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EPIDEMIOLOGICAL CHARACTERISTICS OF Q FEVER IN THE SREM DISTRICT OF VOJVODINA, FROM 2011 TO 2020

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Abstract

Q fever is a globally widespread zoonosis, which has a large number of animal reservoirs. In humans, Q fever is asymptomatic in 60% of cases but may appear in the form of acute or chronic disease. The disease is mostly asymptomatic in animals but may be a cause of abortions or stillbirths. The aim of this study was to present and analyze the epidemiological characteristics of Q fever in Srem district, in the Autonomous Province of Vojvodina, Republic of Serbia. We conducted a descriptive study using data from the registries of infectious diseases of the Institutes of Public Health of Vojvodina and Institute of Public Health Sremska Mitrovica in the period 2011-2020. A total of 76 human cases of Q fever were registered in Srem district over ten-year period. The majority of patients (89.47%; N = 68) were regis-

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tered in municipalities of Sremska Mitrovica and Šid. One third of patients were hospitalized (32.89%; N = 25). Males were 3.2 times more affected than females (M : F = 3.22 : 1). Working age population (20–59 years) were most affected (82.89%; N = 63) with a significantly higher incidence compared to the age category 0-19 years ($p < 0.05$). The majority of cases were registered in February (60.53%; N = 46). Probable routes of transmission of *Coxiella burnetii* were: direct contact with animals and the airborne route of transmission (50.00% vs. 47.37%). The highest seroprevalence of Q fever recorded in goats (55.54%) and sheep (11.88%) in the municipality of Šid, which is connected to outbreak in Kukujevcu 2017. The high seroprevalence in goats, recorded in Indija (22.87%) was not accompanied by Q fever in humans. Q fever still represents a significant problem of both veterinary and human medicine and therefore continuous disease monitoring and more efficient cooperation of the veterinary and human health care sectors is necessary.

Key words: Q fever, zoonosis, disease outbreaks, epidemiology, incidence, Srem

EPIDEMIOLOŠKE KARAKTERISTIKE Q GROZNICE U SREMSKOM OKRUGU, U VOJVODINI, U PERIODU OD 2011-2020. GODINE

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Kratak sadržaj

Q groznica je globalno rasprostranjena zoonoza, koja ima veliki broj rezervoara među životinjama. Kod ljudi, Q groznica je asimptomatska u 60% slučajeva, ali se može javiti u formi akutne ili hronične bolesti. Bolest je uglavnom asimptomatska kod životinja, ali može biti značajan uzrok pobačaja i mrtvorodenosti. Cilj ovog istraživanja bio je da prikaže i analizira epidemiološke karakteristike Q groznice u Sremskom okrugu, u Autonomnoj Pokrajini Vojvodini, Republika Srbija. Sproveli smo deskriptivnu studiju koristeći podatke iz registara zaraznih bolesti Instituta za javno zdravlje Vojvodine i Zavoda za javno zdravlje Sremska Mitrovica u periodu 2011-2020. godine. Ukupno 76 humanih slučajeva Q groznice je registrovano u Sremskom okrugu tokom desetogodišnjeg perioda. Većina obolelih (89,47%; N = 68) registrovana je na teritoriji opština Sremska Mitrovica i Šid. Trećina pacijenata je bila hospitalizovana (32,89%; N = 25). Muškarci su 3,2 puta češće obolevali u odnosu na žene (M : Ž = 3,22 : 1). Radno sposobno stanovništvo (20-59) je bilo najviše pogođeno (82,89%; N = 63) sa značajno višom incidencijom u poređenju sa starosnom grupom 0-19 godina ($p < 0,05$). Većina slučajeva registrovana je u februaru (60,53%; N = 46). Verovatni putevi prenosa *Coxiella burnetii* su bili: direktni kontakt sa životinjama i aerogeni put prenosa (50,00% prema 47,37%). Najviša seroprevalencija Q groznice zabeležena je kod koza (55,54%) i ovaca (11,88%) u opštini Šid, što je bilo povezano sa epidemijom u Kukujevima 2017. godine. Visoka seroprevalencija kod koza, zabeležena u Indiji (22,87%), nije bila praćena Q groznicom kod ljudi. Q groznica u Sremskom okrugu i dalje predstavlja značajan problem humane i veterinarske medicine zbog čega je neophodan kontinuirani nadzor i još efektivnija saradnja veterinarskog i sektora zdravstvene zaštite ljudi.

