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Seroprevalence of Q Fever and Risk Factors Affecting Transmission of *Coxiella burnetii* in Industrial Slaughterhouse; A Survey from Northeastern Iran

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Abstract

Background: Q fever is a generally neglected infection caused by *Coxiella burnetii*. Slaughterhouse workers exposed to livestock are among occupationally at-risk people.
Objectives: This study was conducted to investigate the seroprevalence of anti-*Coxiella burnetii* (Q fever) IgG antibody among industrial slaughterhouse workers and factors affecting the risk of infection.
Methods: In this cross-sectional study serum samples were taken from 91 individuals working at the central industrial abattoir in Mashhad, Iran using a convenient sampling method. Sera were kept at -80°C until assayed for specific anti-*Coxiella burnetii* IgG antibodies (phase 1) using the commercial ELISA kit. The participants filled out a checklist addressing potential risk factors of acquiring the infection. SPSS 11.5 was used for data analysis considering a significance level of $P < 0.05$.
Results: The participants' mean age was 38.7 ± 8 years. Fifty-six percent of the studied individuals (51 out of 91) were found positive for anti-*Coxiella burnetii* antibodies. The most prevalent cases were sheep (29, 57%) and cow (18, 35%) butchers. The odds of Q fever infection increased among those with a history of accidental hand cuts of more than five times during the previous years (OR = 2.56, CI95% = 1.02 - 6.33, P-value = 0.04) and those dealing with sheep as the primary livestock (OR = 2.9, CI95% = 1.09 - 7.66, P = 0.02).
Conclusions: The high seropositivity rate of anti-*Coxiella burnetii* IgG reflects high exposure rate of workers to this potentially serious pathogen in slaughtherhouses; therefore, careful education, follow-up, and revision of decontamination policies and improved occupational care and environmental hygiene should be strictly implemented in slaughterhouses to reduce the risk.

Keywords: Q Fever, Abattoir, *Coxiella burnetii*, Iran

1. Background

Zoonotic diseases are serious occupational hazards. Theses potential threats have drawn remarkable attention to public health surveillance systems for early detection, prevention and control strategies (1). Diverse types of occupational contacts with animals, such as livestock handlers, farmers, veterinarians, butchers, as well as slaughterhouse workers, are at-risk occupations. According to a report issued by WHO, more than 200 zoonotic diseases have been identified (2, 3), among which, *Coxiella burnetii*, the cause of Q fever is listed as a neglected zoonosis.

Q fever is an old, globally distributed rickettsial disease, with yet unanswered questions (4). Ticks are critical in circulating the pathogen between animals (5, 6). The major animal reservoirs for *Coxiella burnetii* are goats, cattle, and sheep (1, 7-9). *Coxiella burnetii* is mainly transmitted to humans by inhalation of contaminated aerosols, contact with infectious animal tissues, consumption of unpasteurized contaminated dairy products, and directly by tick bites (10-12). Human-to-human transmission has been reported through sexual contact, tissue transplantation, or close family contacts mainly through aerosol spread from contaminated clothing (13, 14). The main known risk factors of infection are occupational exposure to the pathogen. Epidemiologic reports show higher risk among occupations such as veterinary personnel, farmers, butchers, veterinary lab workers, as well as wool and leather industry workers. However the risk factors contributing in each occupation vary from the others, and risk assessment studies exploring each type of occupation are still ongoing (4).

It is estimated that nearly sixty percent of people infected with Q fever remain asymptomatic. However, the acute form of infection may manifest as a self-limited flu-like febrile illness, atypical pneumonia, or abnormal liver function tests (15-18). In chronic from, chronic fatigue syndrome, endocarditis, hepatitis, and osteomyelitis are predominant clinical manifestations (19-22). In the endemic area for Q fever, $\geq$ 12% of the population show antibodies against *C. burnetii*. Among the infected individuals, approximately 1% become chronic, with the considerable risk of life-threatening endocarditis (19, 23). Little is known about seroprevalence of infection in general Iranian population, and most studies have been performed among high-risk groups. Based on one meta analysis conducted in 2017, including ten studies, overly 1111 human sera were analyzed, among which, the seroprevalence of IgG phase I and II antibodies against Q fever were 19.80% (95% CI: 16.35 - 23.25%) and 32.86% (95% CI: 23.80 - 41.92%), respectively (24). However, such estimates should be interpreted with caution, because most included studies were conducted in particular geographic regions of the country and mainly among high-risk groups and thus such estimations do not necessarily reflect the status of infection in general Iranian population. The other types of epidemiologic studies have been conducted in animals as the primary source of human infections. According to one meta-analysis in Iran, the seroprevalence of Q fever in animals was estimated to be about 27% (CI 95%: 23 - 32%) (25).

