EPIDEMIOLOGICAL ANALYSIS OF LEPTOSPIROSIS IN BULGARIA, 1999-2018

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Abstract. Background: The aim of the study was to characterize the epidemic process of leptospirosis in Bulgaria. **Material and methods:** Data was collected from the National Centre for Public Health and Analysis official database of infectious diseases for the period 1999-2018 year. Graphical methods, absolute and relative values were applied when analyzing the data. A regression analysis was used to search for trends in incidence rate and mortality rate over a period of time. **Results:** For the period 1999-2018, a total of 414 cases of leptospirosis were registered in Bulgaria, 35 of them were lethal. Incidence ranged from 0,10 per 100 000 population (2012, 2017 year) to 0,63 per 100 000 (1999 year). Using the regression analysis method a model $p = 0,03 < 0,05$ was constructed, which most adequately described the tendency of leptospirosis incidence rate in Bulgaria. Mortality rate was the highest in 2000 – 0,09 per 100 000 and was zero for six years of the survey period. An adequate model was developed $p = 0,005 < 0,05$, which showed the trend of leptospirosis mortality rate. The case-fatality rate was high and reached 27,27% in 2010. The highest incidence rate of leptospirosis was in the areas of Yambol and Shumen. Leptospirosis in Bulgaria had a seasonal trend. Risk factors for the disease were male gender and age over 55 years. **Conclusions:** Global environmental changes, including extreme weather conditions, increase the threat of severe epidemics of leptospirosis worldwide. An unfavorable impact on the spread of leptospirosis is the intensive migration of the population and travel-associated cases. Modern control over leptospirosis should be constant, complex and ubiquitous. Therefore, leptospirosis in Bulgaria should not be underestimated.

Key words: leptospirosis, cases, incidence rate, mortality rate, case-fatality rate

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INTRODUCTION

Leptospirosis, a disease caused by pathogenic spirochetes belonging to the *Leptospira* genus, represents a worldwide public health problem affecting both industrialized and developing countries. Annually, approximately 500 000 severe cases occur worldwide, with a mortality rate of 5-20% [1].

Humans are infected through direct contact with infected animals, or through contact with water or soil that has been contaminated by urine of infected animals; occasionally, through drinking of water and ingestion of food contaminated with urine of infected animals, often rats; also through inhalation of droplet aerosols of contaminated fluids. Disease transmission is strongly driven by environmental factors

including heavy rainfall, flooding, natural disasters, population growth, urbanization, and poor sanitation and hygiene [2, 3, 4, 5]. In addition, infection risk depends on individual behaviour (e.g. swimming in fresh water, working outdoors), and contact with animals including livestock, rodents, pets and wildlife [2, 4]. Risk factors for infections and drivers of outbreaks depend on interactions between humans, animals, and the environment, and vary significantly between locations based on environmental, cultural, and socio-demographic factors [4].

MATERIALS AND METHODS

The aim of the study was to characterize the epidemic process of leptospirosis in Bulgaria. Data was collected from the National Centre for Public Health and Analysis official database of infectious diseases for the period 1999-2018 year.

Graphical methods, absolute and relative (dynamic and intensive) values were applied when analyzing the data. A regression analysis was used to search for trends in incidence rate and mortality rate over a period of time. The incidence trend was calculated according to the following formula: incidence rate per 100 000 = $27,873 - 0,14 * \text{Year}$, the year is an independent variable and incidence rate is dependent. To find the mortality rate trend, the following equation was used: Mortality rate per 100 000 = $5,086 - 0,003 * \text{Year}$, with the year being an independent variable and mortality rate – a dependent one.

RESULTS

For the period 1999-2018, a total of 414 cases of leptospirosis were registered in Bulgaria, 35 of them were lethal. Incidence rate ranged from 0,10 per 100 000 population (2012, 2017) to 0,63 per 100 000 (1999 year). Using the regression analysis method a model $p = 0,03 < 0,05$ was constructed, which most adequately described the tendency of leptospirosis incidence rate in Bulgaria. Mortality rate was the highest in 2000 – 0,09 per 100 000 and was zero for six years of the survey period (Table 1, Fig. 1). An adequate model was developed $p = 0,005 < 0,05$, which showed the trend of leptospirosis mortality rate. The case-fatality rate was high and reached 27,27% in 2010 (Table 1, Fig. 2).

