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# THE MOST COMMON ANTHROPOZOONOSES IN THE REPUBLIC OF SRPSKA IN THE PERIOD 2015 – 2020

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## Abstract

Zoonotic diseases are increasingly becoming an emerging public health threat, partially due to the risk of spillover events at the human-wildlife interface. Their potential for infecting people with exotic pathogens originating from unusual pets should not be overlooked. The aim of the study is to present and analyze the trend of zoonoses in the 2015-2020 period using the descriptive method. The source of data is reports of single cases of infectious diseases, which is in accordance with the applicable legislation governing this area. The incidence of anthropozoonoses was the highest in 2017 amounting 16.5/100,000, while the lowest value in this five-year period was in 2020, with 1.1/100,000. The share of anthropozoonoses in the total incidence of infectious diseases was also the lowest in 2020, with the value of 0.02%, while the highest share of this group of diseases was recorded in 2017 with a value of 1.42%. In the specified period, the three most commonly reported anthropozoonoses are Q-febris, leptospirosis, and brucellosis. In 2020, the most frequently registered anthropozoonosis was toxoplasmosis, while in the previous 5 years, this disease was not reported among the three most common. It is necessary to raise awareness about the presence of zoonoses in the overall incidence of infectious diseases in the Republic of Srpska, because due to the common non-specific clinical picture, zoonoses are not the first to be considered in differential diagnosis. In the fight against zoonoses, a coordinated approach to "One Health" is necessary, which will enable design and implementation of programs, policies, legislation and research in the area of public health.

Key words: zoonosis, incidence, One Health, Republic of Srpska

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# NAJČEŠĆE ANTROPOZOONOZE U REPUBLICI SRPSKOJ U PERIODU 2015 - 2020

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#### Kratak sadržaj

Zoonotske bolesti sve više postaju nova prijetnja javnom zdravlju, djelomično zbog rizika od bliskog kontakta i narušavanja granice čovjeka i divljeg svijeta. Ne treba zanemariti ni mogućnost zaražavanja ljudi egzotičnim patogenima porijeklom od neobičnih kućnih ljubimaca. Cilj studije je prikazati i analizirati kretanje zoonoza u periodu 2015-2020. godine korišćenjem deskriptivnog metoda. Izvor podataka su pojedinačne prijave slučajeva zaraznih bolesti, što je u skladu sa važećom zakonskom regulativom koja uređuje ovu oblast. Incidencija antropozoonoza je najviša bila 2017. godine i iznosila je 16,5/100.000, dok je najniža vrijednost u ovom petogodišnjem periodu bila u 2020.godini i iznosila je 1,1/100.000. Učešće antropozoonoza u ukupnom obolijevanju od zaraznih bolesti najniže je bilo takođe u 2020. godini i iznosilo je 0,02%, dok je najveće učešće ove grupe oboljenja zabilježeno 2017.godine sa procentom učešća od 1,42%. U posmatranom periodu, tri najčešće prijavljivane antropozoonoze su Qfebris, leptospiroza i bruceloza. U 2020. godini je najčešće registrovana antropozoonoza bila toksoplazmoza, dok u prethodnih 5 godina ova bolest nije bila prijavljena ni u tri najčešće. Neophodno je podizanje svjesnosti o prisustvu zoonoza u ukupnom obolijevanju od zaraznih bolesti u Republici Srpskoj, jer zbog veoma često ne specifične kliničke slike, zoonoze nisu prve u razmatranju u diferencijalnoj dijagnostici. U borbi protiv zoonoza neophodan je koordinisan pristup strategiji "Jedno zdravlje" koji će omogućiti dizajniranje i primjenu programa, politika, zakonodavstva i istraživanja u javnom zdravlju.

