

Acute Q fever among febrile patients in Zahedan, southeastern Iran

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Aim: So far, few studies have been conducted on Q fever in Iran. The objective of this study was to determine the frequency of acute Q fever in febrile patients admitted to Boo-Ali Hospital in Zahedan (southeastern Iran).

Materials and methods: In this study, 105 febrile patients suspected of having brucellosis were examined using indirect immunofluorescent assay kit for the detection of *Coxiella burnetii* IgM and IgG phase antibodies in their serum. Serum with a phase II IgG titer of ≥ 256 and a phase II IgM titer of ≥ 50 was predictive for acute Q fever. Additionally, a 4-fold rise in antibody titers was considered diagnostic of Q fever. Results were analyzed using SPSS 17.0 for Windows.

Results: Among 105 patients (male: 52, female: 53), 35.2% (37/105) febrile patients had a positive serology test for acute Q fever. The prevalence of acute Q fever in women and men was 17/37 (45.9%) and 20/37 (54%), respectively. There was serological evidence of past infection in 36 (34.3%) patients.

Conclusion: According to the results of our study, acute Q fever is highly prevalent in this province. Thus, it is necessary to pay attention to this disease to prevent its transmission in this region.

Key words: *Coxiella burnetii*, microimmunofluorescence, Q fever, Iran

1. Introduction

Q fever is caused by a pleomorphic gram-negative coccobacillus called *Coxiella burnetii* (1). It was found in 1930 and has occurred in most geographical regions, except New Zealand and Antarctica (2). Major reservoirs of this infection for humans are infected cattle, sheep, and goats (3). However, cats, rabbits, dogs, birds, and ticks may also transmit *C. burnetii* to humans. A sensitive host will catch the infection following inhalation of *C. burnetii* via aerosols (1).

Q fever is considered an occupational disease, and it is prevalent among people who are in direct contact with animals, such as farmers having livestock, veterinarians, and workers in slaughterhouses. In some cases, drinking contaminated milk, autopsy of an infected corpse, and blood transfusions have caused infection in humans (3). After 14–39 days of latency, symptoms of the disease appear, of which the most frequent in early stages of the disease are severe headache, fever, chills, fatigue, and myalgia (1). Of cases of infection 40% are asymptomatic,

while the rest of the patients acquire febrile illness, hepatitis, and pneumonia (4).

Q fever is diagnosed using serological methods. Microscopic agglutination, complement fixation, immunofluorescence, and enzyme-linked immunosorbent assay (ELISA) tests can be effective in the serological diagnosis of the disease. An indirect immunofluorescence antibody (IFA) test is the best way to diagnose acute and chronic Q fever (along with the evaluation of phase I and II antibodies). An increase in acute-phase and convalescent-phase serum antibody titer can usually be seen in acute Q fever. Moreover, cases of cross-reactions have been observed between *Bartonella* and *Legionella micdadei* antibodies and the *C. burnetii* antibody that occurs with IFA, which is tested less than other serological methods. In cases of tissue samples, the polymerase chain reaction (PCR) technique can be used as a diagnosis method (1,4).

Some case reports on Q fever have been previously published in Iran (5). Additionally, some of the serological

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studies that have been performed showed domestic animals infected with *C. burnetii* in eastern Iran (6,7).

Only 1 study examined Q fever serology in 75 febrile patients in Kerman (eastern Iran), using the ELISA method. In that study, 24% and 36% of the patients had phase I antibodies and phase II antibodies, respectively (8).

There are some published studies of countries neighboring Iran in relation to prevalence of Q fever (4,9–11). Therefore, the aim of this study was to investigate the presence of anti-*C. burnetii* antibodies among febrile patients in southeast Iran.

2. Materials and methods

The present study assessed the prevalence of Q fever in febrile patients admitted to Boo-Ali Hospital, which is a reference hospital for infectious diseases in Sistan and Baluchestan Province (Zahedan, southeastern Iran) (Figure). In this descriptive cross-sectional study, all febrile patients admitted to our hospital with brucellosis-like systemic symptoms in the winter of 2011 were studied, after informed consent was given.

Upon admission and 3–4 weeks later, 2 mL of blood was drawn from the patients. The serum samples were frozen at -20°C in the serum bank of the infectious diseases research center.

A questionnaire containing demographic, epidemiological, and clinical features of Q fever was completed for each patient. The information included age, sex, history of contact with livestock and animal products, and patient's clinical signs. Samples were tested for the presence of IgM and IgG antibodies against *Coxiella burnetii* phase II antigen by using an IFA test with a commercial kit (VIRCELL, S.L., Granada, Spain).