2. Objectives

Being exposed to animal products, abattoir workers are thought to be at occupational risk of acquiring the infection. The present study was conducted to investigate the seroprevalence of Q fever among workers of the central industrial slaughterhouse in Mashhad city area, Iran. In addition, the risk factors affecting the transmission of infection to these workers were explored.

3. Methods

3.1. Study Population

This study was performed in the main Mashhad's industrial slaughterhouse. The slaughterhouse has almost 450 workers who work in daytime shifts consisting of 120 to 150 workers in different working areas. Sample size was calculated based on determining a qualitative variable in a population. Considering an alpha error of 5% and a prevalence of 68% based on similar study in Iran (26) with a precision of 10%, the sample size was calculated as 84 participants. Considering a dropout rate of almost 10%, the final considered sample size was 94. Due to working shift changes, the present field study was performed in three separate day times. In each sampling round, the sampling team was sent to the slaughterhouse with cooperation of the veterinary center of the province and sampling was performed in the site thorough convenient sampling method. Finally, 91 serum samples were included in the present cross-sectional study using a convenient sampling method (participation rate of $\sim$ 20%). About 5 ml venous blood was taken from volunteers working at different job positions in separate working area. These occupations consisted of caw butchers, sheep butchers, and administrative staff. The inclusion criteria was all the registered personnel who had a history of more than 6 months working in the slaughterhouse and agreed to participate the study. The exclusion criteria was the serum samples which were hemolyzed and laboratory unacceptable to be assayed in ELISA technique.

The consent was obtained from all participants and then a checklist was filled which addressed subscales of demographic data, history of working in the site, type of occupation (slaughtering vs. administration), kinds of animals dealt with (sheep/gout vs. caw), history of relevant risk factors in the last year including tick bites, hand-cut, contact with visceral secretions and application of personal protective equipments, PPE (mask, gloves, boots, aprons, eye protection).

3.2. ELISA

The sera were collected and kept at -80°C until the experimental assay. Specific Q fever IgG antibodies (phase 1) were measured using the anti-*Coxiella burnetii* (Q fever) phase 1 IgG ELISA kit (Abcam, UK) base on kit manual. Briefly, 100 μL of controls and diluted samples were added to the wells of ELISA microplate pre-coated with *Coxiella burnetii* capture antigens. After incubation phase for binding of IgG antibodies, the wells were washed and *Coxiella burnetii* anti IgG-HRP (peroxidase) conjugated was added to the wells. Thereafter, unbound material were washed out and the substrate, TMB (tetramethylbenzidine) was added to the wells. Next, the enzyme reaction was stopped by sulphuric acid (2N), and the plates were read using an ELISA reader at 450 and 620 nm wavelengths. The positive and negative controls provided by the kit were used in the experimental procedure. Finally, the OD values were interrelated based on the kit manual. According to the manufacturer's instructions, the test sensitivity and specificity was more than 90 and 98% respectively.

3.3. Statistical Analysis

The descriptive measures such as mean and standard deviation (SD) or median and intra quartile range

(IQR) were reported for continuous parametric or non-parametric data, respectively. Also frequency and percentage were used for categorical data. Kolmogorov–Smirnov test was used for evalution of normality. The quantitative variables were analyzed using Student's t-test or Mann–Whitney U test based on normality distribution, and the chi-square test estimated the association between the categorical variables. Binary logistic regression was performed to evaluate the risk factors for positive cases and the odds ratio (OR) was reported alongside with 95% confidence interval (CI). The data were analyzed using SPSS 11.5 and the significance level was considered as $P < 0.05$.

4. Results

Ninety-one male individuals were included the study. The participants' mean age was 38.7 ± 8 years with a mean working duration of 13.4 ± 6.9 years. The participants' demographic characteristics are shown in Table 1.

Of the participants, 56% (51 cases) were positive for Q fever immunoglobulin, while 37% (34 cases) were negative. There were also 7% (six people) of non-defined cases based on the commercial ELISA kit used in the study. The most common occupations among the positive cases were sheep butchering (29, 57%) and cow butchering (18, 35%). The odds of Q fever infection increased among those dealing with sheep as the primary livestock (OR = 2.9, CI95% = 1.09 - 7.66, P = 0.02).

We found no relationship between age (P = 0.51) or duration of employment (P = 0.53) with Q fever seropositivity. A significant relationship was not found between using PPE, including mask, glove, boot, and gown with the risk of acquisition of Q fever (Table 2). However, individuals who always used a mask were significantly younger (36.3 ± 8.7 years) than individuals who rarely/never (40.2 ± 7.3 years) used it (P = 0.02).