Ključne riječi: zoonoze, incidencija, Jedno zdravlje, Republika Srpska

#### INTRODUCTION

Six in ten human cases of infectious disease arise from animal transmission (Center for Disease Control, 2018). Fifty years ago, following the wide-

scale manufacture and use of antibiotics and vaccines, it seemed that the battle against infections was being won for the human population. Since then, however, and in addition to increasing antimicrobial resistance among bacterial pathogens, there has been an increase in the emergence of zoonotic diseases originating from wildlife, sometimes causing fatal outbreaks of epidemic proportions. Zoonosis is defined as any infection naturally transmissible from vertebrate animals to humans. In addition, many of the newly discovered diseases have a zoonotic origin. Due to globalization and urbanization, some of these diseases have already spread all over the world, caused by the international flow of goods, people and animals. However, special attention should be paid to farm animals since, apart from the direct contact, humans consume their products, such as meat, eggs, and milk. Therefore, zoonoses such as salmonellosis, campylobacteriosis, tuberculosis, swine and avian influenza, Q fever, brucellosis, STEC infections, and listeriosis are crucial for both veterinary and human medicine. Consequently, in the suspicion of any zoonoses outbreak, the medical and veterinary services should closely cooperate to protect the public health (Libera et al., 2022). Zoonotic diseases, particularly those associated with livestock and poultry, are becoming an increasing threat for public health for various reasons. For example, the predictions suggest that the global human population will constantly increase and reach almost 10 billion by 2050. Consequently, it will result in a higher food demand (United Nations, 2019). One Health is an effective approach for the management of zoonotic disease in humans, animals and environments. Examples of the management of bacterial zoonoses in Europe and across the globe demonstrate that One Health approaches of international surveillance, information-sharing and appropriate intervention methods are required to successfully prevent and control disease outbreaks in both endemic and non-endemic regions. Additionally. One Health approach enables effective preparation and response to bioterrorism threats (Cross, 2018).

Diagnostics plays a key role in disease surveillance. Misdiagnosis results in inappropriate treatment, or missed opportunities to prevent further disease transmission. The zoonoses discussed in this paper often present as undifferentiated febrile illnesses, and so a detailed history is key to diagnosis. More common ailments with similar symptoms are initially suspected, and diagnosis may be missed altogether in self-limiting cases (Gunaratnam et al, 2014).

It is almost certain that large-scale zoonotic disease outbreaks will almost certainly continue to occur regularly in the future. Therefore, a better general understanding of the factors affecting variation in the severity of outbreaks is critical for well-being of the global community (Stephens et al, 2021). Endemic zoonoses continue to be relatively neglected, often with a lack of local and international realization of the extent to which they impact human health and well-being. This is partly due to the issues surrounding local capacity and knowledge and partly because, unlike emerging infectious diseases, they are not seen as a threat to people in the developed world. Both EIDs and endemic zoonoses, however, can be tackled using the One Health approach, which includes the identification and mitigation of human activities that lead to disease emergence and spread (Cunningham et al, 2017). In the fight against zoonoses, a coordinated approach to "One Health" is necessary, as it will enable the design and implementation of programs, policies, legislation and research in the field of public health.

The aim of the study is to present and analyze the trend in zoonoses during the 2015-2020 period using the descriptive method. The source of data is reports of single cases of infectious diseases, which is in accordance with the applicable legislation governing this area.

### MATERIAL AND METHODS

No ethical approval was obtained because this study did not involve laboratory animals. Only non-invasive procedures were used.

As part of epidemiological surveillance, an analysis of the data obtained from monitoring the trend of anthropozoonosis according to European Union (EU) case definitions was performed (European Commission, 2018). EU definitions have been part of the national legislation for years now, and they are regulated by law. Using the descriptive method, the data obtained from all 54 primary health centers, as well as 10 hospitals in Republic of Srpska, were analyzed. The data were obtained through the Notification of Infectious Diseases, which is an official and binding document for every doctor who registers and thus reports an infectious disease, which is regulated by regulations and law. The disease reports are sent from these institutions to the Public Health Institute of the Republic of Srpska which analyzes the data and generates official reports. The trend of anthropozoonoses in the mentioned period is described and the three most common anthropozoonoses for each year are determined. The case of each disease is classified as possible - probable - confirmed on the basis of the national case definition criteria. Using statistical analysis with statistical software SPSS 23, we compared the incidences of these diseases, while patient demographics were analyzed and statistically processed using chi-squared ( $\chi^2$ ) test. This test was used to determine whether there is a statistically significant difference between the observed frequencies of the three

diseases in the observed groups and the frequencies of the same groups in the general population.

#### RESULTS

The incidence of anthropozoonoses was the highest in 2017 with 16.5/100,000, while the lowest value in this six-year period was in 2020, amounting to 1.1/100,000 (Figure 1).