Ključne reči: Q groznica, zoonoza, epidemije, epidemiologija, inciden-cija, Srem.

INTRODUCTION

Q fever is a globally widespread zoonosis caused by the small obligate intracellular gram-negative bacterium *Coxiella burnetii* (*C. burnetii*) (Angelakis and Raoult, 2010). The large number of reservoirs, the possibility of transmission by different routes, the resistance of the microorganism and the small infectious dose place *C. burnetii* in category B on the list of agents suitable

for biological weapons (Parker et al., 2006). Among the many reservoirs, for humans the most important are ruminants: goats, sheep and cattle. Infected animals shed pathogens via body fluids. Q fever is mostly asymptomatic in animals, but it causes abortions and stillbirths (Fournier et al., 1998).

The most common route of transmission of *C. burnetii* to humans is by inhalation of contaminated dust or aerosols from infected feces, urine and birth products (Reimer, 1993; CDC, 2019), thus Q fever is an occupational hazard. Q fever is less commonly transmitted through the consumption of raw milk and unpasteurized dairy products, blood transfusions, from a pregnant woman to her fetus, or through sexual contact (Fournier et al., 1998; Maurin and Raoult, 1999; Milazzo et al., 2001). In humans, Q fever is asymptomatic in 60% of cases and in the rest of symptomatic cases, it may occur in the form of acute or chronic disease (Ristić et al., 2018). Due to asymptomatic course, Q fever is often an unrecognized and under-registered disease.

In aim to better understand the reasons for the endemic maintenance of Q fever, we analyzed the epidemiological characteristics of Q fever in Srem district, in the Autonomous Province of Vojvodina (APV), Republic of Serbia, for ten consecutive years (from 2011 to 2020).

MATERIAL AND METHODS

Study area and data collection

The study was conducted in Srem district, located in its southwestern part of the APV, with a population of 312,278 inhabitants according to the latest population census (SORS, 2011). The source of data was the database from the registries of infectious diseases of the Institute of Public Health of Vojvodina and the Institute of Public Health of Sremska Mitrovica responsible for the surveillance on communicable diseases. The data of Q fever in humans included individual case reports, epidemiological studies, epidemiological questionnaires, reports on laboratory tests, reports of outbreaks and annual reports for the observed ten-year period (2011-2020). According to the European Center for Disease Prevention and Control (ECDC) case definition, we classified Q fever cases as probable and confirmed cases (ECDC, 2018).

Laboratory confirmation of human Q fever

Laboratory diagnosis of human Q fever from sera samples was confirmed by the enzyme-linked immunosorbent assay (ELISA) at the Serbian Reference Laboratory for Q fever, the Institute of Public Health of Zrenjanin. A specific

antibody response to *C. burnetti* (IgM and/or IgG to phase II antigen) was used as a laboratory criteria for the confirmation of Q fever. Paired serum samples tested at least two weeks apart were taken for patients whose first serum test results were equivocal or negative.

Veterinary data and laboratory confirmation of animal Q fever

Data on Q fever laboratory confirmation of animals in Srem district were obtained from the Scientific Institute of Veterinary Medicine, Novi Sad. Samples of goats, sheep and cattle were tested under the auspices of mandatory annual monitoring. By order of the Republic Veterinary Inspection, the Veterinary Scientific Institute, Novi Sad conducted epizootiological investigation in the households with livestock in the case of Q fever in humans. In the case of reports of abortions in domestic animals, serological analysis was performed and in case of positive findings, again, an epizootiological investigation in the household was conducted. The ELISA method was used for the analysis of blood samples (detection of IgM/IgG antibodies against *C. burnetti*) of goats, cattle and sheep (OIE, 2021). Data about results of molecular analysis and data about seroprevalence of Q fever in specific years (2011, 2012 and 2013) are lacking and are not presented.

Data analysis and statistics

Descriptive method was applied. The data were analyzed chronologically, demographically, and topographically for the observed period. We used the basic statistical indicators, general and specific incidence rates. Statistical data processing included descriptive analysis (mean, minimum and maximum, as well as standard deviation). The Mann-Whitney U test was applied to test the differences of Q fever incidence between two of each age group (0 - 19, 20 - 59, ≥ 60 years). For all data analyses the SPSS software, version 21.0 was used and p -value < 0.05 was considered statistically significant. For mapping, we used the program Quantum GIS (QGIS) version 3.4.