The cutoff points for diagnosis of acute Q fever antibody IgM and IgG were ≥ 1.50 and ≥ 1.256 , respectively. A 4-fold rise in titer between acute and convalescent sample was diagnostic of Q fever. Lower titers that did not show any increase 3–4 weeks later were considered as a previous infection.

2.1. Statistical analysis

The statistical analysis of the results was carried out using SPSS 17.0 for Windows to calculate significant differences and $P \leq 0.05$ was considered statistically significant.

3. Results

In this study, a total of 105 febrile patients admitted to Boo-Ali Hospital were examined. Of these patients, 52 (49.5%) were male, and 53 (50.5%) were female. Based on IFA serological tests, 37/105 patients (35.2%) had acute Q fever. From these patients, 14 cases had IgM and IgG greater than or equal to 1:50 and 1:256, respectively. Furthermore,



Figure. The location of the region investigated in this study (Zahedan is the capital of Sistan and Baluchestan Province).

23 individuals showed a 4-fold rise in convalescence phase samples. There were 36 out of 105 cases (34.3%) that had lower IgG titers, indicating a previous infection.

Of the 73 individuals who were serologically positive for *Coxiella* infection, 31 (42.5%) were female and 42 (57.5%) were male. Of the 37 patients who had acute Q fever, 20 were male and 17 were female. Only 2 male patients (1.6%) were younger than 18 years old, while in 16 cases, ages ranged between 18 and 35 years. The mean age was 39.5 ± 19.1 years, with a range between 18 and 35 years in the seropositive group. The means of ages in the seropositive and seronegative groups were 39.5 and 40.1, respectively (P = 0.64). There was no significant difference between seropositive and seronegative groups regarding sex (P = 0.45).

Of the 73 patients who had positive serology for Q fever, 70 patients had a history of contact with livestock and had recently consumed unsafe dairy products. However, only 27 individuals from the seronegative group had this history (P = 0.05). Among the above studied patients, 76/105 patients (72.4%) lived in urban areas and 29/105 patients (27.6%) lived in rural parts of the province. There was no significant difference between the 2 groups regarding their residence (P = 0.63) (Table 1).

In respect of symptom frequency, all the participants were febrile. Moreover, 14 (37.8%), 22 (59.4%), 2 (5.4%), 16 (43.2%), and 2 (5.4%) patients had arthralgia, myalgia, cough, headache, and gastrointestinal problems, respectively. Only 2 patients did not have any symptoms other than fever (Table 2).

Table 2. Clinical characteristics of acute Q fever patients.

Symptoms	No.	%
Fever	37	100
Arthralgia	14	37.8
Myalgia	22	59.4
Cough	2	5.4
Headache	16	43.2
Diarrhea	2	5.4

4. Discussion

The present study is among the few studies conducted on Q fever in Iran. In this study, the prevalence of acute Q fever in febrile patients admitted to Boo-Ali Hospital was 35.2%. Furthermore, 34.3% of the patients had serological evidence of past infection. In this study, no significant difference was found between the prevalence of this infection in men and women (P = 0.45). Furthermore, the mean age of those infected with Q fever was 41 years. About 97% of those with Q fever had contact with livestock and also had consumed unsafe dairy products (P = 0.05).

The results of the present study, using a microimmunofluorescence method, were comparable with the statistics of acute Q fever in a study performed in Kerman on Q fever using the ELISA method (36% had anti-*Coxiella burnetii* phase II antibodies) (8).

Table 1. Epidemiological characteristics based on serological evidence for anti-phase II *Coxiella burnetii* among febrile patients.

Variable	Seropositive patients			Seronegative	P
	Acute Q fever	Past infection	Total		
Sex					
Male	20 (19%)	22 (20.9%)	42 (57.5%)	10 (9.5%)	0.45
Female	17 (16.2%)	14 (13.3)	31 (42.5%)	22 (20.9%)	
Total (105)	37 (35.2%)	36 (34.3%)	73 (69.5%)	32 (30.4%)	
Age, years (Mean ± SD)*					
	41.2 ± 18.4	37.2 ± 19.7	39.5 ± 19.1	40.1 ± 16.1	0.64
Residence					
Urban	26 (24.8%)	26 (24.8%)	52 (49.6%)	24 (22.8%)	0.63
Rural	11 (10.5%)	10 (9.5%)	21 (20%)	8 (7.6%)	
History of contact with:					
-Livestock	23 (21.9)	19 (18.1%)	42 (40%)	18 (17.1%)	0.05**
-Unsafe animal products	12 (11.4%)	16 (15.2%)	28 (26.7%)	9 (8.6%)	
No contact	2 (1.9%)	>1 (0.9%)	3 (2.8%)	5 (4.8%)	

*: Student's t-test, SD: standard deviation.

