characteristics and Clinical Manifestations of Brucellosis and Q Fever Among Humans from Northeastern Inner Mongolia

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Objective: To investigate the distribution, epidemiology, and clinical symptoms of brucellosis and Q fever in northeastern Inner Mongolia.

Methods: In this study, 64 townships of Bairin left flag and Alukerqin flag, Jarud flag and Horqin right front flag in four counties with frequent brucellosis and Q fever were selected. Epidemiological characteristics, clinical features, and exposure to risk factors were identified and descriptively analyzed in patients from these areas.

Results: There were 367 brucellosis cases in the four regions and 78 positive cases of Q-fever infection. In addition, 24 cases of brucellosis and Q-fever co-infection were identified, with a co-infection rate of 1.13%. Brucellosis and Q fever were mainly concentrated in the 30–65 and 40–55 age groups. For brucellosis, the difference between age groups was statistically significant ($\chi^2 = 29.121$, P < 0.05). The sex distribution for brucellosis was 225 men (61.31%) and 142 women (38.69%), and 45 men (57.69%) and 33 women (42.31%) had Q fever. Those with brucellosis and Q fever were mainly farmers, accounting for 79.19% and 78.38% of the total number, respectively. Of the 367 cases of brucellosis infection, the main symptoms were joint pain (52.59%), fatigue (47.14%), lower back pain (38.96%), fever (33.24%), hyperhidrosis (28.88%), and muscle pain (20.44%). Of the 78 cases of Q-fever infection, the main symptoms were joint pain (35.90%), fatigue (30.77%), lower back pain (26.92%), fever (21.79%), and hyperhidrosis (17.95%). Muscle pain also accounted for 12.82%.

Conclusion: Occupational distribution suggests that we should strengthen the protection measures against diseases infected through animal husbandry. Among the clinical symptoms, fever, hyperhidrosis and fatigue were associated with brucellosis, while fever, headache, and fatigue were significantly associated with Q fever.

Keywords: distribution, clinical characteristics, brucellosis, Q fever, northeastern Inner Mongolia

Introduction

Brucellosis is a common zoonosis that affects more than 500,000 people per year and usually presents as fever and constitutional symptoms (excessive sweating, fatigue, headaches, joint and muscle pain, and so on).[1–3] The main origin of infection of brucellosis is sheep, cattle, pigs, deer, and other large economic animals. It can infect humans through the respiratory tract, digestive tract, and direct contact with the skin and mucosa.[4] Brucellosis can affect any organ or system, and the presenting symptoms of the infection are not specific; therefore, it can easily be confused with other diseases. Conversely, the overdiagnosis of brucellosis may lead to adverse drug effects, and, equally importantly, other serious infectious or noncommunicable diseases may be overlooked. Therefore, the proper diagnosis of brucellosis and adequate management of patients are essential not only for early diagnosis but also for public health management.[4] In recent years,

the incidence of human brucellosis in China has increased dramatically, and national surveillance data have shown that the total incidence of human brucellosis in mainland China has increased from 0.92 cases per 100,000 people in 2004 to 4.2 cases per 100,000 people in 2014.[5] In foreign countries, brucellosis has also continued to circulate and is difficult to control, for example Bulgaria has been free of brucellosis since 1958, but during 2005–2007, human and animal diseases reemerged.[6] In Greece, despite animal control measures, brucellosis has been endemic from 2005 to 2020, with cases in both vaccination and eradication areas.[7]

Q fever is the zoonosis caused by *Coxiella burnetii* (also known as Q rickettsia).[8] Domestic animals, such as cattle, sheep, and goats, are the main source of human Q fever.[9] Q fever is significantly seasonal.[10] Humans usually contract the disease by inhaling contaminated aerosols emitted from infected livestock.[11] The main clinical manifestations are fever with chills, headache, muscle aches, and fatigue. Antibiotic treatment is effective in the early stage of the disease. Delayed treatment can lead to chronic Q fever, with a long treatment period, the tendency to relapse, and a high mortality rate.[12] However, the clinical symptoms of Q fever are extensive, disguising it as other diseases. Acute infections are more common and usually asymptomatic, and 4–5% of the patients have a persistent local infection with poor progression, making an early and accurate diagnosis of Q fever difficult.[13] There have been many outbreaks of Q fever in China in the 1960s and 1980s,[14] and in addition to outbreaks, Q fever has been prevalent in China, with occasional case reports of Q fever. Q fever has also outbreaks or long-term epidemics in many foreign countries. Greece has been reported by cases of Q fever during 2001–2013, totaling 731 cases, which is a relatively large number.[15] The Netherlands has had a large outbreak between 2007 and 2010, followed by Q-fever epidemics.[16] From March to April 2007, Q fever broke out in a school in Slovenia.[17]

Brucellosis and Q fever are worldwide zoonoses.[18] They are extremely similar in terms of infectious agents, transmission routes, and clinical symptoms and can easily turn into chronic infections. Because it is difficult for clinicians to make an accurate diagnosis in time, misdiagnosis and delays in treatment are common, leading to chronic infections. According to the literature, combined brucellosis and Q-fever infections exist in Xinjiang Province and Inner Mongolia.[19] In 2022, the Chinese Journal of Endemiology also revealed that from 2018 to 2020, a total of 40,665 cases of brucellosis were reported in the Inner Mongolia Autonomous Region, with an annual incidence rate close to 53.47/10,000.[20] The present study therefore explores the differences in the distribution of brucellosis and Q fever in northeastern Inner Mongolia and the differences in infection between sexes, age stages, and occupational groups. It also summarizes the clinical symptoms of brucellosis and Q fever and analyzes their potential differences. It is hoped that this data collection and analysis in the field will provide a theoretical basis for the diagnosis, precise monitoring, and early warning of brucellosis and Q fever.

Materials and Methods
Definition of Cases
Brucellosis: Brucellosis is a zoonotic disease caused by Brucella infection, and the source of infection is mainly infected animals, mainly through direct or indirect contact with sick animals, meat products and excreta.[21] Definitions of confirmed cases, clinically diagnosed cases, suspected cases, and invisible infection cases refer to the Diagnosis of Brucellosis (WS269-2019).

