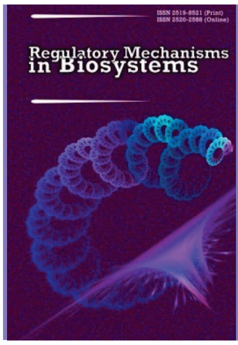

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Epizootological and epidemiological aspects of leptospirosis in Ukraine for the period 2003–2022

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Zoonotic leptospirosis is an infectious disease caused by pathogenic *Leptospira* bacteria that can be transmitted from animals to humans. Animals, especially wild and domestic mammals, are reservoir hosts that carry and excrete the bacteria in their urine. A retrospective analysis of the incidence of leptospirosis in animals and humans in Ukraine from 2003 to 2022 was conducted based on reports from regional state laboratories of veterinary medicine and the Center for Public Health. GIS mapping was used to analyze and visualize the data. The incidence and prevalence of leptospirosis among different animal species, including farm, domestic and wild animals, were analyzed. These studies included a retrospective analysis of blood serum samples from different animal species for leptospirosis and analysis of the results to determine the level of seropositivity. The study analyzed a total of 6,543,934 samples, with an overall seropositivity rate of 3.3%. Among cattle, 4.1% of the samples were positive. For pigs, 2.1% were positive. Horses had a seropositivity rate of 7.9%, while dogs and cats had seropositivity rates of 17.5% and 13.1% respectively. Wild boars showed a positivity rate of 2.2%. The number of seropositive animals of different species in Ukraine showed different dynamics from 2003 to 2022. The highest number of positive cases was found among cattle, pigs and horses. However, the number of positive cases decreased significantly after 2015, which coincides with a significant reduction in the number of farm animals. Trends of increasing seropositivity among dogs and cats in the period 2007–2015 indicate that these species are also active carriers of *Leptospira*, as are the leading agricultural species. Wildlife species with stable seropositivity serve as both sources and reservoirs of *Leptospira*. Wild pigs are becoming the main bacterial carriers in all regions of Ukraine. There is a marked disproportion between the number of positive cases among farm animals and wildlife, indicating that seropositivity in these populations exists largely autonomously. A total of 7,937 people were infected in Ukraine between 2003 and 2022. Certain regions, such as Lviv, Kherson, Kyiv, Mykolaiv, and Vinnytsia, account for a larger share of the total number of cases, ranging from 4.8% to 7.3%. The incidence of human leptospirosis has fluctuated over the years, peaking at 473 cases in 2014, followed by a decline: 301 cases in 2015, 323 cases in 2016 and 330 cases in 2017, and in subsequent years the number of cases remained relatively stable, ranging from 142 to 295 cases per year. The study emphasizes the need to improve preventive measures and raise public awareness of the disease, especially in rural areas. It is important to adopt a comprehensive interdisciplinary approach involving collaboration between veterinary medicine, public health and environmental authorities to better understand and address the complexities of leptospirosis transmission and reduce its impact on animal and human health.

Keywords: *Leptospira*; epizootology; cattle; pigs; small ruminants; horses; wild animals; serological monitoring; mapping.

Introduction

Leptospirosis is a naturally occurring zoonotic disease that is globally distributed and affects a wide range of animal species, with severe damage to the internal parenchymal organs and nervous system. The natural reservoirs of infection are insectivores, rodents, domestic animals, wild animals, and fur-bearing animals (Haake & Levett, 2015; Pongpan et al., 2023). After significant numbers of human leptospirosis cases were reported worldwide (Hartskeerl et al., 2011), the disease was classified by the WHO as having re-emerged. The disease is considered to be neglected by humanity, due to reduced reporting and lack of awareness of its wider spread (Moseley et al., 2018). The morbidity burden of leptospirosis is significantly higher than some other important neglected tropical diseases, including visceral leishmaniasis and severe Dengue fever, including echinococcosis and cysticercosis (Hotez et al., 2010). The disease is prevalent mainly in tropical, subtropical and temperate climates (Azócar-Aedo, 2023). Currently, more than 300 serovars of this pathogen have been identified, classified into approximately 32 serogroups according to their antigenic homology (Caimi & Ruybal, 2020). Certain geographical areas of the world are characterised by serogroups/serovars which have been defined by the ecology of the places, the prevalence of the disease and the distribution of serovars, which differ between different countries and even between regions within any country (Adler & de la Peña Moctezuma, 2010; Harran et al., 2022). Each serovar is adapted to one or more mammals that act as "sustaining hosts", harbouring the bacteria without showing clinical signs, but the latter excrete the microorganism in their urine for many months, acting as reservoirs (Guerra, 2009). In rural areas, cattle, pigs, sheep and goats are at high risk of infection (Gay et al., 2014). Serovar *Pomona* is associated with pigs, cattle and wild animals such as skunks and opossums, and serovar *Autumnalis* is associated with rodents, while serovar *Bratislava* is adapted to rats, pigs and horses (Azócar-Aedo, 2023). In urban areas, rodents, in particular rats, are the main reservoirs of *Icterohaemorrhagiae* (Goarant, 2016); however, rodents can also be reservoirs of the *Ballum*, *Autumnalis* and *Copenhageni* serogroups (Levett, 2001; Perez et al., 2011; Esfandiari et al., 2015; Azócar-Aedo, 2023). Domestic carnivores are reservoir and occasional hosts of *Canicola* serovar (Gay et al., 2014; Azócar-Aedo, 2023).

