Journal of Zoonotic Diseases
2021, 5 (3): 1-7
doi: 10.22034/jzd.2021.48437.1129
https://jzd.tabrizu.ac.ir/article_13858.html

Mini Review

A review of the epidemiology of Q fever disease in Iran

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(Received 15 October 2021, Accepted 13 November 2021)

Summary
Q fever is caused by *Coxiella burnetii*, which infects lots of hosts, including animals and humans. It is a zoonosis that is considered a public health problem. Because of little epidemiological information about the status of this disease in various parts of Iran, this study was carried out to evaluate the epidemiology of Q fever among human cases and animals. Misdiagnosis with inadequate information and inattention about Q fever can lead to widespread epidemics in livestock and human communities. One of the most critical ways of transmitting Q fever in humans is respiratory aerosols or dust contaminated with animal parturition fluids. In some studies conducted in Iran, the incidence of human infection was 3.6 and 5.1%. In some studies performed in different parts of Iran, the prevalence of Coxiellosis was 33%, 27%, and 17% in goats, sheep, and cattle, respectively. Also, 27.08% of raw milk, 6.25% of yogurt, 4.35% of cheese, and 4.16% of doogh were reported positive. In conclusion, based on the evidence obtained, it seems that Q fever is currently present in Iran, and due to the lack of studies, this disease is not considered or mistaken for other febrile diseases such as influenza and brucellosis. Performing more serological studies in different parts of Iran is required to determine the epidemiological features of the disease.
Keywords*: Coxiella burnetii*, Public health, Q fever, Zoonosis

Introduction

C.burnetii is a gram-negative intracellular obligatory bacterium belonging to the *Rickettsiaceae* family that causes Q fever in humans and animals. The q stands for the query because the cause of the disease was long a question mark. It was reported for the first time by Derrick in 1973 after a flu-like disease outbreak among the workers of a Slaughterhouse in Brisbane, Australia (Derrick, 1983). The first case report of Q fever was reported in Iran in 1952. Since then, human cases and reports of serum prevalence of the disease in the human population have been published from different regions of Iran (Mostafavi et al., 2012). From 1976 onwards, Q fever was forgotten in Iran, and no investigation or report of the human cases and outbreak has been published. In 2009, antibodies against Q fever were reported in patients in southeastern Iran (Khalili et al., 2010). Subsequent studies showed that Q fever is an endemic disease in many parts of Iran (Mohabbati Mobarez et al., 2017). *C.burnetii* produces spore-like structures in the environment and is resistant to adverse environmental conditions and physical and chemical stresses. The disease has been reported in all countries except New Zealand (Rahmdel et al., 2018). The Center for Disease Control and Prevention (CDC) has classified *C.burnetii* as a group B pathogen, because it can be used as a biological weapon due

to its rapid spread over long distances in a short time. It is also a zoonosis, so there are many hosts for this bacterium. The bacterium has been reported to be present in a wide range of animals, including livestock, birds, and pets (Pal et al., 2017). Most parts of Iran suffer from reduced rainfall, which accelerates the transfer of this factor. Also, sandstorms blowing from Iran's western neighbors such as Kuwait and Iraq are involved in the transmission of *C.burnetii*, and respiratory transmission has been reported in Kuwait and Iraq (Jaafari et al., 2018). Recently, acute and chronic cases of this disease have been reported in Iran (Khalili et al., 2010; Mostafavi et al., 2012; Mohabbati Mobarez et al., 2017). Due to the zoonotic nature of Q fever, the present study aimed to evaluate *C.burnetii* and its pathogenesis and transmission routes and to review the reports related to the prevalence of the disease in different regions of Iran.

Methods

This paper collected the data from databases such as Google Scholar, Scopus, and PubMed. All included studies were published before January 2021. The data were obtained from research and review articles on the epidemiology of Q fever disease in Iran and were summarized to form a comprehensive review article. The following search terms in the title and abstracts were used to search the databases: *Coxiella burnetii*, Public health, Q fever, Zoonosis, Prevalence, and Iran.

Routes of Transmission and Pathogenicity

Transmission of the organism to humans could happen via three major routes: the respiratory tracts (aerosols), digestive system (consumption of contaminated products), and skin (bite of ticks and dermal ulcers) (Hsi et al., 2020). Human infection occurs through the inhalation of respiratory droplets contaminated with this bacterium, which is present in the urine, feces, milk, and placental discharges of infected animals. Excretion of this agent through milk, feces, and vaginal secretions of contaminated animals continues for several months (Ahmadizadeh et al., 2015). The dose required for the pathogenicity of *C.burnetii* is low, and 1 to 10 organisms can create disease in humans (Brooke et al., 2015). This factor multiplies rapidly after entering the body inside monocytes and macrophages. Ticks have also been shown to be the leading carriers of this bacterium in animals. Ixodidae ticks are the primary carriers of *C.burnetii* in animals. These ticks are also considered as reservoirs of *C.burnetii*, and the continuation of the long-term presence of this microorganism in the environment in terms of transmission from one stage of growth to another (transstadial transmission) and from generation to generation (transovarial transmission) is essential (Buysse et al., 2021).