Q fever: Q fever is a natural epidemic zoonosis caused by Coxiella burnetii.[22] Suspected cases: with Q fever-related clinical symptoms and epidemiological characteristics. Confirmed cases:[23] positive specific antibody test.

Inclusion and Exclusion Criteria
Inclusion criteria: Meets diagnostic criteria for suspected cases of brucellosis and Q fever; resides in the area of the study; absence of psychiatric disorders.

Exclusion Criteria: Not meeting diagnostic criteria for suspected cases of brucellosis and Q fever; permanent residence outside the study area; mental illness and inability to cooperate.

Study Area

The study was cross-sectional and was conducted from April 2018 to April 2021. The study area includes four banners: the Bairin Left Banner and Alukerqin Banner of Chifeng City, Jarud Banner of Tongliao City, and Horqin Right Front Banner of Hinggan League, which are located in the grasslands and semi-agricultural and semi-pastoral areas located at the southeastern foot of the Hinggan Mountains and north of the Xilamulun River. The geographical coordinates of Bairin left flag in Chifeng city are 118 ° 44 ′ −119 ° 48 ′ E and 43 ° −48 ° 48 ′ N latitude. Balinizuo flag temperate semi-arid climate. In the four seasons, the annual average temperature is 5.3 ° C; the average sunshine hours are around 3000 hours, slightly more in the south than in the north; the annual average precipitation is around 400 mm, and the annual average wind speed is 3–4 m/s.[24] The Alukerqin flag is located at 43 ° 21 ′ 43 ″ to 45 ° 24 ′ 20 ″ N and 119 ° 02 ′ 15 ″ to 121 ° 01 ′ E. Average altitude 430 meters.The average annual temperature is 5.5 ° C, the annual sunshine hours are 2760–3030 hours, the annual average accumulated temperature is 2900–3400 ° C, and the average annual rainfall is 300–400 mm, which is a typical continental climate.[25] Jarud Banner in Tongliao City is located between 119 ° 13 ′ 48 ″ – 121 ° 56 ′ 05 ″ E longitude and 43 ° 50 ′ 13 ″ – 45 ° 35 ′ 31 ″ N latitude. Lubei Town, where the flag is located, is 265 meters above sea level. Zarut Banner belongs to the mid-temperate continental monsoon climate. The average annual temperature is 6.6 ° C and the average annual sunshine duration is 2882.7 hours. The average annual rainfall is 382.5 mm, the average annual humidity is 49%, and the average annual wind speed is 2.7 m/s.[26] Horqin 's right front flag is located at 119 ° 49 ′ 49 ″ −122 ° 49 ′ 15 ″ E and 46 ° 22 ′ 25 ″ −46 ° 49 ′ 36 ″ N. Family right front flag continental monsoon climate.The annual mean temperature is 5.8 ° C in the south, and the mean annual precipitation is 423.7 mm in the south and 416.1 mm in the north.[27]

Samples

This study used random sampling of households, a questionnaire survey, and blood sample collection. In the selected four banners, each banner and county selected 3–5 townships (sum) and 6–10 natural villages to identify suspected cases of brucellosis and Q fever for each study year. Suspected cases of brucellosis and Q fever were identified based on case definitions, and a total of 500 cases were identified from each flag county for questionnaire survey and blood sample collection.

Sample size calculation: $N = u_\alpha^2 \pi (1 - \pi)/\delta^2$, where u_α is the value of u corresponding to the test level (taken as u0.05 = 1.96), π is the estimated incidence rate of 0.3% (based on the average of previous incidence rates), and δ is the allowable error (taken as 0.5%). The sample size was calculated to be 460, taking into account any missing cases, and at least 500 cases from each flag county were selected for the study.

For the blood samples, 3–5 mL of venous blood was collected from patients in ordinary blood collection tubes and centrifuged for 4 h, and then serum was separated for storage and frozen for the assay.

Questionnaire

A total of 2,052 valid questionnaires were collected in this study (Final questionnaire validated by infectious disease specialist).

Ethics Statement

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee (Batch 2020031901). Signed informed consent was obtained from all participants.

Brucellosis Detection

The samples were reviewed using a test tube agglutination test, in accordance with the National Brucella Diagnosis Criteria (WS269-2019). Result determination: The samples were tested using the Tiger Red plate agglutination test, and those with positive results were considered suspected positive samples. The suspected positive samples were tested using a test tube agglutination test, and those with positive results of 1:100++ and above were considered confirmed positive samples.

Q-Fever Detection

An indirect immunofluorescence test trial[28] was conducted at the National Key Laboratory of Microbiology of the Academy of Military Medical Sciences. A serum screen was performed with a 1:50 dilution of a Phase II antigen and through micro-immunofluorescence. IgG anti-phase II antibody titers ≥200 and IgM anti-phase II antibody titers ≥50 are considered specific.

Statistical Treatment

Excel 2015 software was used to establish the database, and the number of tests and number of positive infections in different groups were counted separately. The positive rate was compared using the χ^2 test, and the difference was considered statistically significant at P < 0.05. Univariate logistic models were applied to analyze the clinical symptoms associated with brucellosis and Q fever for superior odds ratio estimation and fixed effects type III tests.

Results

Infection and Distribution of Brucellosis and Q Fever

Infection Situation

To gain a preliminary understanding of the infection situation in the four flag districts, a total of 2,122 human serum samples were investigated and collected for Brucella antibody testing and Q-fever testing. The results revealed that a total of 367 serum samples were positive for Brucella antibodies, with an average infection rate of 17.30%; 78 cases were positive for Q fever, with a positive infection rate of 3.68%; 24 cases were positive for a mixed infection of brucellosis and Q fever, with a positive infection rate of 1.13% (see Table 1).

There were differences in the positive rates of brucellosis and Q fever in samples from different banners. The positive rate of brucellosis infection was 12.48%, the positive rate of Q-fever infection was 4.34%, and the mixed infection rate was 0.90%. In Jarude Banner, the positive rate of brucellosis infection was 24.60%, Q-fever infection was 2.28%, and the mixed infection rate was 0.68%. The positive rate of brucellosis infection was 13.91%, Q-fever infection was 6.09% and mixed infection rate was 1.04%. In Bailin Zuoqi, the positive rate of brucellosis infection was 19.86%, Q-fever infection was 1.62%, and the mixed infection rate was 1.80% (see Table 1).