Leptospira transmission occurs directly through contact of a susceptible animal with the urine or other bodily fluids of an infected animal. In other cases, it can be transmitted through water or soil contaminated with the pathogen (Markovych et al., 2019). It has been shown that domestic mammals (any livestock and companion animals) and animals in the wild are reservoirs for *Leptospira* (Matono et al., 2015). The literature describes cases of isolation of the leptospirosis pathogen directly from water sources (Samir et al., 2015). Animals can be asymptomatic after infection, but they can also become seriously ill. However, in all cases, animals infected with the leptospirosis pathogen are sources of leptospirosis, including for humans. Leptospirae have been isolated from more than 160 species of mammals, as well as reptiles, amphibians, fish and invertebrates (Desachy, 2008; Ko et al., 2009; Senthilkumar et al., 2023). The most dangerous sources and reservoirs of this pathogen for humans are small mammals, namely wild and domestic rodents (rats and mice), insectivorous mammals (shrews and hedgehogs) and domestic animals (cattle, pigs, sheep, goats, horses and dogs). Currently, researchers note that the pathogen has also been isolated from birds, amphibians, reptiles and fish (Cilia et al., 2021).

Significant incidence rates of leptospirosis are recorded in the Seychelles, Malaysia, New Caledonia, Suriname (20.0–100.0 per 100 thousand people); Barbados, Brazil, Trinidad and Tobago (10.0–20.0); Jamaica, Costa Rica, Sri Lanka, Thailand, El Salvador, New Zealand (2.5–10.0); average incidence rates are recorded in Uruguay, Nicaragua, Croatia, Ukraine, Dominican Republic, Cuba, Ecuador (1.0–2.5), Argentina, Portugal, Denmark, Latvia, Slovenia, Romania, Australia, Philippines, Slovakia, Taiwan (0.4–1.0); insignificant incidence rates in Iran, China, India (0.1–1.0); low incidence is recorded in the UK, Italy, Spain, USA, Canada, Germany (0.01–0.10) (Pappas et al., 2008; Al-Abri et al., 2015; Costa et al., 2015; Torgerson et al., 2015). In general, the incidence of leptospirosis in temperate areas is 0.1–1.0 per 100,000 population per year, but the highest incidence of leptospirosis in humans is recorded in countries of the subtropical and tropical zones (more than 100 cases per 100,000 per year), where a significant number of people are involved in epidemic outbreaks (Terpstra, 2003; Hartskeerl, 2006; Lau et al., 2010). The annual mortality rate from leptospirosis has been estimated to be 0.84 deaths per 100,000 people worldwide (Costa et al., 2015). Due to changes in climatic conditions, cases of leptospirosis have been reported in the northern territories of the globe (Zakharova et al., 2020). In the European Union, the incidence is estimated at 1–4 cases per million population, depending on the country (Garvey et al., 2014).

The mortality rate of human leptospirosis can be 1–20%. The most severe illness is caused by *L. icterohaemorrhagiae*, the causative agent of leptospirosis. In 5–10% of cases, people develop jaundice or hepatonephrotic syndrome, also known as Weil's disease, which is characterized by severe multiorgan dysfunction (López-Robles et al., 2021). Accurate epidemiological data on this infection in humans are not available, but researchers indicate that most reported cases have a severe clinical course, and often the mortality rate is more than 10%, and the incidence can be as high as 500,000 cases per year worldwide. According to other reports, the morbidity and mortality rate from leptospirosis is estimated at 1 million and 60 thousand cases, respectively (Costa et al., 2015). However, leptospirosis still remains a low-risk disease, when a significant number of sick people are not detected (Schneider et al., 2013), especially in the Americas (Hotez et al., 2014).

In humans, the disease is often manifested by respiratory tract infections, hepatitis, gastroenteritis and enterocolitis, fever, meningitis, meningoencephalitis, joint damage and skin rashes. In the absence of timely treatment, leptospirosis can lead to severe damage to the kidneys, liver, and other organs and death. The variety of clinical manifestations of leptospirosis impairs timely diagnosis and, accordingly, leads to a serious condition of patients. In fact, more than 50% of leptospirosis cases in humans are severe and their treatment requires intensive care (Adler & de la Peña Moctezuma, 2010). The disease is not always correctly diagnosed due to the large number of clinical manifestations and difficult diagnosis. Leptospirosis in humans is often diagnosed as aseptic meningitis, influenza, liver disease, fever of unknown origin or tropical diseases such as malaria or yellow fever, as well as other infectious diseases (hantavirus infection, rickettsiosis, borreliosis, brucellosis, toxoplasmosis), due to the variety of symptoms observed in humans (Bharti et al, 2003; Verma et al., 2020; Azócar-Aedo, 2023).