RESULTS

A total of 76 cases of Q fever were registered in the period 2011 - 2020, in Srem district. Of the total number of cases, 92.11% ($N = 70$) were laboratory confirmed and 7.89% ($N = 6$) were classified as probable cases. Males were 3.2 times more affected compared to females ($M : F = 3.22 : 1$). The highest incidence rates of Q fever were reached in 2012 (14.41/100,000; $N = 45$) and in

2017 (7.04/100,000; N = 22) (Figure 1). There were no registered cases of Q fever during the four years (2016, 2018, 2019, and 2020) of this observed period.

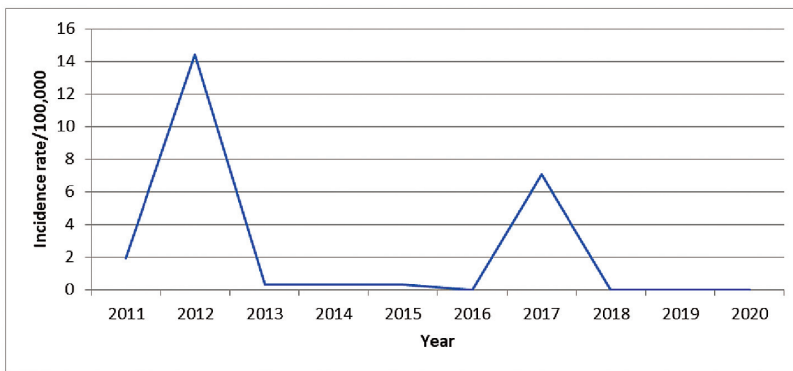


Figure 1. Incidence rate of Q fever in Srem district, in the period 2011 – 2020

Cases of Q fever were registered in all age categories, except in children aged < 10 years. The mean age (\pm standard deviation) of patients was 39.51 ± 14.17 years. The youngest patient was 14, and the oldest was 75 years old. Age-specific incidence of Q fever during the observed ten-year period is shown in Figure 2. The highest age-specific incidence rates were recorded in 2012, in the age groups 20 - 29, 30 - 39 and 40 - 49 (32.17/100,000; 28.76/100,000; 18.38/100,000 respectively) and in 2017, in the age groups 30-39, 40-49 and 50-59 (16.78/100,000; 16.08/100,000; 7.82/100,000; respectively).

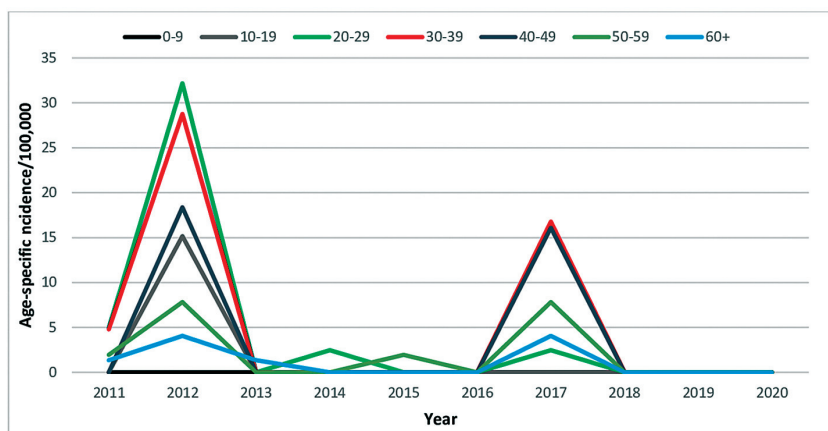


Figure 2. Specific incidence rate of Q fever cases by age in Srem district, in the period 2011 – 2020

The majority of patients (82.89%; N = 63) belonged to the working-age population (aged 20 – 59 years). Age specific incidence (mean, minimum and maximum, as well as standard deviation) are shown in Table 1.

Table 1. Analysis of the age-specific incidence of Q fever in Srem district, in the period 2011 – 2020

Age group (years)	Population ¹	Mean incidence ²	SD ³	Minimum incidence	Maximum incidence ²
0 - 19	61,541	0.76	3.39	0	15.16
20 - 59	176,795	3.66	7.83	0	32.17
≥ 60	73,942	1.08	1.66	0	4.06

¹ according to the latest Census (SORS, 2011)

² per 100,000 population

³ standard deviation

Based on the Q fever data in Srem district during the ten-year period (2011 - 2020), a statistically significantly higher incidence of Q fever was observed in the age category of the working-age population (aged 20 - 59 years) compared to the age category from 0 - 19 years (U = 291.5; p = 0.022) (Table 2).

