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ORIGINAL ARTICLE

Epidemiological Characteristics of Serologically Confirmed Q Fever Cases in South Korea, 2006–2011

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Abstract
Objectives: Q fever has been reported worldwide; however, there was almost no official report of Q fever in Korea. In this study, we describe the current status of human Q fever occurrence in Korea.
Methods: Demographic data of Q fever patients were collected from the National Notifiable Diseases Surveillance System from 2006 to 2011. Case investigation reports from regional public health departments were used for additional information, like risk factors and clinical manifestation, of the patients since 2008.
Results: There were 65 serologically confirmed cases during the study period. The annual notification rate of Q fever was 0.22 cases per million persons. The majority of cases were men (87.7%), adults (98.5%), and urban inhabitants (67.7%). Relevant exposures to risk factors were identified in 45.7% of patients. The most common symptoms of acute Q fever were fever (89.3%), myalgia (67.9%) and asthenia (53.6%). Two cases with endocarditis were identified in chronic Q fever.
Conclusion: This study suggests that Q fever has a low endemicity in Korea. However, management and research at national level is required for prevention of a future epidemic.

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1. Introduction

Q fever, a zoonosis caused by *Coxiella burnetii* (*C. burnetti*), has been reported in most parts of the world [1]. The primary animal reservoirs are cattle, sheep, and goats, but they are usually asymptomatic, except for reproductive disorders in females. Most human infection is through direct contact with infected livestock or inhalation of contaminated aerosols. The clinical manifestation is characterized by prolonged fever, headache, myalgia, pneumonia or hepatitis in an acute form, as well as endocarditis and vascular infection in its chronic form [2]. There has been no known outbreak of the disease in Korea, but there were a few reports of patients with Q fever. Seroepidemiological studies showed relatively high infection rates in animals and a concern for the risk of human Q fever [3, 4]. In 2006, Q fever was included in the National Notifiable Infectious Diseases, and management at a national level was initiated. The number of hospital consultations for confirmed diagnosis of Q fever increased during 2006−2011. We reviewed the general characteristics, clinical spectrums, and risk factors of patients with Q fever from nationally reported cases during this period.

2. Materials and Methods

2.1. Study subjects

We identified 72 patients with Q fever registered in Korea Centers for Disease Control (KCDC) National Notifiable Diseases Surveillance System from 2006 to 2011. We excluded seven patients without serological diagnosis, and thus reviewed the epidemiological data of 65 patients. Patients' information, such as sex, age, job, region and disease onset date, was available from the surveillance records. Additional information such as risk factor exposures and clinical characteristics had been collected for 35 patients since 2008, when the regional public health departments began epidemiological investigations of all reported cases of Q fever, with the disease-specific case report form.

2.2. Serological methods

Serological diagnosis was performed by indirect immunofluorescence antibody assay (IFA) using *C. burnetii* Nine Mile strain. If immunoglobulin G (IgG) antibodies level against the *C. burnetii* phase II antigen from the convalescent phase, is >four times the amount from the initial acute phase, or the IgG titers are ≥1:256, or IgM titers to phase II antigen are ≥1:16, then the sample was considered positive for acute infection. Further, an IFA diagnosis kit (Commercial Slide, Focus Diagnostics, Cyprus, California, USA) was used to reconfirm the initial diagnosis, by determining the presence of phase I and phase II antibodies in the samples. If IgG titers to phase I antigen were >1:800 in the diagnosis kit, Q fever patients were classified as having chronic infection [5]. All testing was performed at Korea National Institute of Health.

3. Results

Acute and chronic Q fever infection was notified continuously since 2006 and we identified 65 serologically confirmed patients (Figure 1). Twelve patients (18.5%) were considered as chronic, based on the serological analysis results. The average annual notification rate of Q fever was 0.22 cases per million persons during the study period. The general characteristics of all patients are shown in Table 1. The mean (±SD) age of the patients was 49.1 years (±14.5), and they were all adults except for one adolescent patient. There were 57 men (87.7%) and eight women (12.3%). Fifteen patients (23.1%) had high-risk occupations for Q fever, e.g., livestock raiser, veterinarian, slaughterhouse worker, and farmer. The number of patients in urban areas (44; 67.1%) was more than twice that in rural areas (21; 32.3%). Among the 16 provinces and metropolitan cities of Korea, Gyeonggi, Daegu, Chungnam, and Gyeongnam accounted for 61.5% of all notified cases of Q fever. Acute Q fever cases occurred throughout the year, but based on the data from 47 patients for whom the disease onset time was verified, the highest incidence was observed in the spring season (Figure 2).