Figures 1–4 reveal that the highest prevalence of brucellosis infection is in Jarude Banner, the highest Q-fever rate is in Alkurqin Banner, and the highest mixed infection rate is in Balinzou Banner. However, because no statistical tests were performed, the differences may not be statistically significant.

Characteristics of Age Distribution

The youngest infected person with positive brucellosis infection was 21 years and the oldest was 81 years. Infections were mostly concentrated in those aged between 30 and 65 years, accounting for 89.06% of the infections. The highest positive rate of infection was found in the 51–55 age group, and the lowest rate was identified in those aged 81 years and above, with statistically significant differences in positive rates between age groups (χ^2 = 29.121, P < 0.05) (Table 2). The youngest infected person with positive Q fever was 21 years and the oldest was 75 years. Infections were mostly concentrated in those aged between 36 and 55 years, accounting for 67.92% of infections. The highest positive rate of infection was detected in the 46–50 age group, and the infection rate was 0 among those in the 66–70 age group, with no

Table 1 Infection of Two Diseases in Different Regions

Area	Brucellosis Infection Rate	Q Fever Infection Rate	Mixed Infection
Bairin Left Banner	19.86%	1.62%	1.80%
Alukerqin Banner	13.91%	6.09%	1.04%
Jarud Banner	24.60%	2.28%	0.68%
Horqin Right Banner	12.48%	4.34%	0.90%
Average infection rate	17.30%	3.68%	1.13%

Brucellosis infection rate

24.60%

19.86%

14.44%
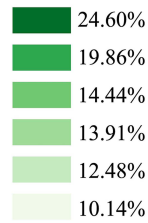
13.91%

12.48%

10.14%

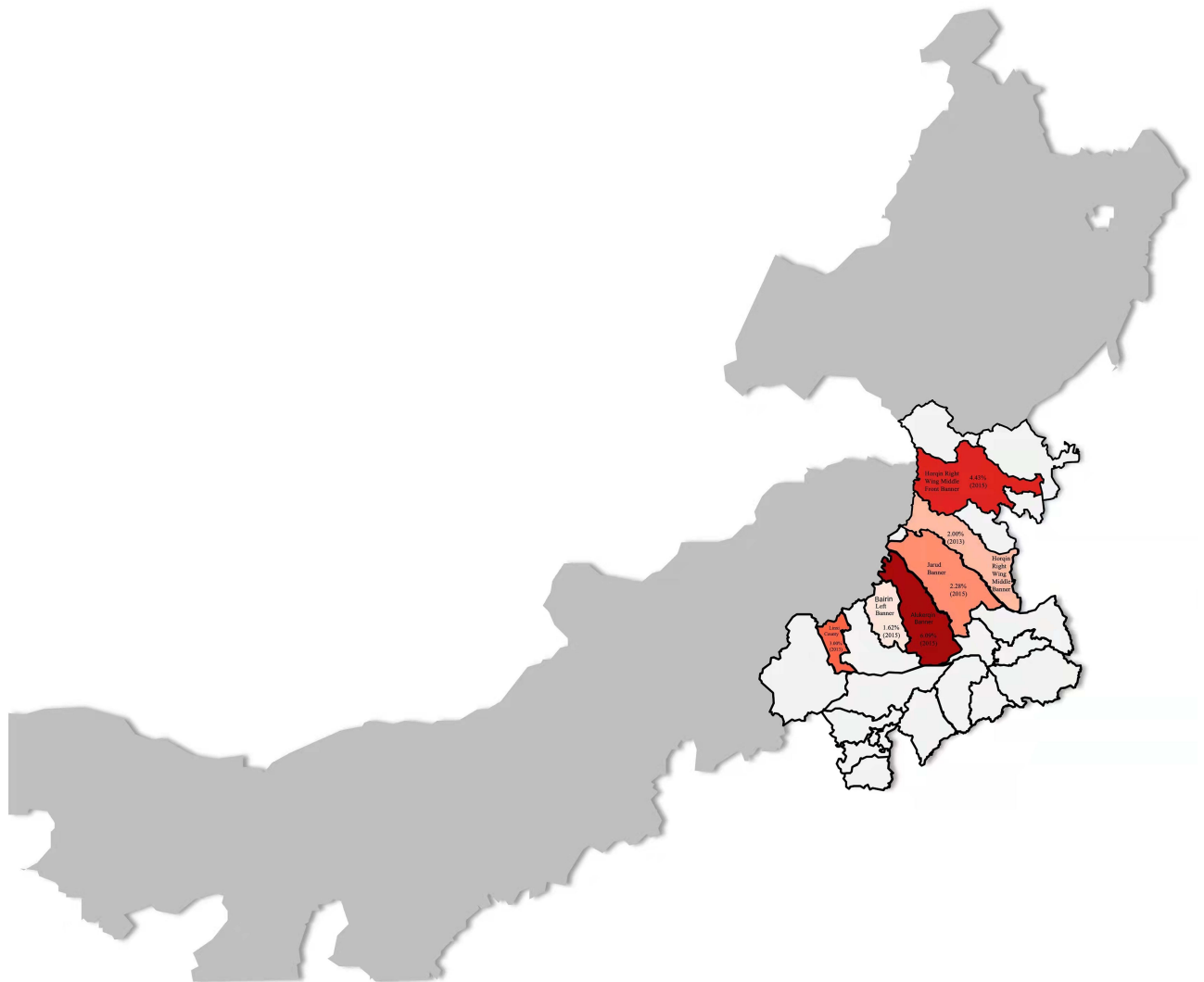**Figure 1** Brucellosis infection rate.

Figure 2 Distribution of brucellosis in eastern Inner Mongolia.

statistically significant differences (χ^2 = 12.271, P > 0.05) (Table 2). The age of patients with mixed brucellosis and Q fever was found to be between 21 and 50 years, with no significant differences (P > 0.05).