The disease has no specific symptoms in animals, but in some cases, stillbirth, abortion, endometritis, and metritis have been reported. The shedding duration of this agent depends on the excretion path and species. *C.burnetii* may be secreted about eight days in ewes and more than 13 months in cattle (van den Brom et al., 2020). Also, in feces, *C.burnetii* could be secreted for more than 20 days in goats and about eight days after lambing in ewes. Goats can shed this factor in two consecutive deliveries periods. Due to the higher susceptibility of females, the prevalence of Q fever is higher in female animals than in males.

Furthermore, pregnancy is one of the crucial parameters in the incidence of Q fever, and reactivation of this factor occurs more in female animals than in male ones. Cases of latent infection are usually the cause of the persistence and spread of bacteria (O'Neill et al., 2014). Contamination of raw milk with *C.burnetii* has raised concerns about the role of milk as a source of transmission to humans. According to reports from different countries, the prevalence of *C.burnetii* in raw milk has been from 4.7% to 47.7%. Milk is a suitable culture medium for many microorganisms, because it is the source of all main nutrients (Khademi et al., 2019). Countries with inappropriate processing of dairy products often have a challenge with foodborne illnesses like Q fever, brucellosis, tuberculosis, and listeriosis. *C.burnetii* was also identified eight months after the production of

traditional cheeses from unpasteurized milk. Livestock workers, veterinarians, butchers, slaughterhouse and laboratory workers, and people who come into contact with domestic animals are at higher risk for Q fever (Khademi et al., 2020). According to the studies conducted in different parts of Iran, the main routes of *C.burnetii* transmission are contaminated dairy products, placental discharges, tick bites, consuming the wild animal's meat, and airborne transmission (Mohabbati Mobarez et al., 2017).

Symptoms of the Disease

The symptoms of this disease are very different in humans, and about 60% of carriers of the disease are asymptomatic (Dadimi and Nishanth, 2020). Clinical symptoms of the acute Q fever include a sudden headache, fever, pneumonia, fatigue, chills, headache, muscle aches, sweating, coughing, nausea, vomiting, chest pain, diarrhea, skin rash, neurological signs, cardiac involvement, bone marrow involvement, cholecystitis, acute lymphadenitis, dermatological signs, myocarditis, pericarditis, meningoencephalitis, and even death. In chronic forms of the infection, endocarditis, bone and joint involvement, vascular infections, chronic lung infection, and chronic fatigue syndrome have repeatedly been reported (Esmaeili et al., 2017). Furthermore, *C.burnetii* infection may lead to premature deliveries, stillbirth, or abortions in pregnant women. Although, Q fever is a benign disease, its mortality in patients with chronic disease is reported to be between 1% to 11% (Honarmand, 2012).

Diagnosis

Doctors and the healthcare system often overlook Q fever disease. Its diagnosis needs to perform so as to increase awareness of physicians and treatment staff and to improve their access to reliable diagnostic laboratory facilities, and thereby preventing acute Q fever from turning into chronic form (Hirai et al., 2005). Indirect immunofluorescence (IF), enzyme-linked immunosorbent assay (ELISA), and complement fixation (CF) are the most common techniques for the detection of the bacterium. The problem of these methods is the delay in diagnosing the causative agent, because the production and detection of antibodies against this bacterium take several weeks. For this reason, the use of serological methods to detect infection with *C.burnetii* is not recommended (Norouzian et al., 2018). However, PCR is one of the most valuable methods in diagnosing *C.burnetii*, because it has no limitations and its sensitivity is high (Malou et al., 2012).

Disease Reports in Different Parts of Iran

As stated above, one of the symptoms of Q fever is chronic endocarditis. In a study conducted from 2016 to 2018 at the Rajaie Cardiovascular Medical and Research Center in Tehran, 30.77% of the patients with symptoms of Infectious Endocarditis (IE) were isolated (Moradnejad et al., 2019). In a study in Kurdistan province, 250 blood serum samples were taken from people at high risk, such as wildlife hunters and their families, butchers, and the medical staff. In the end, 27.83% of the serum samples were reported positive (Esmaeili et al., 2014). In a systematic review and meta-analysis based on the data reported from different parts of Iran (2005 to 2016), Mohabbati Mobarez et al. (2017) reported that the overall seroprevalence of IgG antibodies was 32.86% in human samples. In a study in Ilam province, 367 blood serum samples were taken from people at high risk, such as farmers (n = 82), animal husbandry workers (n = 113), park rangers (n = 35), and slaughterhouse workers (n = 61) (Mostafavi et al., 2019). In the end, 27.83% of serum samples were reported positive (Mostafavi et al., 2019). Soleimani and Jaydar (2021) investigated the seroprevalence of Q fever in the veterinary staff at Lorestan province and found that among 92 serum samples, 77 (83/69%) samples were positive and 15 (16/3%) samples were negative. Some reports of Q fever prevalence in different parts of Iran are shown in Table 1.