The risk factors and clinical symptoms of 35 patients, who were investigated by local health departments from 2008, are summarized in Tables 2 and 3. The most common risk factor was contact with animals (15; 42.9%), followed by visiting animal farms (7; 20%), and participating in animal birthing (6; 17.1%). The most frequently contact was with cattle. The other 19 patients (54.3%) had not been exposed to any such known risk factors. However, in three cases, ingestion of raw beef

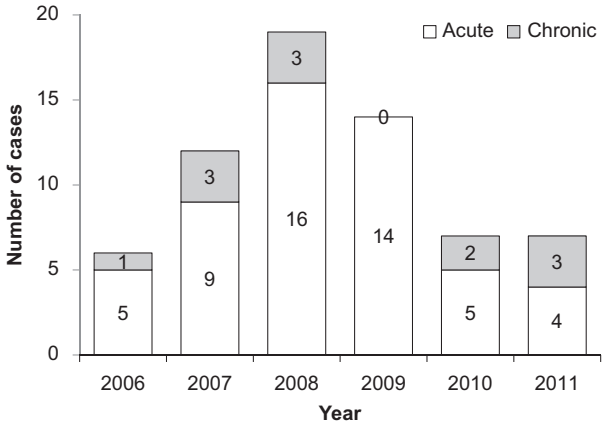

Figure 1. Notified cases of human Q fever in Korea, 2006−2011. Gray bars indicate chronic cases and white bars indicate acute cases.

Table 1. General characteristics of Q fever patients in Korea, 2006−2011

		All cases (n = 65)	
		n	%
Sex	Male	57	87.7
	Female	8	12.3
Age (y)	<20	1	1.5
	20−29	6	9.2
	30−39	11	16.9
	40−49	11	16.9
	50−59	20	30.8
	≥60	16	24.6
Occupation	Livestock raiser	5	7.7
	Veterinarian	2	3.1
	Slaughterhouse worker	2	3.1
	Agricultural farmer	6	9.2
	Others	50	76.9
Inhabitant area	Urban	44	67.7
	Rural	21	32.3
Region	Seoul	6	9.2
	Busan	0	0
	Daegu	10	15.4
	Incheon	3	4.6
	Gwangju	1	1.5
	Daejeon	1	1.5
	Ulsan	0	0
	Gyeonggi	16	24.6
	Gangwon	3	4.6
	Chungbuk	4	6.2
	Chungnam	7	10.8
	Jeonbuk	2	3.1
	Jeonnam	0	0
	Gyeongbuk	4	6.2
	Gyeongnam	7	10.8
	Jeju	1	1.5

or deer blood was the only possible risk factor. The proportion of risk exposures by sex was 48.3% in men and 33.3% in women. Fever was present in 85.7% of all patients. Hepatitis and pneumonia were present in 21.4% and 10.7% of acute patients, respectively, and one patient had a rare complication of encephalitis. Among seven chronic patients, endocarditis was observed in two patients who previously had valvular heart disease. No mortality was identified.

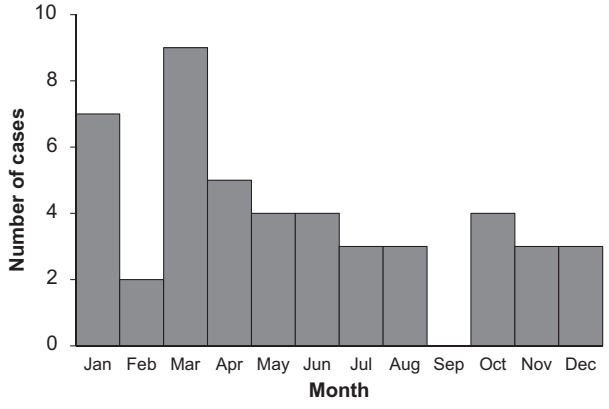

Figure 2. Monthly distribution of 47 cases of acute Q fever in Korea, 2006−2011.