In Ukraine, leptospirosis is reported in all regions of the country, but in recent years, the highest intensity of the epidemiological process has been recorded in Zakarpattia, Kyiv, Kirovohrad, Mykolaiv, Chernihiv, and Chernivtsi regions (Vynohrad et al., 2018). According to the Ministry of Health of Ukraine, intensive incidence rates ranged from 0.69 per 100,000 population (316 cases) in 2012 to 1.38 per 100,000 population (632 cases) in 2010. In 2014, the incidence rate increased by 31.6%, with 473 cases registered, and the intensity rate was 1.04 per 100 thousand people.

The causative agent of leptospirosis belongs to the type Spirochaetes, order Spirochaetales, family Leptospiraceae. Two schemes are used to classify leptospirae. The first is based on serology and is useful for epidemiological purposes, in order to define serogroups and serovars. The other uses molecular taxonomy to identify species, known as genomospecies (Guernier et al., 2018). Currently, based on phylogenetic analysis, Leptospirae are divided into three lineages reflecting the level of pathogenicity: saprophytic (n = 26; referred to as groups *S1* and *S2*), intermediate (n = 21; referred to as group *P2*) and pathogenic (n = 17; referred to as group *P1*) (Mousavi et al., 2017; Vincent et al., 2019; Caimi & Ruybal, 2020; Verma et al., 2020; Harran et al., 2022). This serological division into serogroups and serovars is associated with the antigenic heterogeneity of open lipopolysaccharides (LPS) (Bharti et al., 2003; Daroz et al., 2021). It is important to note that serological and genetic classifications are not related, and different serovars may belong to the same genus (Levett, 2015). Since leptospirosis pathogens affect many species of domestic and wild animals, as well as humans, leptospirosis is classified as a zoonosis (Di Azevedo & Lilenbaum, 2021). The etiologic structure of leptospirosis in patients and suspected cases in Ukraine is represented by 14 serogroups of the diagnostic kit. The basis of the etiologic spectrum is the serogroup *Icterohaemorrhagiae*, *Hebdomadis*, *Canicola*, *Grippotyphosa*, *Pomona*, *Tarassovi* and others.

In farm animals, the asymptomatic form of infection in the form of leptospirosis and immunizing subinfection prevails. Carrier animals with chronic renal infection, mainly rats, dogs, cattle, horses, sheep, goats and pigs, are a constant reservoir of *Leptospira* in nature. These animals can excrete *Leptospira* in their urine for many years (Ukhovskyi, 2014). Dogs are a fairly common source of human infection (Adler & de la Peña Moctezuma, 2010; Narkkul et al., 2021). Mouse-like rodents and rats are almost lifelong carriers of the pathogen and pose a particular epizootic and epidemiological threat (Boey et al., 2019).

In Ukraine, leptospirosis is characterized by summer–autumn seasonality. The peak incidence of leptospirosis in different regions occurs in July–September. The pathogen enters water bodies in the urine of patients, recovered patients, and reservoir animals, where it survives for a long time. Humans are often affected by the leptospirosis pathogen when they swim in such bodies of water, consume raw water or contaminated food. In general, the waterborne route of transmission prevails – swimming, fishing, agricultural work in humid areas. The contact route of transmission is also of great importance, it can be the care of animals or various contacts with rodents, the actual reservoir species of the pathogen (Tsarenko, 2019). Leptospirosis can be an occupational disease (e.g., for farmers, travelers, or workers in sewage systems and slaughterhouses) (Al-Abri et al., 2015). Outbreaks have been reported among people involved in water sports and recreation "on the water" (Agampodi et al., 2014). Leptospirosis also has a broader public health impact in poor regions among farmers (Sethi et al., 2010), farmers and pastoralists in tropical regions (Crump et al., 2013). The disease has become a health threat in the new environment due to the impact of globalization and climate change. It is now recognized that natural disasters and extreme weather events trigger epidemic outbreaks (Lau et al., 2010). Similar outbreaks have been reported in Thailand (Wuthiekanun et al., 2007) and Sri Lanka (Agampodi et al., 2010).

Based on the analysis of epizootic and epidemic features of leptospirosis in animals and humans for the period 2003–2022, we aim to identify the established enzootic areas in our country, provide appropriate recommendations and proposals for disease control.

Materials and methods

A retrospective epizootic and epidemiological analysis of leptospirosis incidence in animals and humans in Ukraine for the period 2003–2022 was conducted by the authors of the article. The study investigated the epidemiological situation of leptospirosis in various domesticated species: domestic carnivores (*Canis familiaris* Linnaeus, 1758), domestic felines (*Felis catus* Linnaeus, 1758), horses (*Equus caballus* Linnaeus, 1758), pigs (*Sus scrofa* Linnaeus, 1758), cattle (*Bos taurus* Linnaeus, 1758), sheep (*Ovis* Linnaeus, 1758), and goats (*Capra hircus* Linnaeus, 1758). Information on leptospirosis testing of zoo animals, camels, rabbits, hamsters, fur-bearing animals, rats, badgers, wolves, raccoon dogs, wild animals, hares, foxes, elk, deer, roes, and wild boars was utilized in the article.