Table 2. Comparison of Q fever incidence rates by age groups in Srem district, in the period 2011 - 2020

Age group (year)	Mean incidence ¹	Mean Rank	Mann-Whitney U test	p-value
0 - 19	0.76	25.08	291.5	0.022
20 - 59	3.66	33.21		
20 - 59	3.66	25.58	197	0.931
≥ 60	1.08	25.20		
0 - 19	0.76	14.33	86	0.237
≥ 60	1.08	17.85		

¹ per 100,000 population

Regarding the seasonal distribution, the majority of confirmed cases were registered in the period from January to May (96.05%; N = 73). The highest percentage of cases (60.53%; N = 46) was detected in February, and then equally in the months of April and May (13.16%; N = 10) (Figure 3).

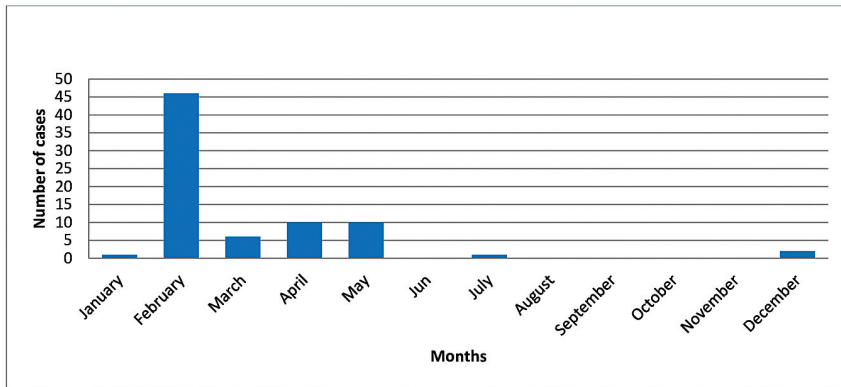


Figure 3. Seasonal distribution of Q fever in Srem district, in the period 2011 – 2020

Most patients (89.47%; N = 68) were registered in the western part of Srem district, in the municipalities of Šid and Sremska Mitrovica (incidence rates 64.35/100,000 and 57.54/100,000; respectively) (Figure 4). The lowest incidence rate (1.52/100,000) was registered in the municipality of Stara Pazova. Cases of Q fever were registered in six out of seven municipalities of the district with the exception of the municipality Indija.

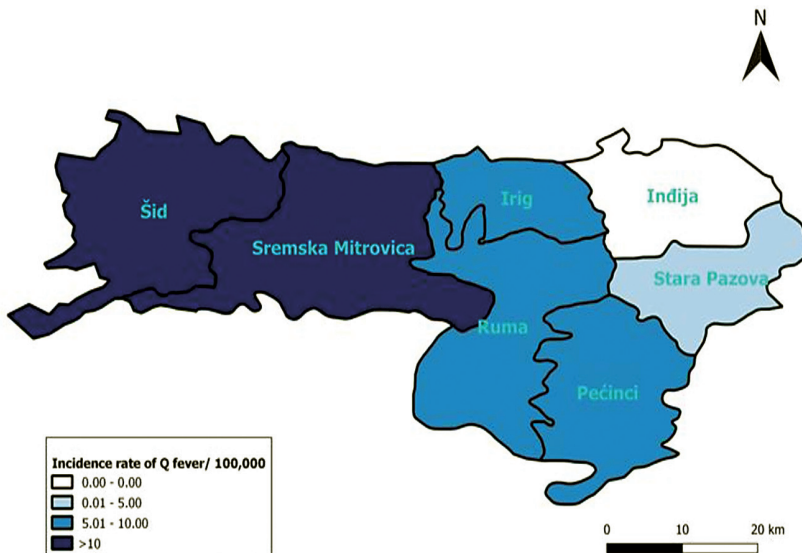


Figure 4. Distribution of Q fever by municipalities in Srem district, in the period 2011-2020

Most (92.11%; N = 70) Q fever cases were detected in outbreaks and the rest (7.89%; N = 6) occurred as sporadic cases. One third of patients (32.89%; N = 25) were hospitalized due to the severity of the disease or complications. There were no registered deaths due to acute Q fever. Direct contact with animals was probably route of Q fever transmission in Srem district, registered in 50.00% (N = 38) of cases (Table 3). Airborne spread of *C. burnetti* was probably route of transmission for the other half of patients (47.37%; N = 36). In only two cases the route of transmission of *C. burnetti* was not established.

