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Q FEVER: EVALUATION OF HUMAN SEROLOGICAL EVIDENCES IN BRAZIL

FEBRE Q: AVALIAÇÃO DAS EVIDÊNCIAS SOROLÓGICAS HUMANAS NO BRASIL

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RESUMO

A Febre Q é uma zoonose causada pela bactéria *Coxiella burnetii*, que tem distribuição mundial, mas poucos casos humanos relatados no Brasil. Animais domésticos e de produção são reservatórios do agente etiológico. Em humanos a doença se caracteriza pela grande quantidade de manifestações clínicas e sistemas acometidos. O presente estudo objetivou traçar um perfil epidemiológico de indivíduos sorologicamente reagentes entre os anos de 2011 a 2017, com base nos dados coletados no Gerenciador de Ambiente Laboratorial (GAL) do Ministério da Saúde. As amostras reagentes foram selecionadas objetivando-se caracterizá-las quanto ao local de ocorrência, data e perfil demográfico. Verificou-se que o estado brasileiro que obteve maior frequência de amostras reagentes foi o do Rio de Janeiro 72,62 % (50/67), o ano com maior número de casos foi 2016 53,73 % (36/67), a zona urbana foi a com maior frequência 46,26 % (31/67) e a maioria dos reagentes eram homens 83,58 % (56/67) em idade adulta economicamente ativa 38,8% (21-30 anos). Ressaltamos neste trabalho a necessidade da realização de mais estudos de cunho investigativo, com vistas a esclarecer melhor o ciclo epidemiológico da doença e assim poder auxiliar os serviços de saúde quanto ao diagnóstico precoce, tratamento e tomada de decisão.

Palavras chaves: *Coxiella burnetti*; Febre Q; Estudo Epidemiológico.

ABSTRACT

Q fever is a zoonotic disease caused by the bacterium *Coxiella burnetii*, with worldwide distribution, but limited human cases reported in Brazil. Domestic and production animals, mainly ruminants, are reservoirs of the etiological agent. In humans, the disease is characterized by the variety of clinical manifestations and affected systems. This study aimed to define the epidemiological profile of serologically reactive individuals between the years 2011 to 2017, based on data collected in the Laboratory Environment Manager (LEM) of the Ministry of Health of Brazil. Reagent samples were selected in order to characterize the

records as to the place of occurrence, date and demographic profile. It was found that the Federated Unit with the highest frequency of reagent samples was Rio de Janeiro, with72.62 % (50/67); the year with the highest prevalence was 2016, with53.73 % (36/67); the urban area had the highest frequency, with 46.26 % (31/67), and most of the reagents were men (83.58 %, 56/67) of economically active age (38.8%, 21-30 years old). We emphasize in this study the need to carry out more investigative studies, with a view to better clarifying the epidemiological cycle of the disease and thus being able to assist health services in terms of early diagnosis, treatment and decision making.

Key words: *Coxiella burnetii*; Q fever; Epidemiological study.

INTRODUCTION

Q fever was first described by Derrick in 1937 as an infectious disease affecting workers in slaughterhouses and farms in Quensland, Australia. According to Brandão et al. (1953), in 1946, after the Second World War, an outbreak of Q fever occurred in Amarilo, Texas, between meat handlers and slaughterhouse workers, where 55 cases and two deaths occurred among 136 employees of the establishment. On this occasion, investigations revealed that the most likely source of infection was cattle.

Coxiella burnetti is usually present in the urine and feces of infected animals, and can be found in large quantities in the placental remains of animals born at term or abortion products and also through the inhalation of bacterial cells suspended in the air or contaminated aerosols, thus enabling entry of the bacteria in the individual's body (DAMASCENO and GUERRA, 2017).

Infections in animals can persist for several years or even for a lifetime. The bacterium is lodged in the mammary glands, supra-mammary lymph nodes, uterus, placenta and fetus, thus, the etiological agent can be found in milk, placenta, uterine discharges, in subsequent pregnancies and lactations (MARES-GUIA, et al., 2015). The clinical diagnosis is difficult, since the symptoms resemble several other diseases such as tuberculosis, sarcoidosis, histoplasmosis, brucellosis, tularemia, syphilis, as well as other bacterial endocarditis.