Sex Characteristics

Of the 367 cases of brucellosis infection, 225 were men (61.31%) and 142 were women (38.69%), with a sex ratio of 1.58:1 and significant sex differences (χ^2 = 13.883, P < 0.05). Of the 78 cases of Q-fever infection, 45 were men (57.69%) and 33 were women (42.31%). The sex ratio was 1.36:1, and the sex difference was not obvious (χ^2 = 0.884,
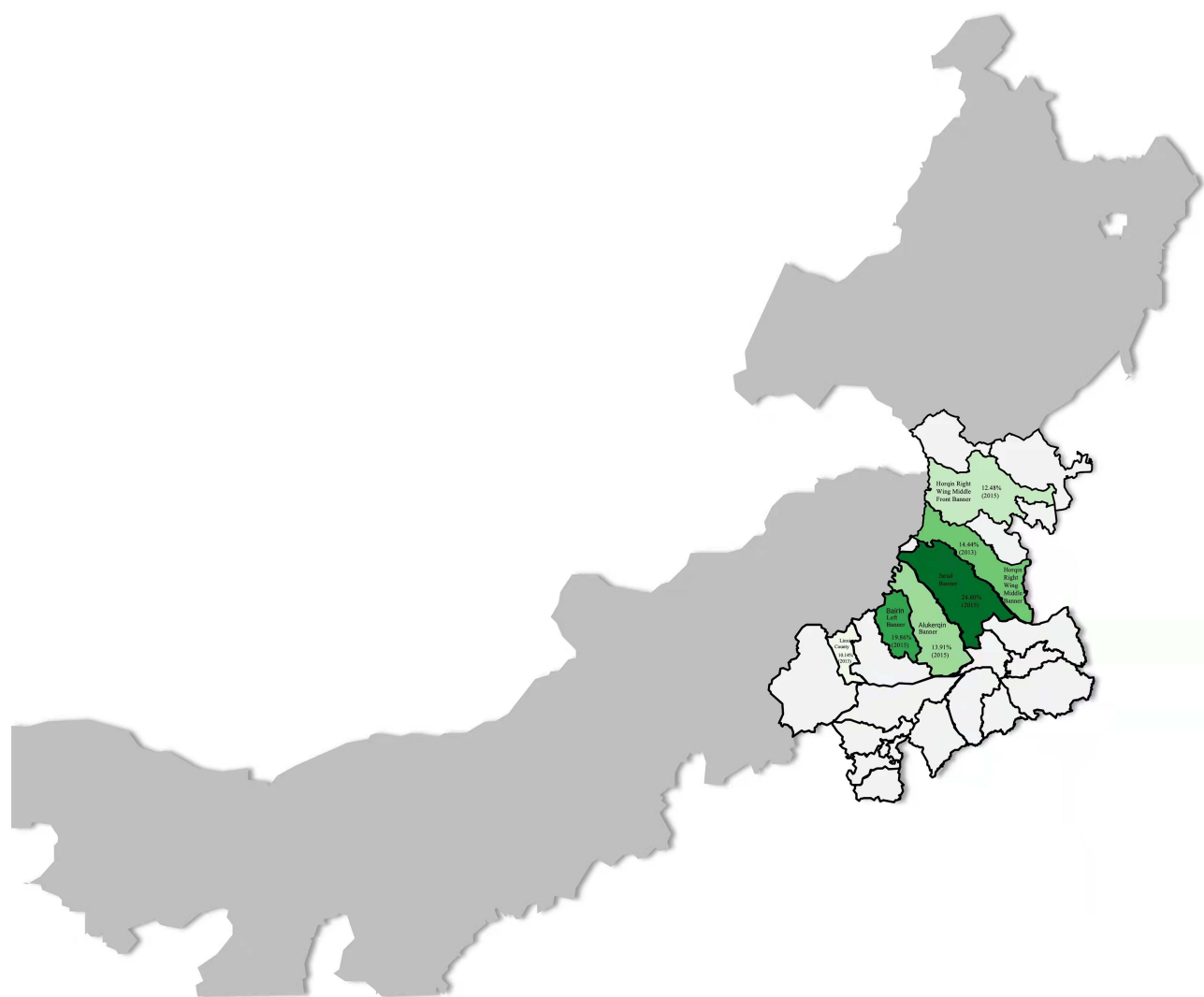
Figure 3 Q-fever distribution in eastern Inner Mongolia.

Q fever infection rate

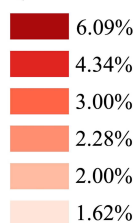|	
■	6.09%
■	4.34%
■	3.00%
■	2.28%
■	2.00%
■	1.62%

Figure 4 Q fever infection rate.

P > 0.05). Of the 24 mixed infection cases of brucellosis and Q fever, 15 were men (62.5%) and 9 were women (37.5%), with a significant difference between sexes (P < 0.05). For brucellosis, the positive rate of infection was 10.6% (225/2,122) in men and 6.69% (142/2,122) in women. For Q fever, the positive rate of infection was 2.12% (45/2,122) in men and 3.27% (33/2,122) in women. For the mixed infection of brucellosis and Q fever, the positive rate of infection was 0.71% (15/2,122) in men and 0.42% (9/2,122) in women (see Table 3).

Table 2 Age Distribution

Age	Brucellosis			Q Fever			Mixed Infection of Brucellosis and Q Fever		
	Test case	Infection Cases (%)	*P*-value	Test cases	Infection Cases (%)	*P*-value	Test cases	Infection Cases (%)	*P*-value
0–20	21	0 (0)	<0.05	21	0 (0)	>0.05	21	0 (0)	>0.05
21–25	40	6 (1.63)		40	2 (2.56)		40	3 (12.5)	
26–30	92	19 (5.17)		92	4 (5.12)		92	3(12.5)	
31–35	184	30 (8.17)		184	7 (8.97)		184	6 (25)	
36–40	190	33 (8.99)		190	8 (10.25)		190	4 (16.67)	
41–45	292	62 (16.89)		292	13 (16.66)		292	5 (20.83)	
46–50	387	64 (17.43)		387	18 (23.07)		387	3 (12.5)	
51–55	305	68 (18.52)		305	14 (17.94)		305	0 (0)	
56–60	256	42 (11.44)		256	5 (6.41)		256	0 (0)	
61–65	190	28 (7.62)		190	6 (7.69)		190	0 (0)	
66–70	97	9 (2.45)		97	0 (0)		97	0 (0)	
71–75	42	3 (0.81)		42	1 (1.28)		42	0 (0)	
76–80	14	2 (0.54)		14	0 (0)		14	0 (0)	
≥81	12	1 (0.27)		12	0 (0)		12	0 (0)	
Total	2122	367 (100)		2122	78 (100)		2122	24 (100)	