Table 3. Possible routes of transmission of Q fever in Srem district, in the period 2011 - 2020

	Direct contact with animals		Aerogenic route of transmission		Unknown route of transmission		Total	
	N ¹	%	N	%	N	%	N	%
Cases in outbreaks	36	51.43	34	48.57	0	0	70	100
Sporadic cases	2	33.33	2	33.33	2	33.33	6	100
Total	38	50.00	36	47.37	2	2.63	76	100

¹ number of Q fever cases

Overall, three outbreaks of Q fever were notified in Srem district in the observed period, in municipalities of Ruma (2011), Sremska Mitrovica (2012) and Šid (2017) with registered 5, 43 and 22 patients, respectively. In the outbreak in the municipality of Ruma, four patients probably contracted Q fever through direct contact with animals (due to occupational exposure), and one patient through airborne transmission. Epizootiological tests were also carried out in six households in the municipality of Ruma (the blood of the sheep and goats was sampled and tested with an ELISA test), and the results for the presence of specific antibodies against the causative agent of Q fever were negative. In the 2017 outbreak, which originated from a goat farm in the village of Kukujevci (Šid), 17 patients contracted infection during direct contact with animals while working on the farm. The other five patients were residents of the village who probably became infected by airborne route of transmission. Then, in the villages of Kukujevci and Bačinci (municipality of Šid) and Kuzmin (municipality of Sremska Mitrovica) an epizootiological investigation was carried out, including serosurvey that proved 436 positive animals (149

sheep and 287 goats), of which 409 were seropositive animals in Kukujevci (278 positive goats on the farm and the rest in the village with the animal keeper) and 27 seropositive animals in one herd in one household in Kuzmin.

During the period from 2014-2020, total of 3,962 animals (821 goats, 3,076 sheep and 65 cattle) were tested for *C. burnetii* in sera samples in Srem district (Table 4). Of all tested animals, the highest seroprevalence was reported in goats (44.58%). The highest seroprevalence was recorded in the municipality of Šid in goats (55.54 %), and also in the municipality of Šid in sheep (11.88%) and in Stara Pazova in cattle (80.00%).

Table 4. Seroprevalence of Q fever in domestic animals in Srem district, by municipalities, in the period 2014-2020

Animal species	Municipalities								
		Indija	Irig	Pećinci	Ruma	Šid	Sremska Mitrovica	Stara Pazova	Total
Goats	T ¹	188	9	20	20	271	2	0	510
	P ²	43	0	0	0	36	0	0	79
	%	22.87	0.00	0.00	0.00	13.28	0.00	0.00	15.49
Sheep	T	304	162	97	337	831	407	114	2,252
	P	7	6	0	3	61	17	2	96
	%	2.30	3.70	0.00	0.89	7.34	4.17	1.75	4.26
Cattle	T	39	2	11	3	0	5	5	65
	P	0	0	1	0	0	0	4	5
	%	0.00	0.00	9.09	0.00	0.00	0.00	80.00	7.69

¹ tested

² positive

DISCUSSION

Our study shows that Q fever is still endemic disease in Srem district with majority of human cases registered in outbreaks. The highest incidence of Q fever in the observed ten-year period was registered in the western part of the Srem district. Men were more affected as well as the working-age population. One third of patients were hospitalized, none with death outcome. Looking at the season, the largest number of infected people was recorded in February while probable routes of transmission were direct contact with animals and airborne spread of infection.

The results of our study showed that there were more cases among men in Srem district, which may be linked to their higher likelihood of occupational exposure. Due to the protective role of sex hormones, women develop symptomatic Q fever less frequently (Leone et al., 2004). Our findings are similar to the results of several published studies showing that the majority of cases were registered in men (Anderson et al., 2009; Gyuranecz et al., 2014; Halsby et al., 2017; Genova-Kalou et al., 2019).