The source of data for the analysis of the epizootology of leptospirosis in animals was the reports of regional laboratories of the State Service of Ukraine for Food Safety and Consumer Protection, research data of the State Research Institute for Laboratory Diagnostics and Veterinary and Sanitary Expertise (Kyiv, Ukraine). The data from the reports of Forms 1-Vet and 2-Vet for 2003–2023 were systematized and analyzed. All the data used were based on the results of diagnostic tests (MAT, PCR, ELISA, bacteriological studies).

For the analysis of leptospirosis epidemiology in humans, reports from the Center for Public Health of the Ministry of Health of Ukraine for the period 2003–2023 were analyzed.

The both datasets excluded data from the temporarily occupied territories of the Autonomous Republic of Crimea, the city of Sevastopol, and parts of Donetsk and Luhansk regions.

Reports of the State Statistics Service of Ukraine were the source of data on the total number of susceptible animals (http://ukrstat.gov.ua).

Cartographic visualization was conducted using Quantum GIS 3.16.0, an open-source software available for download at www.qgis.org/ru/site/forusers/download.html. The vector layers depicting the boundaries of Ukrainian oblasts were obtained from the free database accessible at www.diva-gis.org/Data. A quantile classification with 5 classes was applied, ensuring an equal distribution of regions within each class.

Results

The analysis of the results of leptospirosis tests among farm, small and wild animals in Ukraine for the period 2003–2022 shows that 222,323 (3.33%) of 6,543,934 samples tested for leptospirosis during this period were positive for leptospirosis (Fig. 1–11). Among cattle, 3,704,116 tests were conducted and 151,903 head (4.1%) were found to be positive. During the analyzed period, 2,367,501 samples from pigs were tested, of which 49,153 (2.07%) were positive. The number of sheep and goats (small ruminants) tested amounted to 224,215, of which 1545 were positive (0.68%). During this period, 167,595 sera from horses were tested, of which 13,277 (7.9%) were positive for leptospirosis. Also, during this period, 33,053 samples from dogs were tested, of which 5,788 (17.5%) were positive. Of the 747 sera from cats tested, 98 (13.1%) were positive. The number of other animals tested (zoo animals, rabbits, hamsters, etc.) amounted to 6,211, of which 4 (0.06%) were positive. During the analyzed period, 22,125 sera from wild boars from different regions of Ukraine were tested, of which 483 (2.18%) were positive. The number of roe deer tested during the period amounted to 8,277, of which 32 (0.38%) were positive. The number of other wild animals tested during this period amounted to 10,094, of which 40 were positive (0.39%). Therefore, despite the fact that less sera were tested from horses compared to other animal species, the seropositivity rate was 7.9%. Quite high seropositivity rates are also observed among dogs and cats (17.5% and 13.1%, respectively) despite the small number of sera tested compared to agricultural animals.

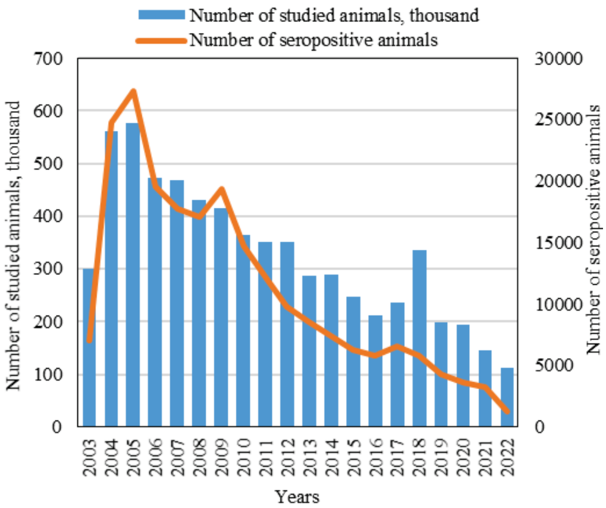

Fig. 1. Dynamics of the number of leptospirosis tests in Ukraine among all animal species and the number of positive test results in Ukraine (2003–2022)

In characterizing the data presented in Figure 1, it is noteworthy that the number of studies conducted among all animal species has significantly decreased. For instance, in 2004 and 2005, the total number of animals tested was 560,467 and 576,234, respectively. However, in 2021 and 2022, it dropped to only 145,283 and 112,085, respectively, indicating a 3.85–5.14-fold decrease in the number of animals tested for leptospirosis. This decline can be attributed to a substantial reduction in livestock across different forms of ownership in Ukraine during those years. Notably, a comparison of the livestock decline from 2003 to 2022 among major farm animal types in Ukraine reveals a 2.92-fold decrease in cattle, a 1.61-fold decrease in pigs, a 13.4-fold decrease in sheep, and a staggering 35.1-fold decrease in horses. Regarding positive leptospirosis cases, there were 24,745 and 27,304 reported in 2004 and 2005, respectively, while this figure decreased to 3,243 and 1,228 in 2021 and 2022, respectively. This represents a 7.63-fold and 22.23-fold reduction in the number of animals testing positive for leptospirosis. Furthermore, in 2005, which marked the peak year in terms of tested livestock and positive cases, the percentage of positive animals across all species stood at 4.73%, decreasing to 1.09% in 2022.

