

The Frequency of Q Fever by Gender in the Human Population of Western Macedonia

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Abstract: Q fever is a widespread zoonosis caused by *Coxiella burnetii*. The aim of the paper is to try and determine the possible gender difference related to the emergence of the Q Fever. People of all ages with different epidemiological conditions were examined. A total of 267 female serums were analyzed, of which 59 samples resulted positive – with a relative frequency of 22.09 % and of 253 male serums which were examined, 55 resulted positive – with a relative frequency of 21.73 %. The positivity has been based on the Cut-off value OD, which is above 0.5 in the positive cases. The serological test was conducted using the ELISA test kit by the German SERION Company. The serum isolates from the blood were kept at -30°C until testing. The sera were properly diluted based on the respective protocol, in the ratio of 1:400, in two phases (dilution 1:100 and 1:4). As regards the relative frequency between the genders, the difference in positive cases is only 0.36%, which implies that the epidemiology of the Q Fever is not gender dependent.

Keywords: *Coxiella burnetii*, age group, frequency, Q fever, seropositive.

1. Introduction

Q fever is a disease caused by infection with *Coxiella burnetii*. [1]

This organism is uncommon, but may be found in cattle, sheep, goats and other domestic mammals, including cats and dogs. The infection results from inhalation of a spore-like small cell variant, and from contact with the milk, urine, feces, vaginal mucus, or semen of infected animals. Rarely, the disease is tick borne. The incubation period is 9–40 days. Humans are vulnerable to Q-fever, and infection can result from even a few organisms. The bacterium is an obligate intracellular pathogen.

Q-fever was first described in 1935 by Edward Holbrook Derrick [5] in abattoir worker in Brisbane, Australia. The "Q" stands for "query" and was applied at a time when the causative agent was unknown; it was chosen over suggestions of "abattoir fever" and "Queensland rickettsial fever", to avoid directing negative connotations at either the cattle industry or the state of Queensland. [6]

The pathogen of Q fever was discovered in 1937, when Frank Macfarlane Burnet and Mavis Freeman isolated the bacterium from one of Derrick's patients. [2] It was originally identified as a species of Rickettsia. H.R. Cox and Gordon Davis elucidated the transmission when they isolated it from ticks in Montana, USA in 1938. [4]. A filter-passing infectious agent isolated from ticks. I. Isolation from Dermacentor andersonii, reactions in animals, and Zfiltration. Public Health Rep. 53:2259-2282.) It is a zoonotic disease whose most common animal reservoirs are cattle, sheep and goats. *Coxiella burnetii* named for Cox and Burnet is no longer regarded as closely related to Rickettsiae, but as similar to Legionella and Francisella, and is a proteobacterium.

C burnetii lives inside acidic lysosomes, a point that has therapeutic implications, [10] and it has 2 morphologic variants. Route of infection determines the clinical manifestations of acute Q fever. The small-cell variant (SCV) (0.2 x 0.7 microns), which survives well in the environment because of its resistance to heat and desiccation, pressure, and chemical agents [9] and the large-cell variant (LCV), which multiplies in the host monocyte and macrophage [11]. These variants are antigenically different.

The small-cell variant is a sporelike structure, enabling the organism to persist on fomites for more than 1 year. After passive entry into the host-cell phagosome, the organism delays the fusion of the phagosome with lysosomes, presumably using this delay to transform from the small-cell variant into the large-cell variant. Thereafter, the large-cell variant exploits and persists within the acidified phagolysosome of the monocytes and macrophages, using it as a nursery. [3]

C burnetii attaches to host macrophages by means of spectrin-binding proteins called ankyrin and is internalized into the cell, where it fuses with lysosomes to form phagolysosomes. The acidic environment of the phagolysosomes has little effect in defending the host against the invading organism, which multiplies and disseminates itself from this environment. This process is thought to occur mainly in the lungs, the main port of entry of *C burnetii*. Marrie and Raoult postulated that these morphologic variants create an impairment in the bacterial responses within the host, enabling the persistence of the illness in chronic cases. (Marrie TJ, Raoult D. *Coxiella burnetii* (Q fever). In. [7] Proliferation of organisms within the phagolysosome eventually ruptures the host cell. The infected pulmonary macrophages are also transported systemically, with the reticuloendothelial system (liver, spleen, bone marrow [most commonly]) being the most heavily infected. Immune responses result in inflammation that manifests as formation of non-necrotizing granulomata, termed doughnut

granulomata due to the characteristic appearance of a fibrin ring surrounding a fat vacuole. Although classically associated with acute Q fever, doughnut granulomata can develop in other conditions, such as visceral leishmaniasis, cytomegalovirus or Epstein-Barr infections, Hodgkin lymphoma, and allopurinol hypersensitivity reaction.