The average annual incidence rate of Q fever in Srem district in the observed period was 1.7 times higher than the incidence rate notified in APV and five times higher than the average annual incidence rate recorded in the Serbia in the same period (IPHS, 2021). The average annual incidence of Q fever in Srem district (2011 - 2020) was approximately two and 1.2 times lower compared to average incidences registered in the endemic areas of Central Banat and South Banat (IPHS, 2018; IPHS, 2021, Ristić et al., 2018). Compared to the average annual incidence rate of Q fever (incidence of 0.17/100,000) in the countries of the European Union (EU), the average annual incidence rate in Srem district was 14.3 times higher in the period 2011 - 2020 (ECDC, 2017; ECDC, 2021).

The lowest incidence of Q fever in EU, in the observed ten-year period was reported in 2020 (ECDC, 2021), when, interestingly, not a single case of the disease was registered in Srem district, nor in the territory of APV. This is explained by the fact that the Coronavirus disease 2019 (COVID-19) emerged in 2020, which is why all communicable diseases, including Q fever, were under-reported. Besides, it is possible that pandemic mitigation measures such as wearing masks and washing hands also reduced the chance of contracting Q fever, since it is an airborne infection.

In our study, there were no registered cases among children < 10 years which is similar to the situation in EU, where the small number of patients with positive samples was recorded in children under 10 years of age (ECDC, 2017). In accordance with the above, we found a statistically significantly higher incidence of Q fever in the working age population (20 - 59 years) compared to the age category of 0 - 19 years old. The reason for this finding may be that children and adolescents infected with *C. burnetti* are more often asymptomatic than adults and may have milder symptoms of the disease, so cases of Q fever are less often registered among them, which is in agreement with other studies (Maltezos and Raoult, 2002; Terheggen and Leggat, 2007).

Seasonal distribution of Q fever, with the majority of patients in Srem district registered in the period January - May, may be related to the fact that during these months the lambing and kidding of sheep and goats are done and other activities in which humans are in contact with potentially infected

animals. During the huge outbreak in the Netherlands, it was observed that the majority of patients appeared, at the end of winter and at the beginning of spring (Schneeberger et al., 2014). Several studies have pointed out the role of high wind speed and low rainfall on the easier transmission of microorganisms and the higher incidence of Q fever (Tissot-Dupont et al., 2004; Medić et al., 2012; Ristić et al., 2018; De Rooij et al., 2018).

Outbreaks in the village of Noćaj (municipality of Sremska Mitrovica - 2012) and in the village of Kukujevci (municipality of Šid - 2017) contributed to the peaks of incidence registered in 2012 and 2017 as well as to the highest incidence rates recorded in these municipalities. The reason for this may be the fact that these two municipalities are close to the border of Croatia, where the highest incidence of Q fever in Europe was registered in 2012 and 2017 (ECDC, 2019). Not a single case of Q fever was registered in Indija, even though there was an outbreak in a goat farm with a high number of positive animals. The most possible reason may be the under-registration of human Q fever cases, as well as the asymptomatic clinical course of the disease.

An extensive epidemiological investigation of Q fever outbreak in village Noćaj (Sremska Mitrovica) established that the most likely route of transmission for more than 2/3 of the patients was airborne, while the rest reported direct contact with animals (Medić et al., 2012). Our results also showed that half of patients had no contact with animals and that they most likely contracted Q fever which was transmitted through the air. This claim is in agreement with previous studies that *C. burnetii* can be transmitted by wind through aerosols and dust over long distances (within 5 km of the source of infection) (Arricau-Bouvery and Rodolakis, 2005; Debeljak et al., 2018). Furthermore, the other half of the cases of Q fever were registered in people who had direct contact with animals, similar to other studies conducted in APV (Ristić et al., 2018; Popov et al., 2019).

Some limitations of our study should be listed. First, documentation of Q fever is limited by the availability of laboratory testing, and it is certain that a majority of asymptomatic infections were not recorded. This suggests that the incidence rates of Q fever are likely to be higher than registered. Earlier studies on Q fever found a positive correlation between the number of infected people and animals in Srem district (Ristić et al., 2018), but more extensive studies are needed to address the low incidence or absence of cases in municipalities where positive animals have been registered. No data for the outcomes of chronic forms of Q fever were obtained during this study.

CONCLUSION

Our results show that Q fever is still an endemic disease in Srem district and represents a significant problem of veterinary and human medicine. More efficient disease control requires strengthening surveillance with continued monitoring the disease in animals, and more effective cooperation between sectors of human and veterinary medicine.