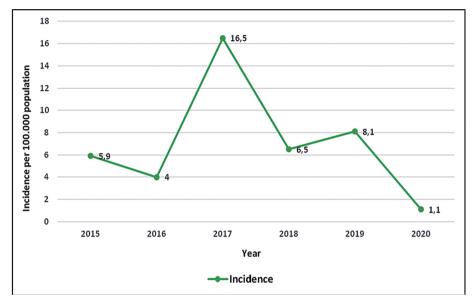


Figure 1. Incidence of anthropozoonosis per 100,000 in the Republic of Srpska 2015-2020

The share of anthropozoonoses in the total incidence of infectious diseases was also the lowest in 2020 and amounted to 0.02%, while the highest share of this group of diseases was recorded in 2017 with a value of 1.42%. In the specified period, the three most commonly reported anthropozoonoses were Q-febris, leptospirosis, and brucellosis.

The analysis of the collected data from epidemiological surveillance in the mentioned period, showed that there was a total of 283 cases of these three diseases, and the incidence trend shows that the incidence was the highest in 2017, high in 2016, 2018 and 2019, while in 2020 the incidence was very low (Table 1).

Year	Total No. of zoono- sis	Brucellosis		Leptospirosis		Q-febris	
		% share in all reported zoonosis	Incidence	% share in all reported zoonosis	Incidence	% share in all reported zoonosis	Inci- dence
2015	83	14.45	1.03	15.66	1.12	10.84	0.77
2016	56	16.07	0.78	14.28	0.69	57.14	2.76
2017	191	6.8	1.13	16.75	2.78	14.65	2.43
2018	75	45.33	2.96	6.66	0.44	21.33	1.39
2019	93	9.67	0.79	25.8	2.10	30.1	2.45
2020	12	50	0.53	33.3	0.35	8.33	0.09

Table 1. Number of reported zoonoses, the percentage and incidence of the 3 most common zoonosis by year

If we separate the incidence for each of these three diseases individually, we come to the following information: a total of 83 cases of brucellosis were reported in that period, and the incidence trend shows that the incidence of brucellosis was the highest in 2018 (2.96% 000), and significantly lower in other seasons. In the observed period, a total of 86 cases of leptospirosis were reported, and the incidence trend was the highest in 2017, with the incidence of 2.78% 000, high in the 2019 season with the incidence of 2.1% 000 and significantly lower in other seasons. 114 cases of Q-fever were reported in the same period, with the incidence trend that was highest in the 2016 season and an incidence of 2.76% 000, high in the 2017 (2.43% 000) and 2019 seasons (2.45% 000) and significantly lower in other seasons (Figure 2).

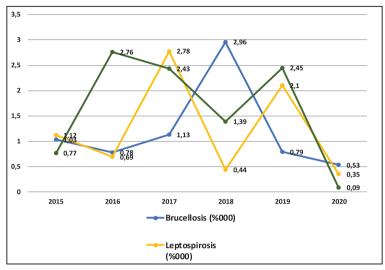


Figure 2. Incidence of Brucellosis, Leptospirosis and Q-Febris in the Republic of Srpska 2015-2020

Based on the results of the  $\chi \wedge 2$  test ( $\chi \wedge 2 = 56.993$ ; p = 0.000), it can be concluded that there was a statistically significant difference in the total number of patients of all three diseases by sex. Statistically significant (*p* =0.000, < 0.05) there was a higher number of male patients than the number of female patients, compared to the number of men and women in general population observed for all three diseases together as well as for each of the diseases individually (Figure 3).

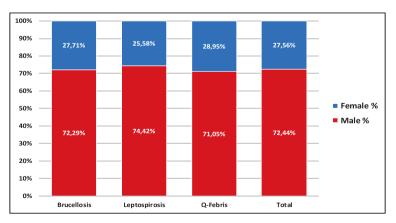


Figure 3. Sex distribution (%) of Brucellosis, Leptospirosis and Q-febris cases in the Republic of Srpska 2015-2020