2. Material and Methods

The study was conducted in the Laboratory of Virology at the Faculty of Veterinary Medicine Tirana-Albania. The serums were separated from blood based on known laboratory methods by centrifugation of 600 rpm for 20 minutes and were preserved in plastic ampoules at -30°C until testing. The check of serum was conducted using the ELISA-SERION highly sensitive test imported from Germany. The results were based on the identification of IgG. Positivity is based on the Cut-off value, which in this case is about 0.5 OD which is considered as positive. Prior to the check, the sera were diluted in the ratio of 1:400 in two steps; first in the ratio of 1:100 and then diluted in the ratio 1:4, in conformity with the protocol of the Serion Company. The study included data on the observation and analysis of possible gender differences concerning the frequency of Q fever in the human population in western Macedonia. The study included 267 female persons and 253 male persons. Details of the sample with male and female persons are divided based on regions: Tetovo, Gostivar, Kicevo, Debar and Struga and in different age groups: 0-20, 20-40 and over

40 years of age. For the epidemiological study of this infection, the serums were gathered from people with various pathologies without any special preference. Data were grouped and processed to determine the spreading of Q fever in both genders.

3. Results and Discussion

Preliminary processing of the data obtained from the initial sample consisting of 267 female persons and 253 male persons shows that the average Q fever in the human populations sample of western Macedonia, which has been subject to serological testing, is present in 22.09% of the female population and 21.73 % in the male population – values that could be considered equal. Hence, 267 sera of female were tested, of which 59 resulted positive and 253 sera of male were tested, of which 55 resulted positive and are presented in the tables below by regions and age groups.

The samples with males or females only:

In order to identify the possible changes in the frequency of the Q Fever in relation to the gender of the community subjects in which the tests were carried out, we included 267 female persons and 253 male persons aged between 0 and 40, spread in five regions. The data have been shown in Table 1.

Table 1: Data of the sample divided into five working regions with men or women of different age groups

i		Xmi (vj)		FEMALES		
				Ni	Yoi (num)	Yoi(%)
REGION	The mean of the age group interval of the regions		Total number of examined persons	Numeric freq. of positive prs. infected with the Q Fever	Relative freq. of positive prs. infected with the Q Feve	
Tetovo	0-20	0,05 – 20,05	26	0	0%	
	20-40	20,05 – 40,05	18	6	33.3%	
	>40	>40,5	38	8	21%	
	Total:		82	14	17%	
Gostivar	0-20	0,05 – 20,05	16	0	0%	
	20-40	20,05 – 40,05	15	0	0%	
	>40	>40,5	30	4	13.3%	
	Total:		61	4	6.55%	
Debar	0-20	0,05 – 20,05	3	0	0%	
	20-40	20,05 – 40,05	4	1	25%	
	>40	>40,5	28	10	35.7%	
	Total:		35	11	31.4%	
Kicevo	0-20	0,05 – 20,05	3	1	33.3%	
	20-40	20,05 – 40,05	8	5	62.5%	
	>40	>40,5	28	12	42.8%	
	Total:		39	18	46.1%	
Struga	0-20	0,05 – 20,05	26	6	23%	
	20-40	20,05 – 40,05	6	2	33.3%	
	>40	>40,5	18	4	22.2%	
	Total:		50	12	24%	
Total Sum:			267	59	22.09%	

i	Xmi (vj)		MALES		
			Ni	Yoi (num)	Yoi(%)
REGION	The mean of the age group interval of the regions		Total number of examined persons	Numeric freq of positive prs. infected with the Q Fever	Relative freq. of positive prs. infected with the Q Feve
Tetovo	0-20	0,05 – 20,05	20	0	0.00%
	20-40	20,05 – 40,05	16	2	15.50%
	>40	>40,5	37	13	35.10%
	Total:		73	15	20.50%
Gostivar	0-20	0,05 – 20,05	20	1	5.00%
	20-40	20,05 – 40,05	19	2	10.50%
	>40	>40,5	40	3	7.50%
	Total:		79	6	7.59%
Debar	0-20	0,05 – 20,05	3	0	0.00%
	20-40	20,05 – 40,05	4	1	25.00%
	>40	>40,5	22	10	45.40%
	Total:		29	11	37.90%
Kicevo	0-20	0,05 – 20,05	4	0	0.00%
	20-40	20,05 – 40,05	6	3	50.00%
	>40	>40,5	25	11	44.00%
	Total:		35	14	40.00%
Struga	0-20	0,05 – 20,05	21	4	19.00%
	20-40	20,05 – 40,05	8	3	37.50%
	>40	>40,5	8	2	25.00%
	Total:		37	9	24.32%
Total Sum:			253	55	21.73%

The data from Table 1 have also been illustrated in Chart 1 with a combination of vertical lines and histograms that illustrate the data for male and female persons respectively.