** : Fisher's exact test. P-value considered significant when ≤0.05.

A study performed on British soldiers with fever of unknown origin in Afghanistan showed that 26% of the 26 soldiers had acute Q fever (9). This issue should be taken into account due to several factors such as the proximity of Iran (Sistan and Baluchestan Province) to Afghanistan, the entry of immigrants (legal and illegal) and livestock to Sistan and Baluchestan Province, lack of adequate control of the production and distribution chain of dairy products, and, finally, traditional ranching methods and proximity of livestock and ranchers.

A study conducted in Turkey estimated a prevalence of 13.5% (4) for Q fever in otherwise healthy people. Q fever was mainly observed in people over 30 years of age, hunters, and slaughterhouse workers.

In the present study, patients over 30 years old also showed the highest prevalence; additionally, patients who had contact with animals showed the highest seropositive prevalence.

However, other studies, performed on blood donors in Turkey, reported that the prevalence of phase II antibody was 35.1% and that the percentage of positive serology in men and women was 32.3% and 21.7%, respectively (10). On the contrary, the present study demonstrated a higher prevalence in men compared to women.

A study in 2005 on 1600 environmental samples obtained from US military bases in Iraq was conducted using the PCR method. The results showed that the prevalence of contamination with pathogen of Q fever was 23%, indicating that people's contact with *Coxiella* was higher than the expected rate (11).

A study investigating the prevalence of Q fever in the United States, using the immunofluorescence method, showed that 3.1% of 4437 samples had positive serology; furthermore, men (3.8%) had slightly more positive serology than women (2.5%) (12). These results showed less prevalence than that seen in the present study; however, similar results were observed in terms of sex.

However, the prevalence of Q fever varies in different countries. A study was carried out in eastern Spain in 1994 and 1995 on the prevalence of Q fever in 595 patients. The prevalence of phase II *Coxiella burnetii* antibody was reported as 48.6% (13).

The prevalence of Q fever in 438 pregnant women studied in London in 2009, using the immunofluorescence method, showed that 4.6% had positive *C. burnetii* IgG phase II and 0.5% had anti-*Coxiella burnetii* IgM antibody (14). Furthermore, a study carried out on the prevalence of *C. burnetii* in rural areas of Senegal using the ELISA method showed that 24.5% of 238 samples had positive

Q fever serology (15). Moreover, 40% of the patients had serological evidence for a previous infection with *C. burnetii* in Mali, of whom 9.5% suffered acute Q fever (16). Similar results were also obtained in the present study (35.5% and 34.3%, respectively). A study performed on Q fever manifestations in Taiwan showed that the disease was much more prevalent in men (98%) compared to women. In that study, most of the disease symptoms were fever (99%), chills (69%), and headache (45%) (17). However, fever, myalgia, and arthralgia were the major symptoms in the present study.

Takahashi et al. reported that 2.5% of 400 patients with symptoms of pneumonia had acute Q fever and their clinical manifestations included fever, generalized fatigue, and liver dysfunction. They stated that Q fever was not a common cause of airway infections (18). Similarly, the current study also showed that 5.4% of patients had cough, and the most prevalent type of Q fever clinical manifestations was self-limited febrile disease.

Based on the above results, it can be concluded that the prevalence of Q fever among febrile patients suspected of having brucellosis is high. The major cause of prevalence of the disease in this province is contact with livestock and dairy products.

Therefore, necessary health measures for disease prevention should be planned and implemented more seriously. However, serological studies on Q fever must be performed in other populations.

Based on the above, the following suggestions are offered: performing further epidemiological studies with more variables in different parts of the province and the country; implementing more training measures related to the disease among various social groups; performing health-related measures in slaughterhouses and centers associated with dairy products; and, finally, checking immigrants and animals entering Iran from neighboring countries including Afghanistan due to the outbreak of the disease in neighboring countries. Some important strategies to control Q fever are training people; consuming pasteurized milk; controlling parasites of cattle, sheep, and goats; and not receiving blood from donors.

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