The data obtained from epidemiological population surveillance from 2015 to 2020 in the Republic of Srpska show that out of a total of 283 patients with brucellosis, leptospirosis and Q-fever, 155 or 54.77% live in urban areas and 128 or 45.23% in rural areas. However, statistical analysis of data for each of the diseases separately reveals that there are significant differences in this regard between these three diseases. Namely, the results of the  $\chi \wedge 2$  test for brucellosis ( $\chi \wedge 2 = 1.157$ ; p = 0.282) and leptospirosis ( $\chi \wedge 2 = 2.110$ ; p = 0.146) show that there was no statistically significant difference in the number of patients according to the type of settlement in which they lived, while in patients with Q fever ( $\chi \wedge 2 = 33,778$ ; p = 0,000) this statistical difference is significant, as indicated by the relatively high value of the  $\chi \wedge 2$  test and the high probability (p = 0.000, <0.05) for the accuracy of that statistical difference (Figure 4).

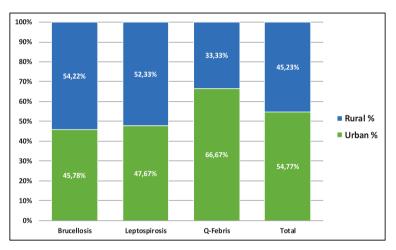


Figure 4. Urban/rural cases distribution of Brucellosis, Leptospirosis and Q-febris in the Republic of Srpska 2015-2020

The average age of patients with brucellosis, leptospirosis and Q-fever in the Republic of Srpska from 2015 to 2020 was  $48.34 (\pm 16.96)$  years. The largest number of patients at the time of illness in the total number and individually in relation to each disease belonged to the age group of 50 - 64 year (34.98%), followed by groups of 30 - 49 years (30.74%), 65 - 79 years (16, 61%) and the 20 - 29 age group (11.31%). These data show that the working age group of population aged 20 to 64 suffered the most (77.03%) (Figure 5).

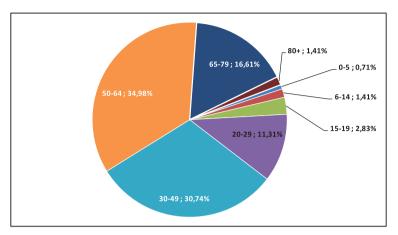


Figure 5. Age distribution of Brucellosis, Leptospirosis and Q-febris cases in the Republic of Srpska 2015-2020

The analysis of the regional distribution of patients by each of the three diseases, and in total, we come to the result that the largest number of reported cases was registered in the Banja Luka region, and lowest in the Trebinje region. When it comes to the reports on the outbreaks of these three infectious diseases in the given period, one epidemic of Q fever was reported in 2016 in Banja Luka, where 30 patients were registered and that correlates with the trend.

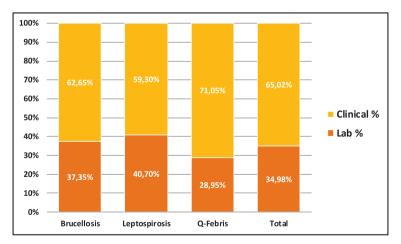


Figure 6. Brucellosis, Leptospirosis and Q-febris cases confirmation in the Republic of Srpska 2015-2020

According to data from population surveillance, the diagnosis of brucellosis, leptospirosis and Q-fever was clinically established in 184 cases (65.02%) (probable cases), which is significantly more than 99 cases (34.98%) in which the diagnosis was confirmed in the laboratory (confirmed cases). There is a similar relationship in terms of the method of establishing the diagnosis for each of the three diseases, with the number and share of clinically made diagnoses (probable cases) being highest in patients with Q fever (81 cases and 71.05%) while there were 33 confirmed cases (28.95%). The number and share of laboratory confirmed cases is the highest in patients with leptospirosis (35 cases and 40.7%), while there were 51 probable cases (59.3%). The number and share of probable cases of brucellosis was 52 (62.65%), while there were 31 confirmed cases (37.35%) (Figure 6).

#### DISCUSSION

Communicable disease epidemiology is closely linked to pathogen ecology, environmental and social determinants, economic factors, access to care, as well as the state of country development (McMichael, 2012). Climate change continues to have both direct and indirect effects on communicable diseases, often in combination with other drivers, such as increased global travel and trade. The frequency, duration, and intensity of heat waves has increased across Europe, and the last decade was the warmest ever recorded (World Meteorological Organization, 2013).