The age structure of leptospirosis incidence rate, for the period 2009-2018, showed that approximately 50% (71/144) of the registered cases were of people over 55 years of age. There were no cases of leptospirosis in children up to 9 years of age. In the age groups of 10-14 and 15-19, single cases of the

disease were recorded (Tabl. 2). Table 3 shows that the highest leptospirosis incidence rate was reached in 2014, in the 55-59 age group (1,96 per 100 000).

The territorial structure of the leptospirosis incidence rate in Bulgaria is presented in Table 4. There were no registered cases of leptospirosis in seven out of the 28 regions in Bulgaria (Kardzhali, Kyustendil, Pernik, Razgrad, Silistra, Smolyan and Haskovo). Three cases of leptospirosis were reported in three areas (Vidin, Pazardzhik and Targovishte). The highest incidence rate of leptospirosis was recorded in 2014 in the following areas: Gabrovo (5,92/100 000), Dobrich (5,41/100 000), Lovech (4,43/100 000) and Yambol, 15/100 000). In 2018, in the region of Gabrovo the leptospirosis incidence rate (4,53/100 000) was significantly higher than the average for the country (0,21/100 000). The leptospirosis incidence rate in Yambol area was several times higher than the average for the country during the survey period, with the exception of 2017 when zero incidence rate was recorded. Shumen region also had an incidence rate above the national average for eight years during the period of 2009-2018.

Leptospirosis in Bulgaria had a seasonal pattern, most cases of which were recorded between June and September (maximum frequency in July and August) (Fig. 3). A risk factor for leptospirosis was the male gender (male/female ratio – 4/1) (Fig. 4).

According to epidemiological studies of the Regional Inspectorates for the Protection and Control of Public Health (RIPCPh), the factors contributing to the spread of leptospirosis were predominantly rodent contaminated food and objects, livestock breeding, less frequent bathing in natural waterbodies [6].

DISCUSSION

In Bulgaria, the official registration of human leptospirosis dated back to 1952. A trend to decrease the incidence of leptospirosis in our country has been observed [7, 8]. In Europe, the incidence rate of leptospirosis decreased during the second half of the last century [9].

In 2017, 931 confirmed leptospirosis cases were reported in 25 European countries [10]. With an overall incidence rate of 0,20/100 000 population, leptospirosis remained a rare disease in EU countries. The highest leptospirosis notification rates were observed in Slovenia (1,16/100 000 population), Portugal (1,13/100 000 population) and Austria (0,78/100 000 population) [10]. The results of our study show that Bulgaria is among the countries with the lowest leptospirosis incidence rate in the EU (0,10/100 000).

Fig. 1. Evolution of leptospirosis incidence and mortality rate in Bulgaria (cases/100 000), 1999-2018

Fig. 2. Evolution of leptospirosis case-fatality rate (per 100) of leptospirosis in Bulgaria, 1999-2018

Fig. 3. Seasonal distribution of leptospirosis cases, Bulgaria, 2014-2018

Fig. 4. Distribution by sex of patients with leptospirosis, Bulgaria, 2009-2018

Table 1. Number of Cases, Number of Deaths, Incidence Rate, Mortality Rate (per 100 000 population), Case Fatality Rate (per 100) of Leptospirosis, Bulgaria, 1999-2018