In confirmed cases, antibiotic therapy is the recommended treatment. In view of the lack of specific symptoms and the difficulty of diagnosis, it is believed that in Brazil the disease is more common, but underdiagnosed. According to Netto et al., (1964), milkers and keepers of cattle herds can be considered highly exposed to the risk of infection, due to the activities that they are responsible for milking, food management, corral cleaning, obstetrics or newborns management.

In 1953, a serological investigation carried out by Brandão et al., (1953) with employees of a slaughterhouse in São Paulo pointed to the presence of positive sera with low antibody titers and other positive sera with high titers. According to Siciliano et al., (2008) some pioneering seroprevalence studies carried out in the 60s and 70s revealed the presence of antibodies against *Coxiella burnetti* at relatively high rates, among potentially exposed individuals.

Knowing the deficit of epidemiological studies on the occurrence of the disease in Brazil, the present study aimed to carry out a survey of the serological evidence in humans, and, based on that, to characterize the reactive samples as to the location, time and demographic profile of the occurrence.

METHODS

In order to contribute to the knowledge about the occurrence of Q Fever in humans in Brazil, we analyzed the data included in the Laboratory Environment Manager (LEM) between the years 2011 to 2017. For this, we used official data from the biological materials registered in the LEM of the Ministry of Health (MH), nationwide. LEM is the information system used by the MH in Brazil for laboratory routines within the scope of Health Surveillance.

The analysis considered data on serology requests using the Indirect Immunofluorescence Reaction technique, performed in reference laboratories, accredited by the Ministry of Health. The detection of anti-Coxiella immunoglobulin G (IgG) antibodies was performed by a test by the manufacturer Scimedx / Medivax®, with titration cut-off values greater than 1/64.

From the information contained in these requests, a database was built on a Microsoft Excel spreadsheet (2013). Subsequently, the data were analyzed to characterize the reagent samples. Thus, thematic maps, graphs and tables were made in order to illustrate the location, date of occurrence and the demographic profile of the reagent samples. The variables used to characterize the location were: State, municipality and area of residence of the reactive individuals; to characterize the date of occurrence: year and month of the serological test request; to characterize the demographic profile: sex, age and race of individuals.

The results are presented in absolute numbers and relative frequencies. The study was carried out with secondary data, presented collectively and no nominal information or information that could identify each individual was accessed, thus not requiring the appreciation of the research ethics committee.

RESULTS

359 samples were submitted to laboratory analysis between the years 2011 to 2017. The serological tests were performed by the Indirect Immunofluorescence technique for Q Fever, the tests were requested by 0.48% (27 / 5,570) of the Brazilian municipalities. Among the samples, 80.77% (290/359) were non-reactive, 18.66% (67/359) were reactive and 0.55% (2/359) were inconclusive for the presence of antibodies against *Coxiella burnetti*.

The highest frequency of reagent samples was recorded in 2016 with 53.73% (36/67), followed by 2017 with 17.91% (12/67), 2013 with 14.92% (10/67), 2015 with 8, 95% (6/67), 2011 with 2.98% (2/67) and 2012 with 1.49% (1/67), as illustrated in Figure 1:

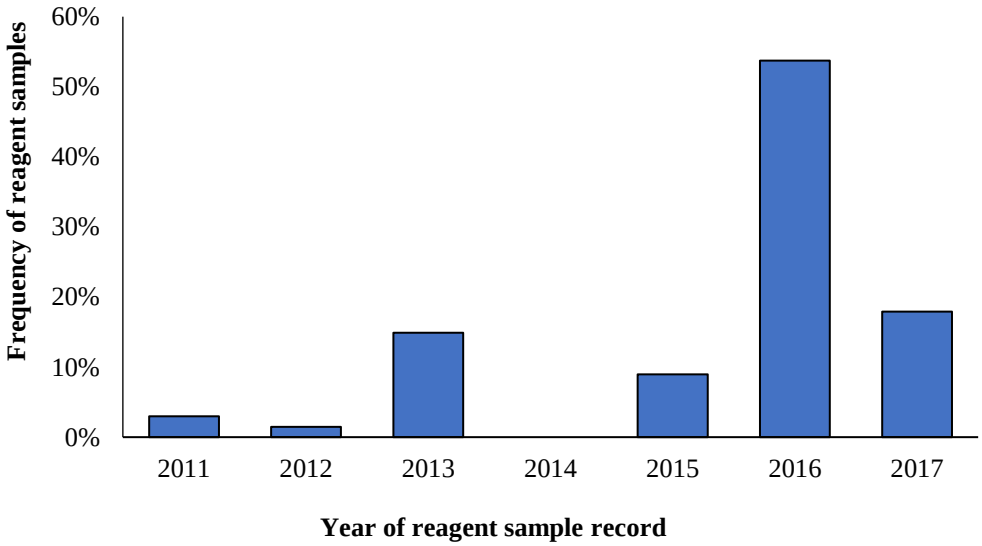

Figure 1- Distribution of reagent samples for Q Fever, per year, in Brazil, 2011-2017.

The monthly frequency, on the other hand, demonstrated that the months with the highest number of reagent samples were March and November, as illustrated in Figure 2:

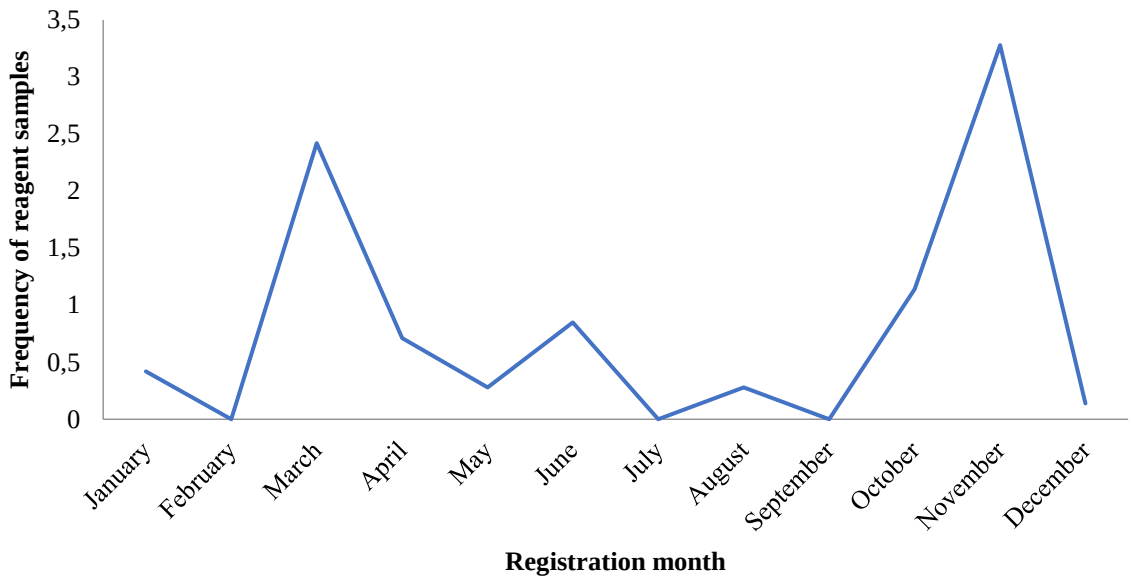

Figure 2- Distribution of the average of reagent samples for Q Fever, per month, in Brazil, 2011-2017.

Results by Federation Unit

Among the federation units that presented reagent samples, Rio de Janeiro had the highest prevalence, 72.62% (50/67), followed by Minas Gerais with 20.89% (14/67), Tocantins with 2.98% (2/67) and Paraná with 1.49% (1/67), as illustrated in Figure 3.