History of hand cuts of more than five times in the previous year during work increased the risk of Q fever by 2.56 times (CI95% = 1.02 - 6.33, P-value = 0.04). The regression model reports crude and univariate odds ratio and since no contextual variables were statistically significant or even has the conservative p value of below 0.1, no multivariate regression was performed (Table 3)

5. Discussion

In the present study, IgG phase 1 antibody against *Coxiella burnetii* was found in 56% of the slaughterhouse workers. IgG phase 1 indicates chronic infection or exposure to *Coxiella burnetii* (27-29). The global prevalence of Q fever varies in different geographic areas. Occupationally related seroconversion has been generally reported from 20% in the United States veterinarians up to 68% in slaughterhouse workers in Kerman, Iran (30, 31). These varieties arise from differences in geographic area, detection method used in the assay, working groups and samples size of the study as well as other minor environmental and occupational issues. One global meta analysis including 19 studies showed a wide variety of seopositivity ranging from 4.7% in Trinidad to 91.7% in Spain among slaughterhouse workers. The pooled estimation of global slaughterhouse workers seropositivity for *C. burnetii* among these workers was calculated as 26% (95% CI: 18 - 35%). Consistent with our results, the meta analysis reported no relationship between seroconversion and the age and years of work experience (26). The present study found higher seroconversion among sheep/goat butchers which is consistent to previous studies in Iran reporting higher *C. burnetii* among sheep (25).

Since only a small percentage of infected individuals become chronic, the high percentage indicates chronic exposure to the pathogen in the workplace. Based on the high persistence of the microorganism in the environment and the transfer of aerosols (13), it seems reasonable that all administrative personnel and butchers are exposed to the infection. Also, administrative personnel do not usually wear PPE during working hours. Noteworthy, *C. burnetii* is an extremely sustainable virulent pathogen and can be easily spread to rather distance area, and only limited numbers of the microorganism is sufficient to cause infection in humans (32). Therefore working in slaughterhouse area is an occupation risk for both butchers and administrative personnel.

Different routes through which pathogens can be transmitted to humans are oral, respiratory, cutaneous wounds, mucus, animal bites or stings of arthropods. These are all potentially conceivable in a working environment such as slaughterhouse. The pathogen can be transmitted through inhaling droplets, aerosols, contaminated dust, and direct contact with contaminated tissues or by-products. In addition, contact with infected animal hides, straw, or wool has been mentioned as other potential routes of *C. burnetii* transmission (13).

We found that hand cuts could increase the risk of seropositivity. It seems reasonable that direct inoculation of the pathogen into the body following hand cuts in a highly contaminated environment might be a possible transmission route. However it should be noted that the number of hand cut injuries may not be accurately remembered and stated and possible information bias should be considered. In addition more hand cut events may be a reflection of carelessness in personal and professional hygiene and that influences the overall susceptibility to the infection. Inconsistent to our results occupational injury

Table 1. The Participants' Demographic Characteristics and Risk of Seropositivity

	Total	Seropositive (%)	OR (95% CI)	P-Value
Age, y				0.51
< 40	44	22 (50)	0.41 (0.16 - 1.01)	
≥ 40	41	29 (71)		
Work history, y				0.53
< 16	49	28 (57)	0.75 (0.31 - 1.82)	
≥ 16	36	23 (64)		
Occupation				0.16
Butcher	75	47 (63)	2.51 (0.65 - 9.7)	
Official	10	4 (40)		

Table 2. Personal Protective Equipment (PPE), Personal Hygiene Behaviours and Risk for Q Fever Seropositivity

	Total	Seropositive (%)	OR (95% CI)	P-Value
Mask				
Always	32	18 (56)	0.77 (0.31 - 1.90)	0.58
Rarely/never	53	33 (62)		
Gloves				
Always	81	49 (61)	1.53 (0.09 - 25.36)	0.99
Rarely/never	2	1 (50)		
Gowns				
Yes	82	49 (60)	0.74 (0.06 - 8.52)	0.99
No	3	2 (67)		
Boots				
Yes	82	49 (60)	0.74 (0.06 - 8.52)	0.99
No	3	2 (67)		
Tools disinfection				
Always	10	6 (60)	1 (0.26 - 3.84)	0.99
Rarely	75	45 (60)		
Face & hand disinfection after work				
Always	13	7 (54)	0.72 (0.22 - 2.43)	0.62
Rarely	72	43 (61)		

has not been identified as a main risk factor of acquiring the infection (33), therefore, still additional investigations are needed to reach a consensus.