4. Discussion

To our knowledge, this is the first official report on the characteristics of Q fever patients in Korea. The annual incidence of Q fever in Korea is much lower than that in France, Australia and Taiwan (0.02 vs. 2.5, 0.1, and 0.38 per 100,000 population, respectively) [5−7]. As the disease has a broad spectrum of clinical manifestations, from nonspecific febrile illness to neurological disorder, and there are no known outbreaks in Korea, it is difficult for physicians to diagnose Q fever without an increased awareness. Serological diagnostic testing is limited, because it is available at only one national laboratory. Therefore, Q fever is likely to be under-diagnosed and under-reported in Korea.

Table 2. Distribution of exposures for Q fever infection among the investigated patients, 2008−2011

	All cases (n = 35)	
Risk factors	N	%
Animal contact	15	42.9
Cattle	7	20.0
Deer	4	11.4
Goat	3	8.6
Horse	1	2.9
Pig	1	2.9
Unspecified	2	5.7
Unpasteurized milk	0	0
Visiting animal farm	7	20.0
Birthing animals	6	17.1
None	19	54.3

Similar to other studies, the majority of Q fever cases were men and adults [8−10]. In this study, men were more involved in the 'at risk' exposures than women, but the gender difference could be explained by the protective role of female hormones [11]. There were no cases of children <15 years old, and it seems to be related with low clinical expression after infection at a young age [12]. A clustering of cases in spring is associated with the animal birth season, as *C. burnetti* is highly concentrated in the amniotic fluids or placental tissues of infected animals [13]. Occupational contribution was not high in comparison with other countries [10,14]. It needs to be interpreted with regards to the workforce structure of Korea. More than half of the patients were not exposed to any risk factors. This suggests that Q fever might occur in urban areas, even without direct contact with primary reservoirs, as the bacteria can spread through contaminated dust by wind from the remote areas and infect humans at very low doses of inhalation [15].

Table 3. Distribution of symptoms and signs among the investigated patients with Q fever, 2008−2011

	All cases, n (%)	
	Acute infection n = 28	Chronic infection n = 7
Fever	25 (89.3)	5 (71.4)
Myalgia	19 (67.9)	0 (0.0)
Asthenia	15 (53.6)	2 (28.6)
Skin rash	1 (3.6)	1 (14.3)
Cough	4 (14.3)	0 (0.0)
Headache	7 (25.0)	1 (14.3)
Dizziness	5 (17.9)	0 (0.0)
Nausea	6 (21.4)	0 (0.0)
Vomiting	2 (7.1)	0 (0.0)
Diarrhea	2 (7.1)	0 (0.0)
Chill	14 (50.0)	4 (57.1)
Sweating	5 (17.9)	1 (14.3)
Splenomegaly	3 (10.7)	0 (0.0)
Hepatomegaly	1 (3.6)	0 (0.0)
Pneumonia	3 (10.7)	0 (0.0)
Hepatitis	6 (21.4)	1 (14.3)
Endocarditis	1 (3.6)	2 (28.6)

Hepatitis or pneumonia are known to accompany symptomatic acute Q fever, but our results indicated that mild illness was dominant [9,16,17]. More detailed clinical reviews of patients are necessary in future studies. Q fever endocarditis, most frequent presentation of chronic infection, was also observed in an acute patient without previous cardiac abnormalities. Q fever testing is recommended for discovering the cause of endocarditis in patients with valvulopathies. In addition, clinical and serological follow-up after acute Q fever should be considered for early detection of cardiac involvement [18]. Raw milk consumption is unusual in Korea, but ingestion of raw beef or deer blood is preferred by some people. Although a recent study showed a low seroprevalence of *C. burnetti* in meat cattle and farm-raised deer in Korea, the risk of transmission to humans by the oral route should be assessed [2,19].

According to national surveys of *C. burnetti* seroprevalence in the Korean population, the seropositivity rate of high-risk occupation groups, such as dairy farmers, slaughterhouse workers, and veterinarians, was 3.7−10.2% (data not shown). Q fever is not currently considered as a significant threat to public health in Korea. Only sporadic cases have been reported to date, but there is a possibility of an epidemic. Therefore, increased awareness among physicians for better detection and treatment of Q fever, expansion of the diagnostic system, and further investigations for undiscovered risk factors, are persistently required.

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