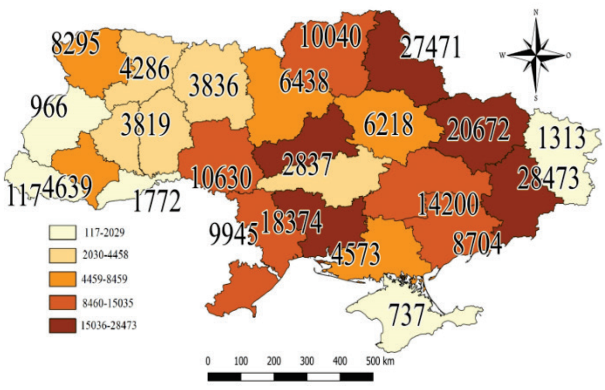

Fig. 2. Maps of the cases distribution of seropositive animals (among all animal species) to leptospirosis in Ukraine (2003–2022)

The analysis of the results of tests for leptospirosis in domestic and farm animals indicates that the largest number of positive animals was found among cattle, pigs and horses. Trends in the number of seropositive animals among different animal species also show a decrease in the number of studies due to the decrease in the number of farm animals in

Ukraine. Figure 5 illustrates the trends in leptospirosis seropositivity in dogs and cats.

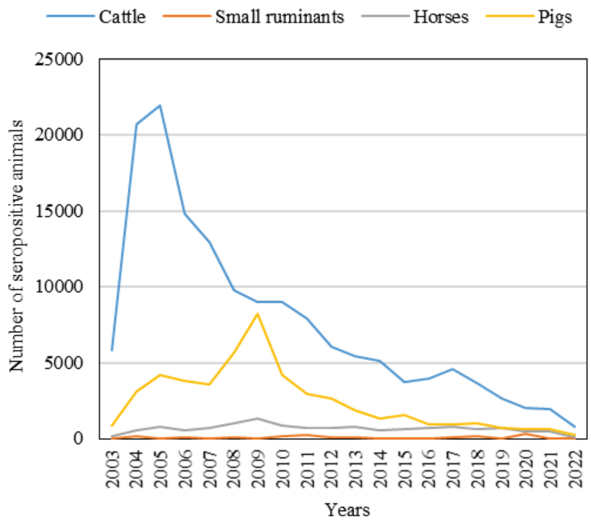

Fig. 3. Dynamics of leptospirosis positive test results among farm animals in Ukraine (2003–2022)

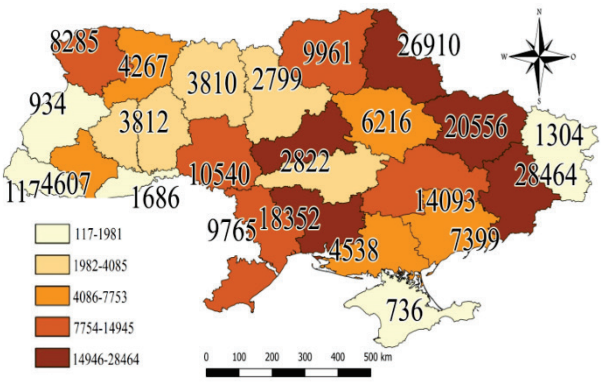

Fig. 4. Maps of distribution of leptospirosis seropositive cases among farm animals (cattle, small ruminants, horses, pigs) in Ukraine (2003–2022)

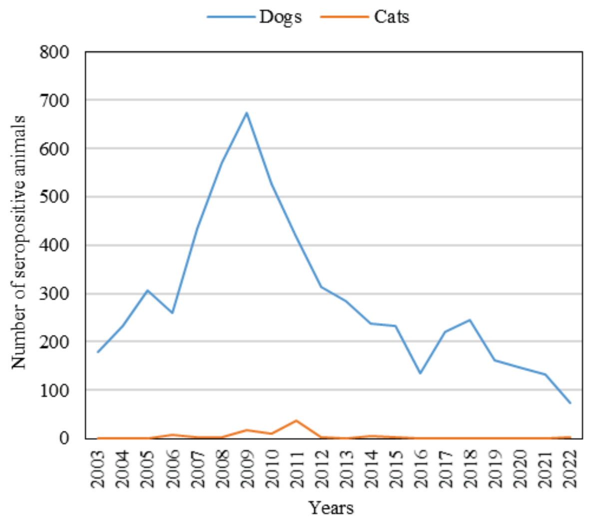

Fig. 5. Dynamics of leptospirosis positive test results among dogs and cats in Ukraine (2003–2022)