Table 1: Reports of *C.burnetii* prevalence in different parts of Iran

NO.	Location	Prevalence (%)	Sample	References
1	Iran (total)	21.03	Sheep	(Mohabati Mobarez et al., 2021)
2	Qom	33.33 35.71 35.71	Cattle Sheep Goat	(Esmaeili et al., 2019)
3	West Azerbaijan	19.3 14.6	Buffalo Cattle	(Khademi et al., 2019)
4	Shahrekord	5.79 5 2.56	traditional bovine cream traditional sheep butter traditional bovine butter	(Reisi et al., 2019)
5	Shiraz	27.08 6.25 4.35 4.16	raw milk yogurts cheese doogh	(Abdali et al., 2018)
6	(Chahrmahal-va-Bakhtiari)	9.72 2.54 2.6	Cattle Sheep Goat	(Nokhodian et al., 2017)
7	Lorestan	15	Sheep	(Lorestani et al., 2016)
8	Shahrekord	16	Cattle	(Karimian, 2016)
9	Isfahan	26	Cattle	(Esmaeili, 2015)
10	Tehran	18	Cattle	(Ahmadizadeh et al., 2015)
11	East Azerbaijan	20	Cattle	(Esmaeili, 2015)
12	Yazd	15	Cattle	(Nasehfar et al., 2015b)
13	Chaharmahal-va-Bakhtiari	33	Cattle	(Nasehfar et al., 2015b)
14	Isfahan	10.76	Camel	(Doosti, 2014)
15	Lorestan	41	Cattle	(Khademi et al., 2014)

Discussion

C.burnetii causes Q fever disease. This study aimed to evaluate *C.burnetii* and its pathogenesis and transmission routes and to review the reports related to the prevalence of the disease in different regions of Iran. *C.burnetii* has been isolated in animals in the reproductive tract, uterus, and mammary glands. Abortion is one of the clinical manifestations of the prevalence of *C.burnetii* in animals and is mainly concentrated during the reproductive season of small ruminants (Khademi et al., 2020). In humans, it causes symptoms such as the flu, hepatitis, and pneumonia. Endocarditis is also possible to be developed in Q fever, especially in chronic and latent causes of the disease. Also, symptoms such as cardiovascular lesions, pericarditis, cardiomegaly, hepatomegaly, and glomerulonephritis are common. The main transmission route is the inhalation of respiratory droplets infected with *C.burnetii*. Environmental contamination is caused by milk, placenta, vaginal discharge, fetal fluids, feces, and urine of infected animals (Maurin and Raoult, 1999). There are various reports of the disease in Iran. The most important reasons that could be mentioned concerning the different reports for the prevalence of *C.burnetii* in dairy products in various areas of the world are the diversities in climate and environment of the geographical areas, the type of survey, the type of samples taken, and the season in which sampling took place. For the detection of *C.burnetii*, there are classical methods such as

cultivation, which have some limitations. However, diagnostic methods based on molecular biology techniques can contribute to the rapid diagnosis and management of the disease. Like other zoonotic diseases, the control of Q fever in humans depends largely on controlling the animal infection. Legislation on compulsory removal of contaminated animals, the transport, and obligatory vaccination of livestock are also important tools to control the disease (Rahimi et al., 2010). Veterinarians, ranchers, and slaughterhouse workers are the most at risk of infection. Among them, veterinarians are most at risk due to the examination and treatment of sick animals, the diversity of covered farms, and the diversity of livestock species. There is no need for close contact to transmit Q fever, and the disease is spread by wind and dust. Finally, due to the zoonotic nature of this disease, it is suggested that the responsible organizations and agencies in the Veterinary Organization, the Ministry of Jihad-e-Agriculture, and subdivisions of the Ministry of Health have extensive and close interactions to identify reservoirs and prevent and control the disease.

Conclusion

Based on the evidence obtained, Q fever is currently present in different regions of Iran, and due to the lack of studies, this disease is not considered or mistaken for other febrile diseases such as influenza and brucellosis. Due to the relatively high prevalence of this disease in Iranian livestock populations and the risk of transmission to humans, animal health and vaccination, pasteurization of dairy products, monitoring the production and distribution of traditional dairy products, and raising farmers' awareness to control *C.burnetii* are recommended.

Acknowledgments

Not applicable

Conflict of interest statement

There is no conflict of interest.

Ethical approval

Not applicable

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