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Author's Contribution:

SP and SM made contributions to conception and design of the article; SP wrote the manuscript. TP contributed in results analysis and the way of results presenting. ND performed the statistical analysis. SS, DB, ML and JJK were involved in the data collection. SM and TP revised the manuscript critically. SP prepared the final draft of the manuscript. All authors read and approved the final manuscript.

Competing interest

The authors declare that they have no competing interest.

REFERENCES

1. Anderson A.D., Kruszon-Moran D., Loftis A.D., McQuillan G., Nicholson W.L., Priestley R.A., Candee A.J., Patterson E.N., Massun R.F. 2009. Seroprevalence of Q fever in the United States, 2003-2004. *American Journal of Tropical Medicine and Hygiene*, 81, 4, 691. doi:10.4269/ajtmh.2009.09-0168.
2. Angelakis E., Raoult D. 2010. Q fever. *Veterinary microbiology*, 140, 3/4, 297-309. doi:10.1016/j.vetmic.2009.07.016.
3. Arricau-Bouvery N., Rodolakis A. 2005. Is Q fever an emerging or re-emerging zoonosis? *Veterinary research*, 36, 3, 327-349. doi: 10.1051/vetres:2005010.

4. Centers for Disease Control and Prevention (CDC) 2019. Q fever-transmission. Available at <https://www.cdc.gov/qfever/transmission/index.html>. Accessed 13.10.2022.
5. Debeljak Z., Medić S., Baralić M., Andrić A., Tomić A., Vidanović D., Šekler M., Matović K., Vasković N. 2018. Clinical, epidemiological and epizootic features of a Q fever outbreak in the border region between Serbia and Montenegro. *The Journal of Infection in Developing Countries*, 12, 05, 290-296. doi: 10.3855/jidc.9918.
6. De Rooij M.M., Van Leuken J.P., Swart A., Kretzschmar M.E., Nielen M., De Koeijer A.A., Janse I., Wouters M.I., Heederik D.J. 2018. A systematic knowledge synthesis on the spatial dimensions of Q fever epidemics. *Zoonoses and public health*, 66, 1, 14-25. doi: 10.1111/zph.12534.
7. European Centre for Disease Prevention and Control (ECDC) 2017. Surveillance report: Q fever - Annual Epidemiological Report for 2015. Available at: https://www.ecdc.europa.eu/sites/default/files/documents/AER_for_2015-Q-fever.pdf. Accessed 05.09.2022.
8. European Centre for Disease Prevention and Control (ECDC) 2018. EU Case definition. Available at: <https://www.ecdc.europa.eu/en/surveillance-and-disease-data/eu-case-definitions>. Accessed 05.09.2022.
9. European Centre for Disease Prevention and Control (ECDC) 2019. Surveillance Atlas of Infectious Diseases. Available at: <https://atlas.ecdc.europa.eu/public/index.aspx>. Accessed 05.12.2022.
10. European Centre for Disease Prevention and Control (ECDC) 2021. The European Union One Health 2020 Zoonoses Report. Available at: <https://www.ecdc.europa.eu/sites/default/files/documents/j-efsa-2021-6971.pdf>. Accessed 05.09.2022.
11. Fournier P.E., Marrie T.J., Raoult D. 1998. Diagnosis of Q fever. *Journal of clinical microbiology*, 36, 7, 1823-1834. doi: 10.1128/JCM.36.7.1823-1834.1998.
12. Genova-Kalou P., Vladimirova N., Stoitsova S., Krumova S., Kurchatova A., Kantardjiev T. 2019. Q fever in Bulgaria: Laboratory and epidemiological findings on human cases and outbreaks, 2011 to 2017. *Eurosurveillance*, 24, 37. doi: 10.2807/1560-7917.ES.2019.24.37.1900119.
13. Gyuranecz M., Sulyok K.M., Balla E., Mag T., Balázs A., Simor Z., Dénes B., Hornok S., Bajnóczi P., Hornstra H.M., Pearson T., Keim P., Dán A. 2014. Q fever epidemic in Hungary, April to July 2013. *Eurosurveillance*, 19, 30. doi: 10.2807/1560-7917.ES2014.19.30.20863.
14. Halsby K.D., Kirkbride H., Walsh A.L., Okereke E., Brooks T., Donati M., Morgan D. 2017. The epidemiology of Q fever in England and Wales 2000–2015. *Veterinary Sciences*, 4, 2, 28. doi: 10.3390/vetsci4020028.