Table 3 Gender Distribution

Gender	Brucellosis			Q Fever			Mixed Infection of Brucellosis and Q Fever		
	Test Case	Infection Cases (Rate)	*P*-value	Test Cases	Infection Cases (Rate)	*P*-value	Test Cases	Infection Cases (Rate)	*P*-value
Male	1113	225 (10.6%)	<0.05	1113	45 (2.12%)	>0.05	1113	15 (0.71%)	<0.05
Female	1009	142 (6.69%)		1009	33 (3.27%)		1009	9 (0.42%)	
Total	2122	367 (17.29%)		2122	78 (5.39%)		2122	24 (1.13%)	

Occupational Distribution

Of the 1,968 people who completed valid questionnaires, the majority were farmers, accounting for 82.11%, followed by herders, accounting for 10.16%. In addition, 95 engaged in the production, processing, and transportation of livestock products, accounting for 4.83%, and the rest accounted for 2.90%. The brucellosis infection was mainly detected among farmers, accounting for 79.19% of the total number of infected cases. Among the three occupations, farmers (274 cases), herdsmen (60 cases), and village veterinarians (8 cases), the number of infections accounted for a relatively high proportion, and the infection rates were 16.96%, 30.00%, and 44.44%, respectively. Farmers also had the highest Q-fever infection cases, accounting for 78.38% of the total infection cases. Village veterinarians (2 cases) and livestock product processing workers accounted for a relatively high number of infections, with infection rates of 11.11% and 8.60%, respectively (Table 4). Mixed infection cases of brucellosis and Q fever were detected mainly among farmers, accounting for 60.87% of the total number of infected cases.

Clinical Characteristics
Clinical Symptoms

Of the 367 cases of brucellosis infection, arthralgia, fatigue, lower back pain, fever, hyperhidrosis, and muscle soreness were the most common symptoms, accounting for 52.59%, 47.14%, 38.96%, 33.24%, 28.88%, and 20.44%, respectively; headache accounted for 16.35%, and other symptoms accounted for just a small proportion. Of the 78 cases of Q-fever

Table 4 Occupational Distribution of Brucellosis/Q Fever

Occupation	Survey Number	Percentage (%)	BBB I		Q Heat		Mixed Infection with Brucellosis and Q Fever	
			Number of Cases of Infection	Infection Rate (%)	Number of Cases of Infection	Infection Rate (%)	Number of Cases of Infection	Infection Rate (%)
Peasant	1616	82.11	274	16.96	58	3.59	14	0.87
Herder	200	10.16	60	30.00	5	2.50	6	3.00
Student	15	0.76	1	6.67	0	0	0	0
Preschool child	3	0.15	0	0	0	0	0	0
Village medical	20	1.02	0	0	1	5.00	0	0
Village veterinarian	18	0.91	8	44.44	2	11.11	3	16.67
Purchase and trafficking of livestock products	2	0.10	0	0	0	0	0	0
Poultry farmers	1	0.05	0	0	0	0	0	0
Processing of slaughtering livestock products	93	4.72	3	3.22	8	8.60	0	0
Amount to	1968	100	346	17.58	74	3.76	23	1.17

infection, arthralgia, fatigue, lower back pain, headache, fever, and hyperhidrosis were the predominant symptoms, accounting for 35.90%, 30.77%, 26.92%, 25.64%, 21.79%, and 17.95%, respectively; muscle soreness accounted for 12.82%. Of the cases of mixed infection, headache, fever, arthralgia, fatigue, and lower back pain accounted for 70.83%, 62.50%, 54.17%, 50.00%, and 50.00% of the symptoms, respectively (Table 5).

Correlation Analysis of Clinical Symptoms and Brucellosis and Q Fever

A univariate logistic model was applied to analyze the relevant clinical symptoms of brucellosis and Q fever identified from the 2,052 valid questionnaires. This was followed by a superior odds estimation and fixed effect type III test. The results demonstrated that fever, hyperhidrosis, fatigue, headache, lower back pain, back pain, arthralgia, muscle soreness, feeling physically drained, and insomnia were significantly associated with brucellosis ($P < 0.01$), whereas fever, headache, and fatigue were significantly associated with Q fever ($P < 0.01$) (Tables 6 and 7).

Table 5 Analysis of the Clinical Symptoms of Brucellosis/Q Fever Infection Cases

Clinical Symptoms	Bucellosis (n=367)		Q Fever (n=78)		Mixed Infection of Brucellosis and Q Fever (n=24)	
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
Fever	122	33.24	17	21.79	15	62.50
Hyperhidrosis	106	28.88	14	17.95	10	41.67
Fatigue	173	47.14	24	30.77	12	50.00
Arthralgia	193	52.59	28	35.90	13	54.17
Headache	60	16.35	20	25.64	17	70.83
Nausea	13	3.54	4	5.13	2	8.33
Vomit	6	1.63	1	1.28	0	–
Cough	19	5.18	7	8.97	4	16.67
Pectoralgia	18	4.90	2	2.56	0	–
Dorsalgia	43	11.72	6	7.69	2	8.33
Low back pain	143	38.96	21	26.92	12	50.00

(*Continued*)

Table 5 (Continued).

Clinical Symptoms	Bucellosis (n=367)		Q Fever (n=78)		Mixed Infection of Brucellosis and Q Fever (n=24)	
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
Abdominal pain	7	1.91	0	–	0	–
Diarrhoea	4	1.09	0	–	0	–
Muscular soreness	75	20.44	10	12.82	4	16.67
Constipation	2	0.54	0	–	0	–
Insomnia	26	7.08	5	6.41	1	4.17
Obnubilation	0	–	0	–	0	–
Anorexia	12	3.27	1	1.28	0	–
Pale	1	0.27	0	–	0	–
Limitation of activity	13	3.54	1	1.28	0	–
Physically-draining	57	15.53	8	10.26	3	12.50

Table 6 Analysis of the Relationship Between Clinical Symptoms and Brucellosis in the Univariate Logistic Model