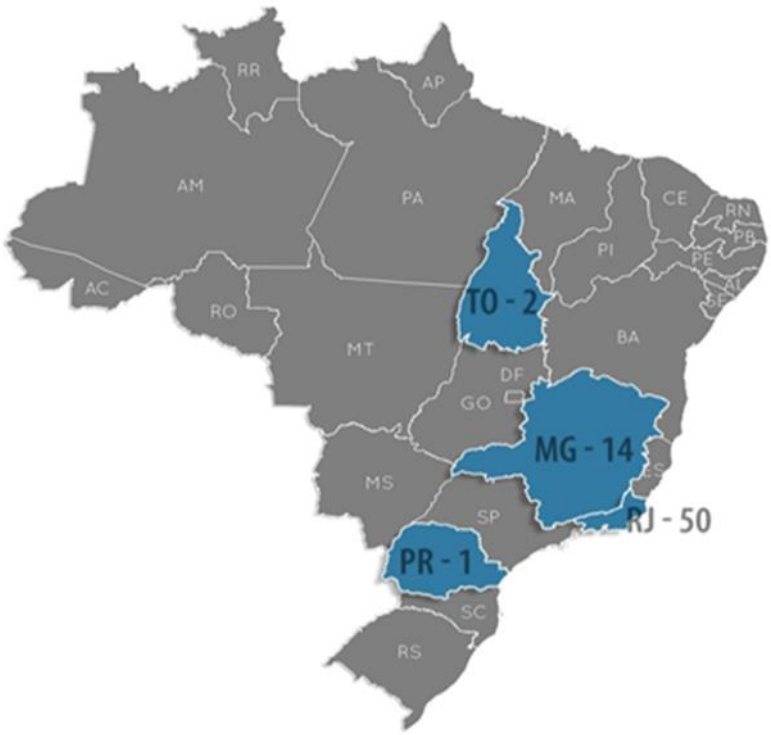

Figure 3-Distribution and number of reagent samples for Q Fever, by Federation Unit, Brazil, 2011-2017.TO: Tocantins; MG: Minas Gerais; RJ: Rio de Janeiro; PR: Paraná.

Rio de Janeiro

Regarding the patient's municipality of residence, it was observed that 64% (32/50) were from Rio de Janeiro, 16% (8/50) from Cachoeiras de Macacu, 8% (4/50) from Maricá, 6% (3/50) from Nova Iguaçu, 4% (2/50) from Itaperuna and 2% (1/50) from Macaé (Figure 4).