As shown in Figure 5, the number of seropositive dogs in 2009 was almost 700. However, among cats, even in the peak years of seropositivity, the number of such animals was less than 50. It is characteristic that the seropositivity among cats is much lower than among dogs. However, the trends of increasing seropositivity in dogs in the period 2007–2015 somewhat coincide with those in cats. The low seropositivity rates (on trends) among dogs and cats do not indicate that these species may be less active carriers of *Leptospira* than the leading species (cattle, pigs, horses, sheep), especially the latter, which indicates a much smaller number of serological studies in small animals.

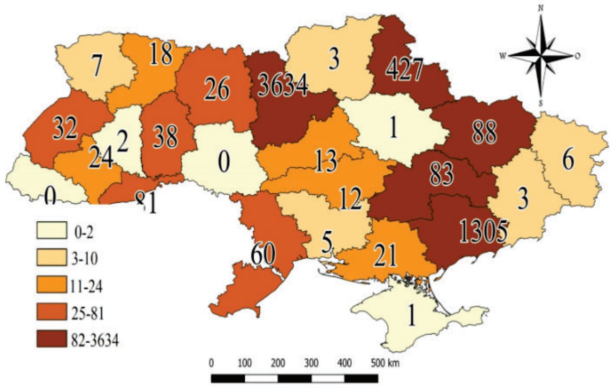

Fig. 6. Map of distribution of leptospirosis seropositive cases among dogs and cats in Ukraine (2003–2022)

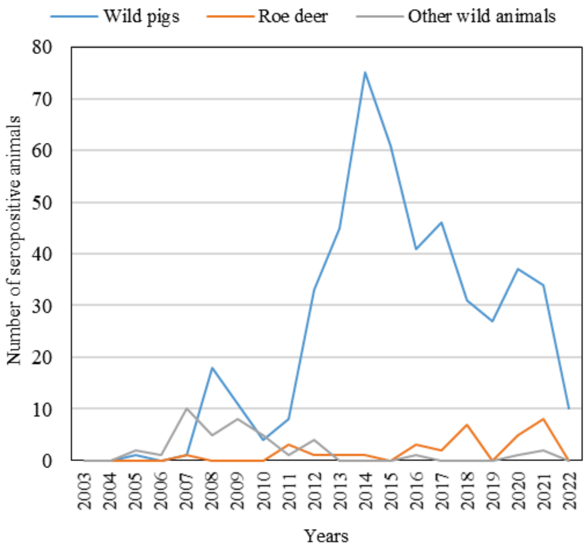

Fig. 7. Dynamics of distribution of leptospirosis seropositive cases among wild animals in Ukraine (2003–2022)

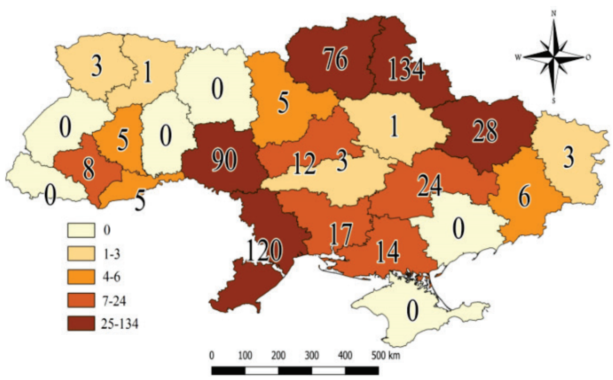

Fig. 8. Maps of the cases distribution of seropositive wild animals to leptospirosis in Ukraine (2003–2022)

The analysis of Figure 7 reveals that the wildlife species investigated in Ukraine serve as both sources and reservoirs of *Leptospira*. Consistent seropositivity is observed among various animal species, including roe deer. However, wild pigs exhibit significant seropositivity trends and emerge as the primary bacterial carriers. In certain years, the seropositivity among wild boars exceeded 70 individuals, spanning across all regions of Ukraine.

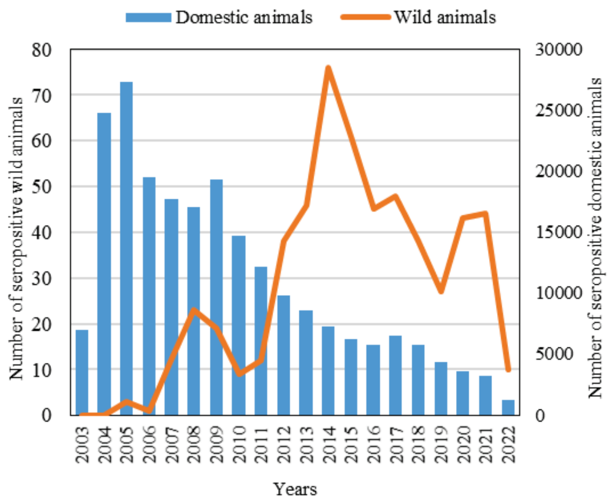

Fig. 9. Dynamics of distribution of leptospirosis seropositive cases among domestic and wild animals in Ukraine (2003–2022)