A global, integrated zoonotic disease surveillance system needs to detect disease emergence in human or animal populations anywhere in the world at the earliest time possible. An effective global, integrated zoonotic disease surveillance system requires effective surveillance at national, regional, and international levels, because information from outbreak investigations is used by human and animal health officials at all levels to implement response measures and evaluate the effectiveness of those responses.

Emerging zoonotic diseases can occur any time in any part of the world. Therefore, it is difficult to predict which pathogens may emerge, which human and or animal populations it may affect, or how these pathogens may spread. From a growing number of experiences, the world has learned that it is crucial to detect and report emerging zoonotic disease outbreaks that occur in a single country or region. Early detection and reporting at the local level give the international community an opportunity to assist national authorities and implement effective response measures (Keusch et al, 2009).

Q fever is a severe, zoonotic disease spread worldwide and caused by Cox-

*iella burnetii*. This disease was first described by Derrick in 1937 following an epidemic fever outbreak among employees at a slaughterhouse in Brisbane, Australia (Derrick, 1937). Q fever can manifest as an acute disease, usually as a self-limited febrile illness, pneumonia, or hepatitis. It may also occur as a persistent focalized infection with endocarditis. The main reservoirs of *C. burnetii* are cattle, sheep, and goats, but infections were detected in other animals such as domestic mammals, marine mammals, reptiles, birds, and ticks (Eldin et al, 2017). *C. burnetii* is most abundant in aborted fetuses, amniotic fluid and placenta after stillbirth or normal birth of offspring from infected mothers, and in the urine, feces and milk of infected animals. Transmission to humans most commonly occurs through inhalation of aerosolized bacteria from the placenta (delivery or abortion), feces, or urine of infected animals. Human-to-human transmission is extremely rare. In humans, the diagnosis of Q fever is mainly established by serology, microbiological cultures, or PCR tests (Pechstein et al, 2018; España et al, 2020).

Brucellosis is caused by the intracellular pathogens from *Brucella* genus. Four *Brucella* species can infect humans: *B. abortus, B. canis, B. melitensis*, and *B. suis*. Brucellosis may be transmitted to humans through contaminated food and dairy products, by occupational contact, or inhalation of infected aerosols. Another important route of infection is the contamination of mucous membranes or open wounds with fetal fluids, making veterinarians, farmers, and abattoir workers the most susceptible to infection. In other cases, transmission from animals to humans is mainly associated with drinking contaminated milk (Amjadi et al, 2019).

Leptospirosis is a widespread bacterial zoonosis occurring most commonly in low-income populations living in tropical and subtropical regions, both in urban and in rural environments. Rodents are known as the main reservoir animals, but other mammals may also significantly contribute to human infections in some settings. Clinical presentation of leptospirosis is nonspecific and variable, and most of the early signs and symptoms point to the so-called 'acute fever of unknown origin' (Goarant, 2016; Adler et al, 2009).

The implementation of the case definition is significant because all reported cases need to be categorized in the same way in accordance with international regulations (Nichols et al, 2014). The introduction of a case definition facilitated the early recognition of these diseases as well as the appropriate direction in their diagnosis and confirmation. This also enables the evaluation of surveillance system through the analysis of the report of each individual case (Mohamed et al, 2019; Katelaris et al, 2019; Debeljak et al, 2018; Boden et al, 2014). Standards for good laboratory practices overlap with standards for good laboratory network operations. Good laboratory practice principles are simply applied to laboratory facilities that meet proper standards for testing, safety, and security; employ a trained and proficiency-tested staff; have standard-ized operating procedures, validated test protocols, and properly functioning equipment; and use a communication system that relies on common platforms and accurately and reliably reports test results in a timely manner.

The Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (WOAH - ex OIE), and the World Health Organization (WHO) recognize a joint responsibility to minimize the health, social and economic impact of diseases arising at the human-animal interface by preventing, detecting, controlling, eliminating or reducing disease risks to humans originating directly or indirectly from domestic or wild animals, and their environments. An important aspect of efforts to mitigate potential health threats at the human-animal ecosystems interface is early warning, supported by robust risk assessment to inform decisions, actions, and timely communication between agencies and sectors responsible for human health, animal health, wildlife, and food safety. In 2006, in response to health threats such as H5N1 highly pathogenic avian influenza (HPAI) and the severe acute respiratory syndrome (SARS), the three organizations consolidated their efforts to establish a Global Early Warning System for Major Animal Diseases Including Zoonosis (GLEWS). GLEWS became one of the mechanisms used by the WOAH, FAO, and WHO together for monitoring data from existing event-based surveillance systems and track and verify relevant animal and zoonotic events (FAO-WOAH-WHO, 2010).