Clinlcal Symptom	Optimum Ratio Estimate	Standard Error	Free Degree	95% CI	F-value	P-value
Give out heat	2.115	0.1410	2052	1.604–2.789	28.22	0.0001*
Hidrosis	2.249	0.1405	2052	1.708–2.963	33.29	0.0001*
Feeble	1.853	0.1241	2052	1.452–2.363	24.67	0.0001*
Headache	1.608	0.1710	2052	1.150–2.248	7.71	0.0055*
Feel like vomiting	0.965	0.3258	2052	0.509–1.828	0.01	0.9126
Cough	1.089	0.2747	2052	0.635–1.867	0.10	0.7560
Pectoralgia	1.205	0.2935	2052	0.677–2.142	0.40	0.5261
Dorsalgia	1.731	0.1870	2052	1.199–2.497	8.61	0.0034*
Lumbago	1.900	0.1312	2052	1.469–2.457	23.93	0.0001*
Abdominal pain	1.606	0.4491	2052	0.666–3.875	1.11	0.2915
Muscular soreness	1.640	0.1662	2052	1.193–2.025	9.30	0.0023*
Lose sleep	2.083	0.2608	2052	1.249–3.473	7.92	0.0049*
Anorexia	2.026	0.3652	2052	0.990–4.146	3.74	0.0534
Limitation of activity	1.949	0.3625	2052	0.957–3.967	3.39	0.0658
Physical decline	2.431	0.1918	2052	1.669–3.541	21.44	0.0001*
Arthralgia	2.015	0.1234	2052	1.582–2.567	32.24	0.0001*

Note: *Indicates $P < 0.05$.

Table 7 Analysis of the Relationship Between Clinical Symptoms and Q Fever in the Univariate Logistic Model

Clinlcal Symptom	Optimum Ratio Estimate	Standard Error	Free Degree	95% CI	F-value	P-value
Give out heat	2.091	0.1257	2052	1.545–2.606	27.11	0.0001*
Hidrosis	0.962	0.3071	2052	0.527–1.757	0.02	0.8998
Feeble	1.894	0.1616	2052	1.495–2.660	0.00	0.0001*
Headache	1.593	0.1152	2052	1.489–2.218	2.39	0.0001*
Feel like vomiting	1.093	0.5421	2052	0.378–3.166	0.03	0.8692
Cough	1.543	0.4260	2052	0.669–3.558	1.04	0.3086
Dorsalgia	0.904	0.4428	2052	0.379–2.155	0.05	0.8200
Lumbago	1.111	0.2746	2052	0.648–10,903	0.15	0.7026
Muscular soreness	0.913	0.3620	2052	0.449–1.858	0.06	0.8023
Lose sleep	1.355	0.4956	2052	0.513–3.581	0.38	0.5398
Physical decline	0.757	0.4016	2052	0.344–1.664	0.48	0.4885
Arthralgia	0.985	0.2520	2052	0.601–1.615	0.00	0.9529

Note: *Indicates $p < 0.05$.

Discussion

In this study, four banners and counties in the grassland and semi-agricultural and semi-pastoral areas located at the southeastern foot of the Hinggan Mountains and north of the Xilamulun River were selected for a comparative analysis of brucellosis and Q-fever infection and their clinical symptoms. The results revealed that all four regions had cases of brucellosis and Q-fever infection as well as mixed infection cases of brucellosis and Q fever. According to the data of the brucellosis monitoring project of the Department of Disease Control, the high-risk population for brucellosis in the four counties constituted 9,863 people in 2020, accounting for 3.43% of the total population of 287,689 in the region.[29] The positive rate of brucellosis in these four regions is high, which is consistent with the high prevalence of brucellosis in the central and eastern regions of Inner Mongolia, spreading from east to west and from north to south.[30] Inner Mongolia is historically an epidemic area for brucellosis. The disease was effectively controlled in the 1980s, but it recovered rapidly after 2004, and 2017 saw a sharp increase in cases.[31] By 2021, the number of reported cases in the region reached 21,910, a record high, accounting for 51.32% of the nationally reported cases. Since 2017, brucellosis has ranked first in China for four consecutive years, becoming the most serious public health concern in the region.[32]

In a study abroad in 2021, it was demonstrated that developing countries, such as those commonly affected by brucellosis, Q fever, and rift valley fever outbreaks, have a high disease burden; co-infection is therefore common.[33] Of the 55 studies collected, 50 different pathogens were coinfected with *Brucella* and *Clostridium baratii*.[33] In 2013, a World Bank Avian and Human Influenza Trust Fund grant project in Inner Mongolia found that 48 of 100 suspected brucellosis samples randomly selected in northern Inner Mongolia were positive for brucellosis and 5 samples for Q fever (including 2 samples in Horqin Right Front Banner and 3 in Linxi County), suggesting that brucellosis and Q fever are distributed across the forest and grassland areas. This suggests that brucellosis and Q fever may overlap in the source of infection, route of transmission, and geographic distribution. Our results indicate that co-infection cases of brucellosis and Q fever were detected in the four regions included in this study, and since no statistical tests were performed, this finding may have been due to chance factors or may have been true and requires further investigation to determine, but this suggests the risk of tick-borne brucellosis and Q fever in the southeast of the Hinggan Mountains and grassland areas north of the West Ramron River and should be noted. People infected with brucellosis and Q fever are mainly farmers and herders. These four banners are semi-agricultural and semi-pastoral areas, with a population mainly engaged in animal husbandry, and the most high-risk groups for these diseases are engaged in animal husbandry and agricultural product processing. The main source of infection for human brucellosis is livestock that has brucellosis, but there is a lack of awareness of brucellosis protection among breeders, who become infected through close contact with sick animal during breeding, and the risk of brucellosis exposure exists all year round. Frequent exchange of animal husbandry in Mongolia, the inflow of sick animals from epidemic source locations, the predominance of free-range farmers in the farming industry, and the weak awareness of farmers in brucellosis protection are the reasons for the high rate of brucellosis infection.[34] In terms of clinical symptoms, brucellosis and Q fever both present with fever, fatigue, hyperhidrosis, lower back pain, and joint pain, which can be accompanied by lymphadenopathy, hepatosplenomegaly, rash, and other symptoms and signs.[35] Therefore, the clinical symptoms of brucellosis and Q-fever infection are similar, making it difficult to distinguish between the two diseases based on the symptom manifestations.