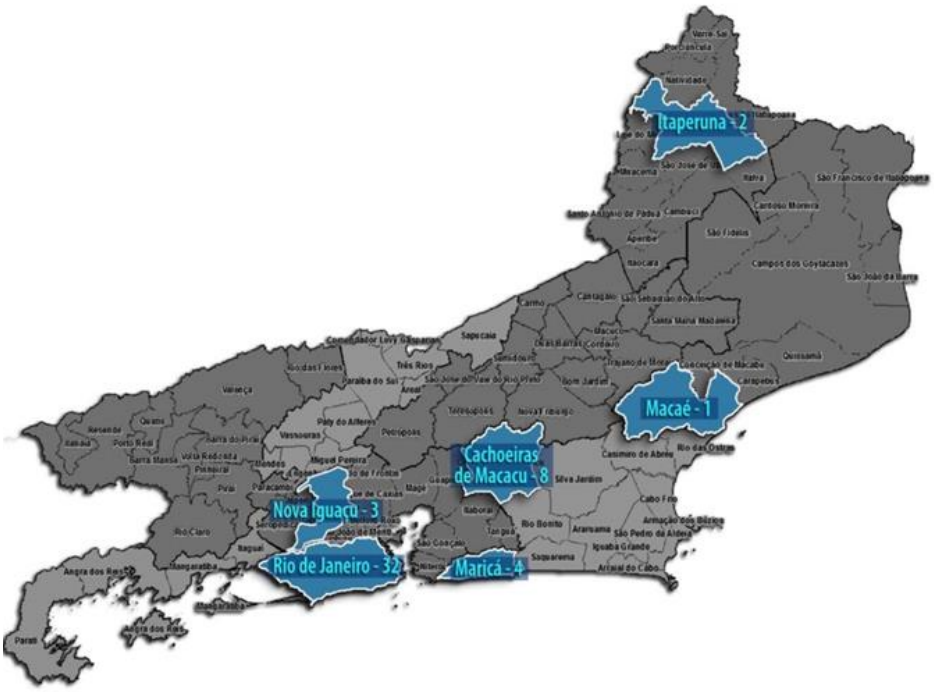

Figure 4 - Distribution and number of reagent samples for Q Fever, by municipality in the State of Rio de Janeiro, Brazil, 2011-2017.

Minas Gerais

In Minas Gerais, we observed that 50% (7/14) of the reagent samples were from Belo Horizonte, 42.85% (6/14) from Betim and 7.14% (1/14) from Caratinga (Figure 5).

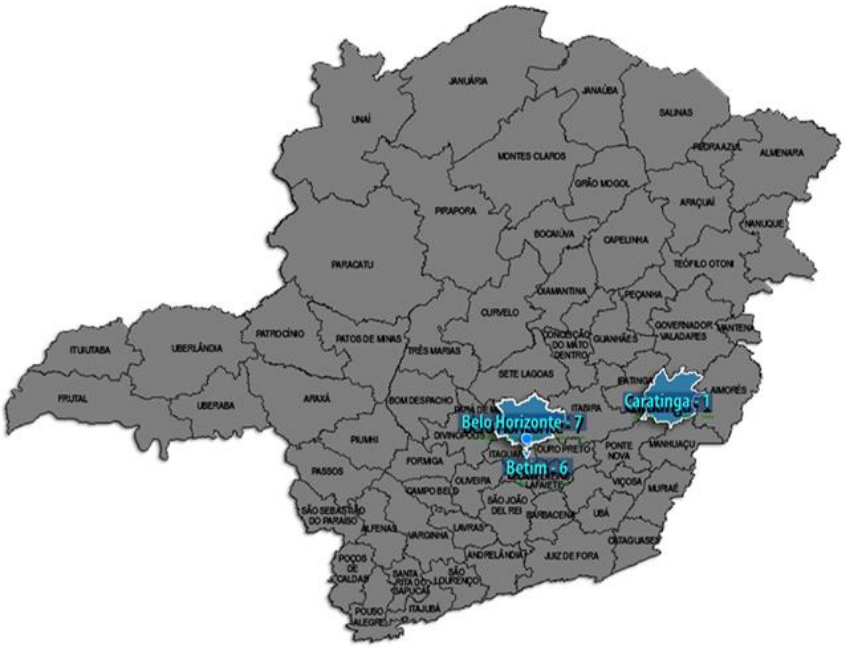

Figure 5 - Distribution and number of reagent samples for Q Fever, by municipality in the State of Minas Gerais, Brazil, 2011-2017.

Tocantins

In Tocantins we observed that 50% (1/2) of the reagent samples were from Palmas and 50% (1/2) were from Miracema do Tocantins. (Figure 6).