Year	Cases (n)	Incidence Cases/100,000	Deaths (n)	Mortality Rate Cases/100 000	Case Fathality Rate per 100
1999	53	0,63	2	0,02	3,77
2000	35	0,43	8	0,09	22,86
2001	22	0,26	3	0,04	13,64
2002	21	0,26	1	0,01	4,76
2003	23	0,29	3	0,04	13,04
2004	28	0,30	1	0,01	3,57
2005	43	0,55	5	0,06	11,63
2006	20	0,26	2	0,03	10,00
2007	16	0,21	2	0,03	12,50
2008	9	0,12	0	0,00	0,00
2009	11	0,14	1	0,01	9,09
2010	11	0,15	3	0,04	27,27
2011	12	0,16	0	0,00	0,00
2012	7	0,10	1	0,01	14,29
2013	8	0,11	2	0,03	25,00
2014	43	0,59	0	0,00	0,00
2015	17	0,24	0	0,00	0,00
2016	13	0,18	1	0,01	7,69
2017	7	0,10	0	0,00	0,00
2018	15	0,21	0	0,00	0,00

Table 2. Distribution of Leptospirosis (Number of Cases) by age groups, Bulgaria, 2009-2018

Year	Age groups/Number of Cases														
	0	1-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65+
2009	0	0	0	0	0	0	1	0	0	1	0	3	1	1	4
2010	0	0	0	0	0	1	0	2	0	2	3	1	0	1	1
2011	0	0	0	0	1	1	0	2	0	2	0	1	0	2	3
2012	0	0	0	0	0	0	0	1	1	2	0	0	1	2	0
2013	0	0	0	0	0	0	2	0	0	1	1	3	0	0	1
2014	0	0	0	0	0	2	3	2	2	4	2	5	10	6	7
2015	0	0	0	0	0	2	1	0	2	0	1	1	3	2	5
2016	0	0	0	0	0	0	0	0	0	0	1	3	3	1	5
2017	0	0	0	0	0	0	0	0	1	0	1	0	1	1	3
2018	0	0	0	1	0	0	0	0	3	0	2	2	2	2	3

Table 3. Leptospirosis Incidence rate by age group (Cases/100 000), Bulgaria, 2009-2018.

Year	Age group, years/ Incidence rate														
	0	1-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65+
2009	0,00	0,00	0,00	0,00	0,00	0,00	0,20	0,00	0,00	0,20	0,00	0,60	0,20	0,20	0,30
2010	0,00	0,00	0,00	0,00	0,00	0,20	0,00	0,30	0,00	0,40	0,60	0,20	0,00	0,20	0,10
2011	0,00	0,00	0,00	0,00	0,28	0,20	0,00	0,30	0,00	0,40	0,00	0,20	0,00	0,38	0,20
2012	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,19	0,18	0,38	0,00	0,00	0,19	0,38	0,00
2013	0,00	0,00	0,00	0,00	0,00	0,00	0,41	0,00	0,00	0,19	0,21	0,60	0,00	0,00	0,07
2014	0,00	0,00	0,00	0,00	0,00	0,46	0,61	0,40	0,36	0,76	0,41	1,00	1,96	1,16	0,49
2015	0,00	0,00	0,00	0,00	0,00	0,49	0,21	0,00	0,37	0,00	0,20	0,20	0,60	0,39	0,35
2016	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,20	0,62	0,60	0,20	0,34
2017	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,19	0,00	0,20	0,00	0,20	0,20	0,20
2018	0,00	0,00	0,00	0,31	0,00	0,00	0,00	0,00	0,60	0,00	0,39	0,43	0,41	0,41	0,20

Table 4. Leptospirosis Incidence in Region, (cases/100 000 population), Bulgaria, 2009-2018

Region / year	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Blagoevgrad	0,61	0,00	0,00	0,00	0,00	0,00	0,32	0,00	0,00	0,00
Burgas	0,71	0,00	0,47	0,00	0,00	0,00	0,00	0,48	0,24	0,24
Varna	0,00	0,21	0,00	0,00	0,42	0,00	0,21	0,21	0,00	0,21
Veliko Turnovo	0,00	0,00	0,00	0,00	0,00	0,00	0,40	0,41	0,00	0,00
Vidin	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	1,15
Vratsa	0,00	0,51	0,52	0,00	0,00	4,48	0,00	0,58	0,00	0,00
Gabrovo	0,00	0,00	0,00	0,00	0,00	5,92	0,00	1,75	0,00	4,53
Dobrich	0,00	0,00	0,00	0,00	0,00	5,41	0,55	0,00	0,00	0,00
Kardzhali	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Kyustendil	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Lovech	0,00	0,00	0,68	0,00	0,73	4,43	1,50	0,00	0,00	1,58
Montana	0,63	0,00	0,65	0,00	0,70	0,71	0,00	0,73	1,49	0,00
Pazardzhik	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,38	0,00	0,00
Pernik	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00