In terms of age distribution, brucellosis infection was mainly identified in those aged 30–65 years and Q-heat infection was identified in those aged 40–55 years, with little difference in age. The main age group of Brucella occurrence is consistent with the study of Li Juanjuan,[36] and the possible reason is that middle-aged people are the main laborers in contact with livestock, followed by apathy of protection awareness, relatively low education level, and the ability to receive publicity and education is not as good as that of young people aged 20–30 years, so they are more likely to cause infection. In terms of gender distribution, both brucellosis and Q fever were more common in men than in women, consistent with other findings.[37,38] The possible reason is that men are the main labor force, and there are many opportunities for contact with sick animals and their metabolites, polluted external environment, and production and processing links related to sick animals; men are not as good as women to pay attention to protecting themselves; and men are not as high as women in their physical health. Health education should pay attention to middle-aged and male publicity and education.

In summary, this article presents an epidemiological study on the existence of mixed infections of brucellosis and Q fever in Inner Mongolia. The number of incidents is increasing annually, and farmers aged 40–60 years who are mainly engaged in animal husbandry constitute the high-risk group. In addition, brucellosis and Q fever both manifest as fever, malaise, excessive sweating, back pain, and arthralgia, which can be accompanied by lymphadenopathy, hepatosplenomegaly, rash, and other signs and symptoms. These findings can provide a reference for the development of future brucellosis prevention and control strategies and prevention and control priorities. However, there are some limitations to this study. The study had a small sample size of cases, which may lead to some bias compared with the real situation. The limited source of cases may not fully reflect the epidemiological and clinical characteristics of our province or even our country. In the process of case collection, because of the incomplete case data of patients and because most patients were discharged after the symptoms improved, the relevant symptoms could not be fully established. We will conduct a more comprehensive investigation to expand the sample collection and increase the content of the research in our province to confirm the reliability of the results in this study. When comparing the infection rates of the two diseases in different regions, no statistical test was performed, and the difference may not be statistically significant. The statistical analysis of the data will be added in the subsequent study to make the study more reference. Because no regression models were developed for each factor, it was not possible to identify which factors were true risk factors, and univariate multivariate logistic regression models were developed for each disease region, age, sex, and occupation in future studies to identify true risk factors.

Conclusion

The population infected with brucellosis and Q fever in northeastern Inner Mongolia mainly consists of men. The age of onset of brucellosis is mainly between 30 and 65 years, and Q fever is between 40 and 55 years, of which farmers and herdsmen are the main infected groups of brucellosis, and farmers and livestock product processing workers are the main infected groups of Q fever. Among the clinical symptoms, fever, hyperhidrosis, fatigue, headache, lower back pain, back pain, arthralgia, muscle soreness, body flu, and insomnia were associated with brucellosis, while fever, headache, and fatigue were significantly associated with Q fever. At present, the infection rate of brucellosis and Q fever remains high in northeast Inner Mongolia, and the risk of brucellosis infection is high, which may be related to frequent contact with livestock without protective measures. Our results may provide a stronger theoretical basis for clinical research on brucellosis and Q fever.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article. Please contact the correspondence author for additional information on the questionnaire.

Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee (Batch 2020031901). Signed informed consent was obtained from all participants.

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Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

References

1. yagupsky P, Morata P, Colmenero JD. Laboratory diagnosis of human brucellosis. *Clin Microbiol Rev.* 2019;33(1):e00073–19. doi:10.1128/CMR.00073-19
2. Bosilkovski M, Krteva L, Dimzova M, Kondova I. Brucellosis in 418 patients from the Balkan Peninsula: exposure-related differences in clinical manifestations, laboratory test results, and therapy outcome. *Int J Infect Dis.* 2007;11(4):342–347. doi:10.1016/j.ijid.2006.10.002

3. Bosilkovski M, Krteva L, Dimzova M, Vidinic I, Sopova Z, Spasovska K. Human brucellosis in Macedonia - 10 years of clinical experience in endemic region. *Croat Med J.* 2010;51(4):327–336. doi:10.3325/cmj.2010.51.327

4. Shakir R. Brucellosis. *J Neurol Sci.* 2021;420(117280):117280. doi:10.1016/j.jns.2020.117280

5. Zheng R, Xie S, Lu X, et al. A systematic review and meta-analysis of epidemiology and clinical manifestations of human brucellosis in China. *Biomed Res Int.* 2018;2018:5712920. doi:10.1155/2018/5712920

6. Russo G, Pasquali P, Nenova R, et al. Reemergence of human and animal brucellosis, Bulgaria. *Emerg Infect Dis.* 2009;15(2):314–316. doi:10.3201/eid1502.081025

7. Kefaloudi C, Mellou K, Dougas G, Vorou R, Mitrou K, Kontopidou F. Human brucellosis in Greece, 2005-2020: a persistent public health problem. *Vector Borne Zoonotic Dis.* 2022;22(3):163–169. doi:10.1089/vbz.2021.0050

8. Gregory AE, van Schaik EJ, Russell-Lodrigue KE, Fratzke AP, Samuel JE. Coxiella burnetii intratracheal aerosol infection model in mice, guinea pigs, and nonhuman primates. *Infect Immun.* 2019;87(12):e00178–19. doi:10.1128/IAI.00178-19

9. Martínez-Dubarbie F, Rollán-Martínez-Herrera M. Peripheral nervous system involvement in Q fever. *Acta Neurol Belg.* 2022;122(1):17–22. doi:10.1007/s13760-021-01791-2

10. Punda-Polić V, Luksić B, Capkun V. Epidemiological features of Mediterranean spotted fever, murine typhus, and Q fever in Split-Dalmatia County (Croatia), 1982–2002. *Epidemiol Infect.* 2008;136(7):972–979. doi:10.1017/S0950268807009491

11. Budgin AM, Abidi MZ, Bajrovic V, Miller MA, Johnson SC. Severe acute Q fever pneumonia complicated by presumed persistent localized Q fever endocarditis in a renal transplant recipient: a case report and review of the literature. *Transpl Infect Dis.* 2020;22(1):e13230. doi:10.1111/tid.13230

12. Eldin C, Mélenotte C, Mediannikov O, et al. From Q fever to Coxiella burnetii infection: a paradigm change. *Clin Microbiol Rev.* 2017;30(1):115–190. doi:10.1128/CMR.00045-16

13. España PP, Uranga A, Cillóniz C, Torres A. Q Fever (Coxiella Burnetii). *Semin Respir Crit Care Med.* 2020;41(7):509–521. doi:10.1055/s-0040-1710594

14. Xiaolu X, Jun J, Bohai W. Strengthening the prevention and control of Q fever in China. *J Parasitol Med Entomol.* 2020;27(04):258–263.