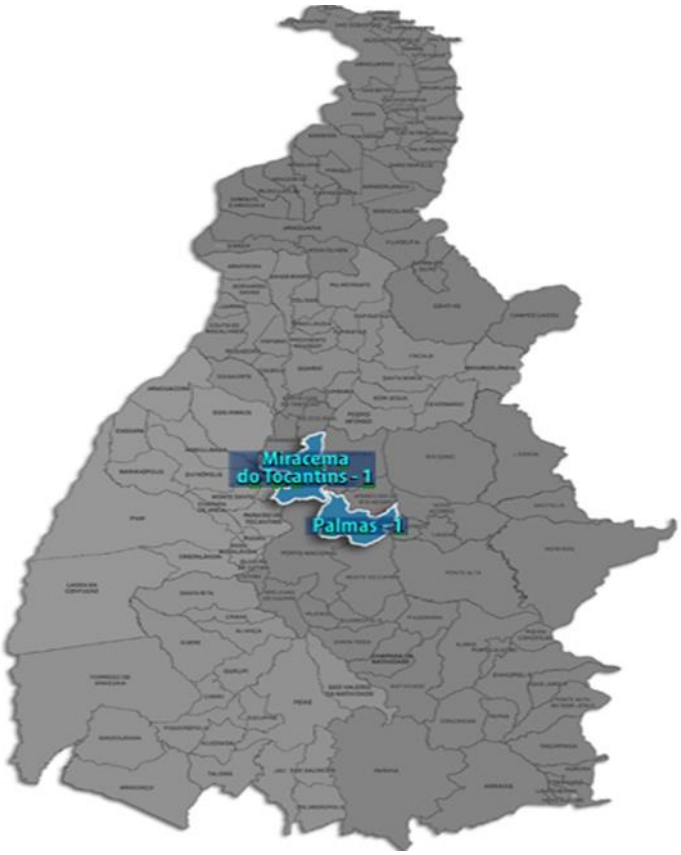

Figure 6 - Distribution and number of reagent samples for Q Fever, by municipality in the State of Tocantins, Brazil, 2011-2017.

Paraná

In Paraná we observed a reagent sample, from Curitiba. (Figure 7).

Figura 7 - Distribution and number of reagent samples for Q Fever, by municipality in the State of Paraná, Brazil, 2011-2017.

Demographic results

The distribution of the age groups of patients with reagent samples is shown in figure 8.

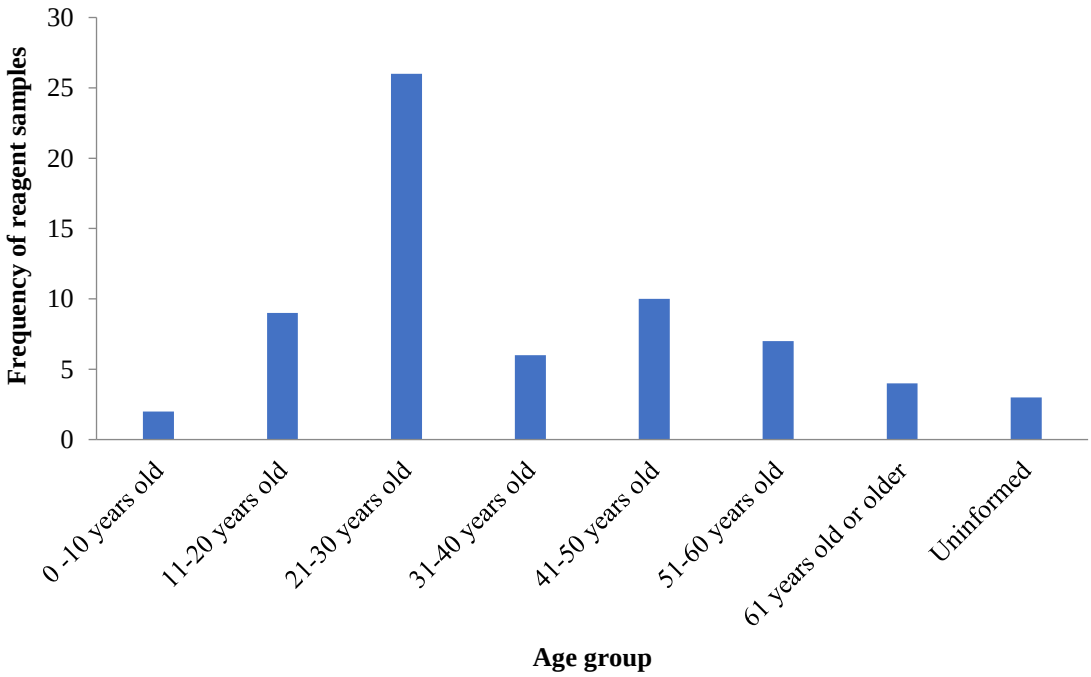

Figure 8 - Distribution of age groups of the reagent samples for Q Fever, Brazil, 2011-2017.