To provide a more accurate picture of the infection in slaughterhouses, the frequency of infection among livestock should be considered. A study in Iran reported that 27.2% of goats and 19.5% of sheep were seropositive for *C. burnetii* (34). Another study from Khorasan Razavi Province reported 36.5% seropositivity for sheep and 29.8% for goats (35). Hence, almost one-third of incoming livestock to abattoirs have a history of infection (25). These animals spread the pathogen through their feces, urine, and milk. Thus, a slaughterhouse is potentially contaminated with infected material. It is known that *C. burnetii* remains viable in the environment and is resistant against routine decontamination strategies. The sporulation-like process of the bacterium is involved in the persistence of the pathogen in environments particularly in dust which can be scattered in the air and easily inhalated (33, 36, 37).

According to our results, the protective effects of PPE, including wearing gown, mask, gloves, and boots, were insufficient. Though, there might be a prestige bias in

Table 3. Occupational Hazards and Risk of Q Fever Infection

	Total	Seropositivity (%)	OR (95% CI)	P-Value
Contact with animal blood and visceral secretions				0.99
≥ Once a week	79	47 (60)	0.73 (0.12 - 4.25)	
< Once a week	6	4 (67)		
Livestock				0.02
Sheep/goat	39	29 (74)	2.90 (1.09 - 7.66)	
Cow	36	18 (50)		
Hand-cut in last year				0.04
≥ 5 times	52	36 (69)	2.56 (1.02 - 6.33)	
< 5 times	32	15 (47)		
ectoparasite bite in last year				0.48
≥ 5 times	31	21 (68)	1.54 (0.6 - 3.91)	
< 5 times	52	30 (58)		

responding due to the workers occupational considerations because all workers are supposed to follow the rules and regulations related to wearing appropriate protective clothing in the slaughterhouses. Still, it seems that current protective approaches are insufficient. In many slaughterhouses, commonly used masks are not standard biologic masks, and yet are not worn correctly. Appropriate use of masks is particularly important to prevent inhalation of contaminated material; thereby specific training and accurate monitoring are needed to improve workers' self-protection. Inconsistent to our results, PPE has been mentioned to be effective for protection (38), indicating the importance of the accurate PPE protocol used by the workers. Also, more efficient environmental hygiene strategies should be taken into account to regular elimination of the pathogen from working area.

The other prevention strategy for those who are exposed to the infection is vaccination. However, it should be considered that the vaccination has significant side effects in people previously exposed to Q fever and a pre-vaccination test and other screenings should be performed before vaccine application (39). These strategies should be applied to reduce the risk of infection with *Coxiella burnetii* in slaughterhouses. It is noteworthy that the families of slaughterhouse workers are frequently exposed to the workers' contaminated clothing, which is ignored in periodic health evaluations related to slaughterhouse personnel. Therefore, observational and prevention strategies might also include the workers' family members (13).

Some limitations of this study should be noted. The IgG phase 1 shows chronic exposure or chronic Q fever infection. The present study aimed to investigate epidemiological exposure to the infection and did not intend to screen clinically acute or chronic infected individuals. Similar to other serologic studies, some possible underlying confounders should be noted. For example people might have acquired the infection from outside the slaughterhouse or previous to their present occupation. In addition, data regarding IgG phase II could provide a more complete picture. The data is lacking in the general population, and a control group of participants other than the high-risk group would be definitely informative. It is also recommendable to conduct cross studies including both animals and human samples, in addition to environmental sampling to investigate the degree of contamination using both serologic and PCR detection approaches. Seroepidemiologic studies among the general population, such as blood donors, could also provide valuable information about this neglected pathogen.

5.1. Conclusions

We found a high level of seroconversion in slaughterhouse workers. Also higher seroconversion was observed in those with more frequent hand cut events. Whether this association reflects a transmission route in slaughterhouses needs to be further investigated. Given the potentially severe outcomes of Q fever for slaughterhouse workers and their exposed families, and because occupational diseases are potentially preventable, prevention strategies should be strictly followed in such working areas.

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Footnotes

Authors' Contribution: Study design: L.J, K.Gh, M.Y; Data gathering: M.K, Gh.A; Drafting of the manuscript: M.K, L.J, K.Gh, M.Y; Final approval: M.K, L.J, K.Gh, Gh.A, M.Y.

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Data Reproducibility: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: The study was performed under ethical principles of the declaration of Helsinki. The research proposal was approved by the Ethics Committee of Mashhad University of Medical Sciences (Ethical approval code: IR.MUMS.fm.REC.1394.441).

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