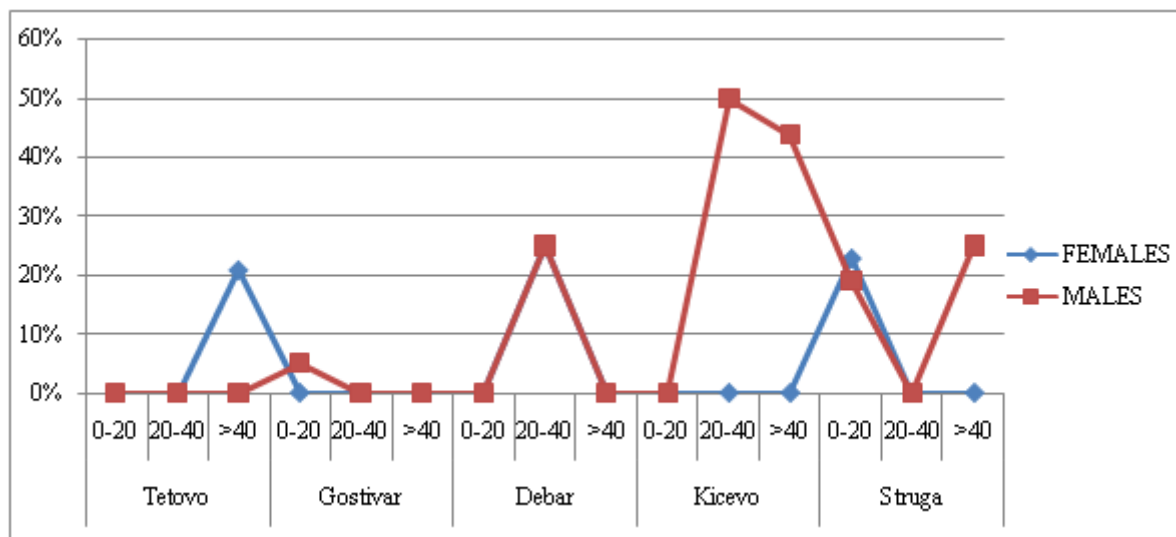


Chart 1: Polygonal lines of the observed relative frequency of people with the Q Fever in males and females respectively

Based on the visual comparisons, we can conclude that the acquired relative frequencies can be considered almost equal or slightly different, i.e. the difference is only 0.36% higher in females, or 22.09% females and 21.73% males; this implies that the epidemiology of the Q Fever does not depend on the gender, which can also be seen from Chart 1; the polygonal lines match in most of the cases (except for the region of Tetovo and Kicevo). Therefore, the presented results show that the Q Fever infection does not depend on

the sex of the infected persons. This slight difference between both sexes is therefore not significant. Having in consideration the factors that cause the spread of the infection, we can say that these factors do not show any preferential impact as regards the sex of the infected persons. The relations with animals, socio-economic conditions, etc. have a common influence on the emergence of this infection. In our opinion, even the ecological conditions of the region in question do not have a considerable impact when it comes

to the infection based on different sexes. Again, as we can see from chart, age plays a crucial role in this respect. The Kicevo region has a majority of female population infected by the Q Fever, with a relative frequency of infected people of 46.1%, of which the age group of 20 – 40 dominates with more than 60%; then we have the region of Debar with 31.4% females, though the age group includes those older than 40 with more than 35%; the region of Struga is next with 24% females, whereupon the age group between 20 and 40 is more exposed, with 33.3%, then Tetovo with infection frequency of 17%, of which the age group between 20 and 40 is the most infected, and finally the region of Gostivar with the lowest frequency of only 6.55%; what is interesting in this case is that only the age group older than 40 has been infected with the Q Fever in this region, with 13.3% of cases. The other chart referring to the male population provides these numerical comparisons: the Kicevo region is again dominant, with a relative frequency of 40% and the most exposed age group of 20-40. Debar follows with 38%, then Struga with 24%, Tetovo with 21% and Gostivar with 8%. The ranking is the same as in the female population. However, the difference between the sexes lies in the frequency of age groups. E.g. in Tetovo, the most affected age group within the male population is the one above 40, compared to females where the most affected age group was the one from 20 to 40. In the region of Gostivar, for example, where the female population of the first two age groups was not affected at all, the male population was affected exactly in those two. Debar, Kicevo and Struga remain proportionally the same in terms of the infection by age groups in both males and females. In this respect, according to our data, the age group between 20 and 40 has been the most affected, in almost all the zones in this region. In our opinion, this has to do with the fact that this particular age group does the greatest amount of work with cattle.

4. Conclusions

As shown above, we have identified the presence of the Q Fever in humans (males and females) in the region of Western Macedonia. This is the first time that a study like this has ever been carried out in this region. Our data show that the Q Fever infection in both males and females in total, in the covered region is almost the same, i.e. 22.09% in females and 21.73% in males. In our opinion, this implies that sex does not play any role in the emergence of this kind of infection. These conclusions can also be statistically verified (Table 1 and Chart 1 above).

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