	0 - 10 years old	11 - 20 years old	21 - 30 years old	31 - 40 years old	41- 50 years old	51 - 60 years old	61 years old or older
Reagent Samples	2/67	9/67	26/67	6/67	10/67	7/67	4/67
Percentage	2.98%	13.43%	38.8%	8.95%	14.92%	10.44%	5.97%

With regard to sex of reagent samples, 83.58% (56/67) were male and 16.41% (11/67) female (Figure 9).

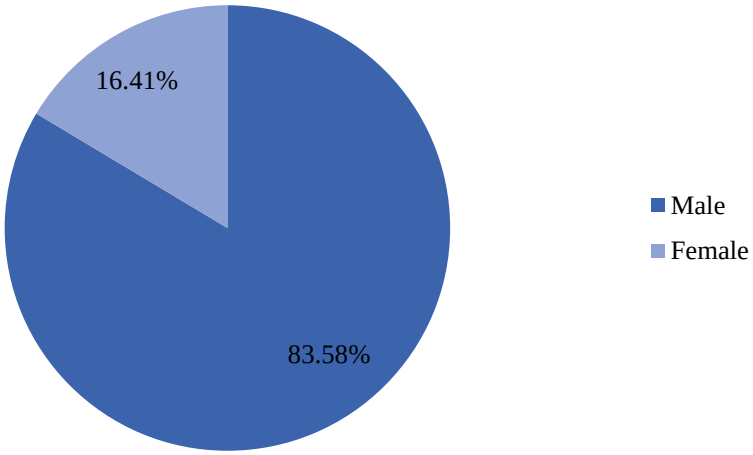

Figure 9- Distribution of reagent samples for Q Fever, by sex, Brazil, 2011-2017.

The race of the reactive samples were 22.38% (15/67) black, 16.41% (11/67) white, 10.44% (7/67) brown and 50.74% (34/67) not informed (Figure 10).

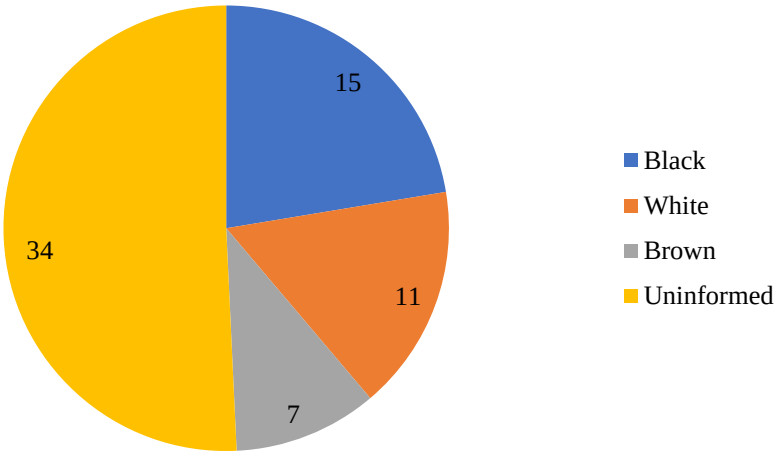

Figure 10- Distribution of reagent samples for Q fever by race in Brazil 2011-2017.

The area of residence of the reagent samples was reported as Urban 46.26% (31/67), Rural 11.94% (8/67) and not reported in 41.79% (28/67) (Figure 11).

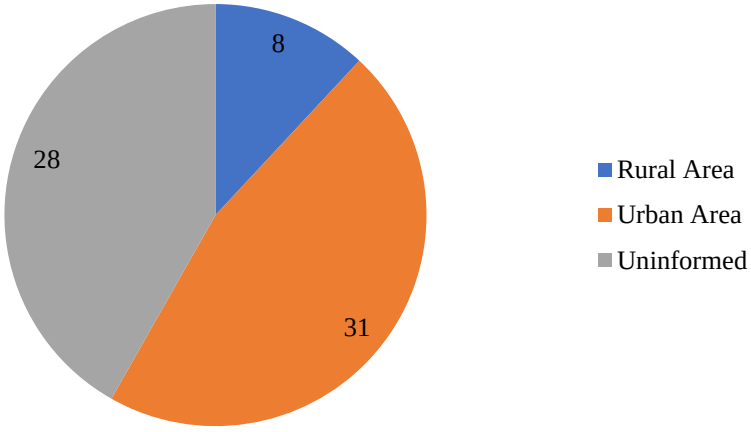

Figure 11- Distribution of reagent samples for Q fever by area of residence in Brazil 2011-2017.