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Pleven	0,00	0,69	0,00	0,75	0,00	0,00	0,00	0,00	0,40	0,41
Plovdiv	0,00	0,00	0,14	0,00	0,00	0,29	0,30	0,00	0,15	0,15
Razgrad	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Ruse	0,00	0,00	0,00	0,00	0,00	0,44	0,00	0,00	0,00	0,45
Silistra	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Sliven	0,48	0,00	0,00	0,00	1,02	0,00	0,00	0,00	0,00	0,00
Smolyan	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Sofia-capital	0,00	0,08	0,00	0,15	0,08	0,08	0,15	0,08	0,08	0,00
Sofia-region	0,39	0,40	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Stara Zaora	0,00	0,00	0,00	0,00	0,00	0,30	0,31	0,00	0,00	0,00
Targovishte	0,76	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Haskovo	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
Shumen	0,51	1,55	2,60	0,00	0,00	1,12	1,13	0,57	0,57	0,58
Yambol	0,71	1,44	0,74	2,31	0,78	3,15	3,18	1,62	0,00	0,83
Bulgaria	0,10	0,15	0,16	0,10	0,11	0,59	0,24	0,18	0,10	0,21

Indeed, most risk factors associated with leptospirosis endemicity (tropical climate, flooding, poor sanitation) are not traditionally encountered in EU countries [3]. This infection occurs most commonly in the tropics because the climate as well as the sometimes-poor hygienic conditions favor the pathogen's survival and distribution [11]. Cyclical changes in the incidence rate of leptospirosis occurring over several years were also affected by adverse weather conditions [12]. In Bulgaria, although there are no specific studies, years of heavy rainfall and floods coincide with the highest levels of leptospirosis incidence rate. During the period 1999-2018, three peaks of leptospirosis were registered in Bulgaria (1999, 2005, and 2014) (Fig. 2). In 1999 torrential rains affected 1/3 of the country, in 2005 75% of Bulgarian territory was flooded [13] and in 2014 eleven districts were affected by floods.

The results of a survey for the period 2010-2011 show that leptospirosis incidence rate in Bulgaria was caused by 5 serovars. The leading serogroup was that of *Leptospira icterohaemorrhagiae* - demonstrated in 14/28 (50%) of the study patients. The rate of infections caused by this serogroup showed a tendency to decrease compared to previous studies [14, 15]. The second most frequent serogroup was the *Leptospira Sejroe*, confirmed by 21,43% of the patients (6/28). There was a significant increase in the relative share of this serogroup compared to previous studies (8,93%) [8, 14, 15, 16]. In all nine leptospirosis patients in 2008, *Leptospira icterohaemorrhagiae* was serologically diagnosed

[6]. Some serovars are generally associated with particular animals (e.g., *Icterohaemorrhagiae* and *Copenhageni* with rats, *Grippotyphosa* with voles, *Hardjo* with cattle, *Canicola* with dogs, and *Pomona* with pigs) but may occur in other animals as well [11]. Despite the limited data in our study, as a risk factor for spreading leptospirosis, an increase in the population of rodents in the inhabited areas can be indicated.

CONCLUSION

For the period 1999-2018, the incidence and mortality rates of leptospirosis in Bulgaria tended to decrease. Despite the limited prevalence of leptospirosis, the case-fatality rate was high. Global environmental changes, including extreme weather conditions, increase the threat of severe epidemics of leptospirosis worldwide. An unfavorable impact on the spread of leptospirosis is the intensive migration of the population and travel-associated cases. Modern control over leptospirosis should be constant, complex and ubiquitous. Therefore, leptospirosis in Bulgaria should not be underestimated.

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