The analysis of Figure 9 reveals interesting findings. From 2003 to 2015, a notable disparity is observed between the number of positive cases in farm animals and the detection of positive *Leptospirillum* carriers in wild animals. This suggests that the seropositivity in wild and farm animals, despite the significant livestock concentration, exists largely independent of each other. However, a shift in the situation occurs after 2015, coinciding with a substantial decline in the number of farm animals. Following 2015, the trends of seropositivity among wild animals align closely with those among domestic animals. It is our opinion that this shift does not indicate an increased frequency of contacts between wild bacterial carriers and domestic animals. On the contrary, the decrease in such contacts is evident. Nevertheless, these studies highlight the independent existence of anthropogenic and natural foci, operating autonomously.

Additionally, Figures 10 and 11 present the results of studies on leptospirosis in humans in Ukraine from 2003 to 2022.

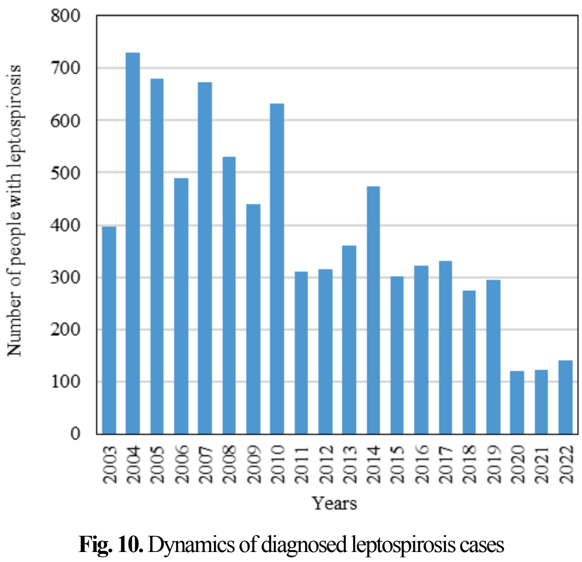

Fig. 10. Dynamics of diagnosed leptospirosis cases among people in Ukraine (2003–2022)

Figure 12 presents data on the number of studies conducted among various animal species, the number of positive responders, and the incidence of human infection in relation to leptospirosis. To facilitate analysis, we compare the percentages (%) of seropositivity among animals and the number of people who contracted the disease. This comparison reveals valuable insights, as a significant number of seropositive animals in a specific area often indicates effective measures such as antibiotic treatment, vaccination, or culling, which contribute to a lower incidence of human infection. Notably, the veterinary medicine service plays a crucial role in identifying and addressing such issues. Encouraging results can be observed in the Vinnytsia, Chernihiv, Mykolaiv, and Kherson regions, where the respective percentages of seropositive animals to sick people for the period 2003–2022 are 4.7/4.9, 4.5/4.7, 8.3/5.9, and 2.1/7.2. These regions demonstrate effective control measures and a relatively low incidence of human infection. However, there are regions where a minimal number of seropositive animals and a comparatively higher number of human cases were identified throughout the analyzed period. Examples of such regions include Zakarpattia, Lviv, and Chernivtsi, where the ratios of seropositive animals to sick people are 0.05/8.5, 0.4/7.1, and 0.8/5.1, respectively. In these cases, concerns may arise regarding the effectiveness of veterinary medicine practices in addressing the issue of leptospirosis in these regions, warranting further investigation and improvements.

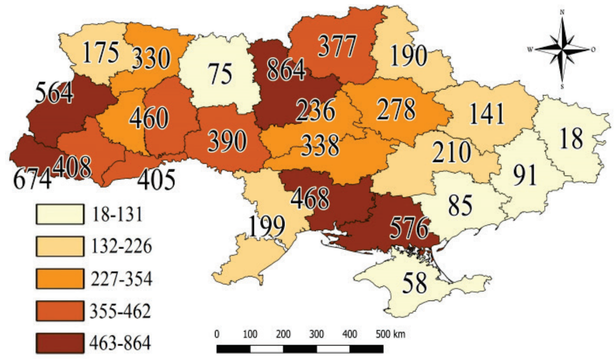

Fig. 11. Maps of the cases of distribution leptospirosis seropositive cases among people in Ukraine (2003–2022)