DISCUSSION

The study showed that 18.66% (67/359) of serological tests requests made in Brazil were reagent, and that the states presenting positive serological evidence were Rio de Janeiro, Minas Gerais, Tocantins and Paraná. We observed that the disease is more common in adults in the economically active age group and that 83.58% (56/67) of the cases were in males,

which is a frequently reported finding, due to outdoor activities, whether they work and / or recreational and contact with animals are more associated with this sex.

Similar to the study by Costa et al., (2006), only a few patients in this study were children, thus showing the highest occurrence in adult individuals, given the greater frequency of outdoor activities, whether for work or leisure reasons.

The study demonstrated that the Q Fever reagent samples are from residents of the urban area in 46.26% of the cases. According to Costa et al., (2006) Q fever is no longer considered an exclusively rural zoonosis and urban outbreaks have been reported. He points out that a recent outbreak in French Guiana found an urban pattern of distribution of infection and the old idea of rural zoonosis was replaced by "everywhere zoonoses", given the multiple forms of transmission of *C. burnetti*, as an expected consequence of its powerful infectivity.

There are few reports of the disease in Brazil, and although the study shows the incidence of cases in different units of the federation, perhaps this is due to the fact that the notification of cases in animals or humans is not mandatory. Because the symptoms are not specific, although known, clinical diagnosis is difficult, and there is no protocol that defines guidelines for medical professionals and veterinarians on the clinical manifestations of the infection, diagnosis, treatment and actions to be taken.

According to Mares-Guia et al., (2016) Q fever is present in Brazil, but in some cases it can be misdiagnosed as other infectious diseases, especially dengue, a fact that has already been observed in the State of Rio de Janeiro.

The present study has some limitations, among them, the impossibility of using the variable "serology" that refers to the antibody titre value, due to a problem of configuration and export of the database, with consequent dubious information and low frequency of filling.Thus, it was decided to use only the information as reagent or non-reagent. Furthermore, the database of the Laboratory Environment Manager has as its main purpose and use, health planning and evaluation, and has few variables that can be used for epidemiological evaluations. This information system lacks clinical data that would be essential for the proper classification of the epidemiological characteristics of Q fever cases.

When analyzing the data, it was possible to perceive a bias that is related to the fact that the number of reagent samplesis probably associated with the greater investment in research, as is the fact of the state of Rio de Janeiro, where there is a Reference Laboratory for Q fever and where in this study concentrated the vast majority of the records presented.

We emphasize in this study the need to carry out investigative studies in the areas where the reagent samples were observed, in order to assess the magnitude of the disease, prioritizing the risk groups already established, seeking to better clarify the epidemiological cycle and thus be able to assist the services regarding early diagnosis, treatment and decision making.

FINAL CONSIDERATIONS

Based on the results obtained through this study, it was noticed that there is a wide range of serological evidence of the occurrence of Q Fever in Brazil and that there is a profile of cases represented mainly by males, in economically active age, residents of the urban areas.

Although Q Fever is a disease that can present itself in a serious way and involve several domestic animals as reservoirs, there is still a lack of knowledge about both the epidemiology and the forms of clinical presentation. In addition, we have an insufficient database, denoted by incomplete data and a reduced number of cases registered in information systems, such as the LEM, which makes it difficult to create public policies aimed at early detection and treatment of cases.

Thus, it is recommended that research lines and investments should be created, both in animal health and in human health, which would allow to improve the understanding of the magnitude of this important zoonosis in Brazil.

INTEREST CONFLICTS

The author declares no conflicts of interest with the topic presented.

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