Based on the results of the study, it can be seen that the incidence of these diseases was the lowest in 2020. The cause of this drastic decline is largely the outbreak of the COVID 19 pandemic and the fact that it cast a shadow on other diseases due to the enormous burden it imposed on the health system. Pandemic certainly did not change the course of these diseases, but it did make their reporting, adequate diagnosis and anti-epidemic action very difficult. But despite the epidemic, doctors who are the first to receive and treat patients do not consider zoonoses as the first option in differential diagnosis, especially because most of them do not have specific symptoms at the beginning of the disease, and in the most severe clinical phase fever, malaise, headache, muscle aches, pneumonia or even meningitis are the symptoms of many other non-zoonotic diseases. Our doctors were somewhat more cautious about zoonoses in the first few years after the catastrophic floods that hit this region in 2014, but that has changed over time due to the impact of several factors.

In the observed period, out of the three most reported diseases, namely brucellosis, leptospirosis and Q fever, the largest number of reported cases were Q fever cases, with the highest incidence in 2016. The reason for this is the registered outbreak of this disease in the area of Banja Luka. Furthermore, a significantly higher number of people with disease fell ill in urban areas than in rural areas. These data may lead to the conclusion that contact of the urban population with the villages through excursions, hiking, visits to rural families and many other activities that bring this population into contact with the rural area, allows immunologically incompetent population contact with *Coxiella* spores. The fact is close contact with the reservoir animals of this disease is not necessary- it is enough to breathe air with spores that carry this causative agent. Thus, in the area of the city of Banja Luka, there were several outbreaks of this disease in the period before 2010.

A statistically significantly higher number of men contracted these three diseases than women, which traditionally described these zoonoses as "male diseases", mostly because men are more likely to engage in livestock, agriculture and other activities in the nature and with animals.

In terms of age groups, the largest number of patients falls in the range of 20-64 year olds, which leads us to the conclusion that these diseases affected the working population the most, namely those who come into contact with animals and their products through agriculture, livestock, etc.

Based on the results of the analysis, the largest number of patients was registered in the region of Banja Luka, which is also the most populated area in the Republic of Srpska. Hospital and diagnostic capacities are the largest in this region, so the increased reporting of these diseases can be related to that fact.

A significantly higher percentage of reported cases of brucellosis, leptospirosis and Q fever was reported based on clinical criteria. This is certainly something that makes a weak point of the system of control over anthropozoonoses and represents a link that requires significant improvements. Adequate and precise diagnostics are necessary to confirm the case of any infectious disease, which makes the system of supervision and control of these diseases stronger and more reliable. Another weakness of the system is the absence of a unique electronic system for reporting of infectious diseases- health institutions are not connected into IT network which would obtain a flow of information on reports of infectious diseases, outbreaks and all other data that is necessary to analyze the situation or other unexpected health events. For this reason, it is impossible to get all the information about each patient, because most of the reporting and data sharing is paper based or via e-mail at our request. That is why establishing a network of health institutions with the Public Health Insti-

tute of the Republic of Srpska would be one of the main factors of the improvement and strengthening of the infectious disease surveillance system.

## CONCLUSIONS

The incidence of anthropozoonoses in the Republic of Srpska in the 2015-2020 period was highest in 2017, and the lowest in 2020. The three most commonly reported diseases were brucellosis, leptospirosis, and Q fever. The reported cases of these three diseases were more common among urban population, the patients being mostly male and a majority of them belonged to the working population. The largest number of cases has been reported as probable without microbiological confirmation, which is stated in the case definition for each disease. It is necessary to improve the reporting of zoonoses in the Republic of Srpska in terms of case confirmation, as well as raising awareness of the frequency and importance of anthropozoonoses of all physicians, especially those who first treat patients.

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## Author's Contribution:

NRV – drafted the manuscript and made substantial contributions to the basic idea, JA – made contributions to the basic idea, JĐD - revised the manuscript critically.

## **Competing interest**

The authors declare that they have no competing interests.

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