15. Institute of Public Health of Serbia (IPHS) 2018. Infectious Disease Report in the Republic of Serbia for 2017. Available at: <http://www.batut.org.rs/download/izvestaji/GodisnjiIzvestajOZaraznimBolestima2017.pdf>. Accessed 03.09.2022.
16. Institute of Public Health of Serbia (IPHS) 2021. Infectious Disease Report in the Republic of Serbia for 2020. Available at: <http://www.batut.org.rs/download/izvestaji/GodisnjiIzvestajOZaraznimBolestima2020.pdf>. Accessed 03.09.2022.
17. Leone M., Honstettre A., Lepidi H., Capo C., Bayard F., Raoult D., Mege J. L. 2004. Effect of sex on *Coxiella burnetii* infection: protective role of 17 β -estradiol. *The Journal of infectious diseases*, 189, 2, 339-345. doi: 10.1086/380798.
18. Maltezou H.C., Raoult D. 2002. Q fever in children. *The Lancet infectious diseases*, 2, 11, 686-691. doi: 10.1016/S1473-3099(02)00440-1.
19. Maurin M., Raoult D. 1999. Q fever. *Clinical microbiology reviews*, 12, 4, 518-553. doi: 10.1128/CMR.12.4.518.
20. Medić S., Nitzan Kaluski D., Šeguljev Z., Obrenović J., Rudan P., Lazarević M., Jandrić Kočić J., Sajenković D., Pušić I., Bugarski D., Vidanović D., Šekler M. 2012. Q fever outbreak in the village of Nočaj, Srem County, Vojvodina province, Serbia, January to February 2012. *Eurosurveillance*, 17, 15. doi: 10.2807/es.e17.15.20143-en.
21. Milazzo A., Hall R., Storm P.A., Harris R.J., Winslow W. Marmion B.P. 2001. Sexually transmitted Q fever. *Clinical infectious diseases*, 33, 3, 399-402. doi: 10.1086/321878.
22. Parker N.R., Barralet J.H., Bell A.M. 2006. Q fever. *The Lancet*, 367, 9511, 679-688. doi: 10.1016/S0140-6736(06)68266-4.
23. Popov S., Štrbac M., Ristić M. 2019. Epidemiological characteristics of the most common zoonoses in the Central Banat district of Vojvodina from 2002 to 2016. *Medicinski pregled*, 72, 3/4, 72-79. doi: 10.2298/MPN-S1904072P.
24. Reimer L.G. 1993. Q fever. *Clinical Microbiology Reviews*. 6, 3, 193-198. doi: 10.1128/CMR.6.3.193.
25. Ristić M., Štrbac M., Savić S., Dragovac G., Ilić S., Medić S., Vidić B., Petrović M. 2018. Factors associated with maintenance of human Q fever in Vojvodina, Serbia. *Vojnosanitetski pregled*, 75, 10, 998-1008. doi: 10.2298/VSP161217034R.
26. Schneeberger P.M., Wintenberger C., Van der Hoek W., Stahl, J.P. 2014. Q fever in the Netherlands - 2007-2010: what we learned from the largest outbreak ever. *Médecine et maladies infectieuses*, 44, 8, 339-353. doi:10.1016/j.medmal.2014.02.006.

27. Terheggen U., Leggat P. A. 2007. Clinical manifestations of Q fever in adults and children. *Travel Medicine and Infectious Disease*, 5, 3, 159-164. doi: 10.1016/j.tmaid.2006.06.001.
28. Tissot-Dupont H., Amadei M.A., Nezri M., Raoult, D. 2004. Wind in November, Q fever in December. *Emerging infectious diseases*, 10, 7, 1264. doi: 10.3201/eid1007.030724.
29. The Statistical Office of the Republic of Serbia (SORS) 2011. Census data - excel table. Population by age and sex, by settlements. Available at: https://www.stat.gov.rs/media/3759/1_stanovnistvo-prema-starosti-i-polu-ponaseljima.xls. Accessed 03.09.2022.
30. World organization for Animal Health (OIE) 2021. Q fever chapter 3.1.16. Available at: <https://www.woah.org/app/uploads/2021/03/3-01-16-q-fever-2.pdf>. Accessed 16.09.2022.

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