15. Vranakis I, Kokkini S, Yachnakis E, Tselentis Y, Chochlakis D, Psaroulaki A. Q fever in Greece: findings of a 13 years surveillance study. *Comp Immunol Microbiol Infect Dis.* 2020;69:101340. doi:10.1016/j.cimid.2019.101340

16. Georgiev M, Afonso A, Neubauer H, et al. Q fever in humans and animals in four European farm countries, 1982 to 2010. *Euro Surveill.* 2013;18(8):20407. doi:10.2807/ese.18.08.20407-en

17. Grilc E, Socan M, Koren N, et al. Outbreak of Q fever among a group of high school students in Slovenia, March-April 2007. *Euro Surveill.* 2007;12(7):E070719.1. doi:10.2807/esw.12.29.03237-en

18. Cadmus S, Salam SP, Adesokan HK, Akporube K, Ola-Daniel F, Awosanya EJ. Seroprevalence of brucellosis and Q fever infections amongst pastoralists and their cattle herds in Sokoto State, Nigeria. *PLoS One.* 2021;16(7):e0254530. doi:10.1371/journal.pone.0254530

19. Wei QQ. Establishment of Brucellosis and Q Fever Detection Method and Co-Infection Study. Shihezi University; 2017.

20. Song LT, Fan MG, Ta N, et al. Epidemical characteristics of human brucellosis in Inner Mongolia Autonomous Region from 2018 to 2020. *Chin J Endemiol.* 2022;41(01):62–65.

21. Jie Z, Guodong Y, Gang C, et al. Characteristics of brucellosis outbreak in Zigong City from 2016 to 2021. *Chin J Zoonoses.* 2022;38(3):5.

22. Xiangxiang S, Lin Z, Wei C. Progress in Q thermal diagnostic techniques. *Chin Anim Quarantine.* 2019;36(05):57–60.

23. Lihong H, Yonglong H. Pharmaceutical treatment practice of patients with suspected Q fever infection: a case report. *J Shanzi Med Univ.* 2016;47(10):959–961. doi:10.13753/j.issn.1007-6611.2016.10.021

24. China Weather Network. Climate background analysis of Balingzuo banner. Available from: https://baike.baidu.com/reference/405429/ff515TnFwzPu20f3GAGmWSMyOlezqkry1mUnAPmc_0_-zYZ4Be27OReyXtjApf52EXbhs7gQwbqrFZk28IsH9ujb9GAwOOr7bjR-mAG-G90. Accessed 01 Nov 2022.

25. Arukorqin Banner People 's Government Network. Overview of Arukorqin banner. Available from: http://www.alkeqq.gov.cn/zjaq/aqgk/202111/t20211115_1697940.html. Accessed 01 Nov 2022.

26. Zarutt Banner People' s Government. Overview of banner situation. Available from: http://www.zhalute.gov.cn/zltq/jbgk/2022-08/12/content_1bb7ff82e06f42b98d5e8296c49e0b45.shtml. Accessed 01 Nov 2022.

27. Horqin Right Wing Front Banner People 's Government. Overview of front banner. Available from: https://baike.baidu.com/reference/7619838/4744hrAgDngRqGbnYmo2UCV0cpN3DCx2t66r7TTbjkg96znKnFWfVi70Qm-5NEJBukcPaXl6mPoadlgmhw8A2tbSmFyP7cqP2JyrJzmLbID2. Accessed 01 Nov 2022.

28. Lili X, Guangle J, Ying Z, Xueqing H, Xiangmei L. Progress in Q fever serological detection methods. *Chin Anim Husbandry Vet.* 2012;39(08):83–86.

29. Zolzaya B, Selenge T, Narangarav T, et al. Representative seroprevalences of human and livestock brucellosis in two Mongolian provinces. Ecohealth. 2014;11(3):356371. doi:. 2014;11(3):356371. doi:10.1007/s10393-014-0962-7

30. Jin Y, Xu Y, Zhang H, Wang P. Epidemiological characteristics and short-term epidemiological trend prediction of human brucellosis in Baotou City, Inner Mongolia, 2003-2017. *Chin J Endemiol.* 2019;1:25–30.

31. Hanwei L. Study on the epidemic profile and infectious factors of brucellosis in Inner Mongolia. Inner Mongolia Medical University, 2020.

32. The Health Commission of Mongolia City. Infectious Diseases and Prevention and Control. Available from: http://wjw.nmg.gov.cn/zwgk/xxgk/zdlyxxgk/crbyq/. Accessed 01 Nov 2022.

33. Middlebrook EA, Romero AT, Bett B, et al. Identification and distribution of pathogens coinfecting with Brucella spp., Coxiella burnetii and Rift Valley fever virus in humans, livestock and wildlife. *Zoonoses Public Health.* 2022. doi:10.1111/zph.12905

34. Zhiqiang Z, Liu L, Xiuying Z. Occupational brucellosis incidence analysis in Inner Mongolia 2010-2014. *Dis Surveill Control.* 2016:2016(5):2.

35. Brookfield CR, Phillips PPJ, Shorten RJ. Q fever-the superstition of avoiding the word "quiet" as a coping mechanism: randomised controlled non-inferiority trial. *BMJ.* 2019;367:l6446. doi:10.1136/bmj.l6446

36. Juanjuan L. Epidemic characteristics of brucellosis and analysis of three serological detection methods for Brucella in Hulunbeier area. Soochow University, 2020.

37. Daohua L, Tengwei H, Jiaxiong W. Analysis of serological surveillance results of human brucellosis in Fujian Province from 2012 to 2017. *Chin J Zoonoses.* 2019;35(9):847–851.

38. S Qiang. Epidemiological and clinical characteristics analysis of 659 cases of brucellosis. *Dis Prevent Control.* 2009;16(23):132–133.