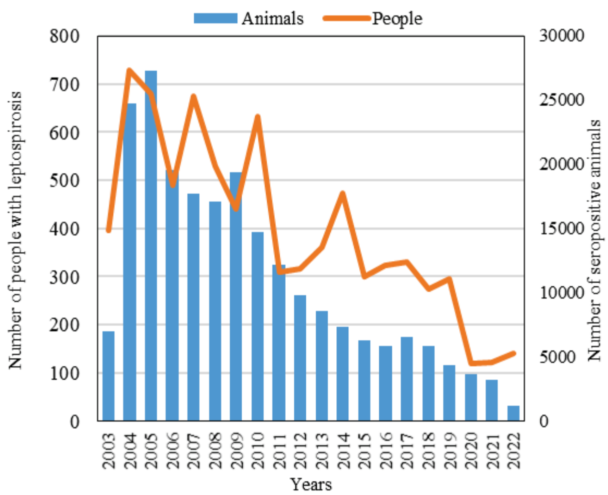

Fig. 12. Dynamics of leptospirosis cases in people and seropositive leptospirosis animals in Ukraine (2003–2022)

The analysis of Figure 12 reveals a notable correlation between the trends in seropositivity among various animal populations, including farm, domestic, and wild animals, and the incidence rates of leptospirosis among humans. This observation provides compelling evidence in support of the hypothesis that *Leptospira*-carrying animals serve as the primary source and reservoir of *Leptospira* for human infections.

During the period under analysis, the number of people who became infected amounted to 7,937. Cluster analysis to identify regions of Ukraine with similar leptospirosis incidence patterns identified four distinct clusters based on reported leptospirosis incidence. Cluster 1 consists of regions with high incidence rates, including Zakarpattia (674 cases, 8.5%), Kherson (576 cases, 7.3%), Lviv (564 cases 7.1%), Kyiv city (480 cases, 6.0%), Mykolaiv (468 cases, 5.9%), Khmelnytsky (460 cases, 5.8%), Ivano-Frankivsk (408 cases, 5.1%) and Chernivtsi (405 cases, 5.1%). Cluster 2 includes regions with moderate incidence rates, such as Vinnytsia region (390 cases, 4.9%), Kyiv region (384 cases, 4.8%), Chernihiv region (377 cases, 4.7%), Kirovohrad region (338 cases, 4.3%), and Rivne region (330 cases, 4.2%), Ternopil (327 cases, 4.1%). Cluster 3 represents the regions with lower incidence rates, including Poltava (278 cases, 3.5%), Cherkasy (236 cases, 3.0%), Dnipro (210 cases, 2.6%), Sumy (190 cases, 2.4%), Odesa (199 cases, 2.5%), Volyn (175 cases, 2.2%), and Kharkiv

(141 cases, 1.8%). Finally, cluster 4 includes the regions with the lowest incidence rates, such as Donetsk (91 cases, 1.1%), Zaporizhzhia (85 cases, 1.1%), Zhytomyr (75 cases, 0.9%), Crimea (29 cases, 0.4%), Sevastopol (29 cases, 0.4%), and Luhansk (18 cases, 0.2%). These clusters provide an idea of the different structure of leptospirosis incidence in different regions of Ukraine. The distribution of cases shows regional differences in prevalence and incidence in Ukraine. Certain regions, such as Lviv, Kherson, Kyiv, Mykolaiv, and Vinnytsia, account for a relatively higher proportion of the total number of cases, ranging from 4.8% to 7.3%. In contrast, regions such as Luhansk and Donetsk oblasts and the Autonomous Republic of Crimea reported fewer cases, accounting for only a fraction of the total number of cases. Such differences in the distribution of cases emphasize the importance of taking into account regional specifics when implementing public health measures. Analyzing the specifics of data distribution in different regions can help to target interventions and allocate resources to effectively manage and control the spread of the disease throughout Ukraine.

The number of registered cases of leptospirosis in humans in Ukraine varied over the analyzed period. In 2003, a total of 379 cases were registered across all regions. Subsequently, the number increased to 729 in 2004 and 679 in 2005. The following years saw fluctuations in the incidence, with 490 cases in 2006, 674 cases in 2007, 530 cases in 2008, and 440 cases in 2009. In 2010, there was a notable increase to 632 cases, followed by a decrease to 310 cases in 2011 and 316 cases in 2012. The number of cases rose again in 2013 to 361 and reached a peak of 473 cases in 2014. Subsequently, a decline was observed with 301 cases in 2015, 323 cases in 2016, and 330 cases in 2017. In the years that followed, the number remained relatively stable, with 274 cases in 2018, 295 cases in 2019, 120 cases in 2020, 122 cases in 2021, and 141 cases in 2022. These figures provide an overview of the fluctuating incidence of leptospirosis in Ukraine from 2003 to 2022.

Discussion

In this article, we studied the epizootic and epidemiological aspects of leptospirosis in Ukraine. The research was based on the results of reports of leptospirosis in different animal species and human morbidity in Ukraine for the period 2003–2022.

Domestic dogs are the primary and occasional hosts of *Leptospira* in urban and rural settings. The main route of transmission of the pathogen to humans is contact with the urine of carrier dogs. Interspecies transmission is facilitated by the behavioral habits of dogs (sniffing and licking), with stray dogs being an important source of infection (Luna et al., 2008; Adler & de la Peña Moctezuma, 2010). The seroprevalence of canine leptospirosis in India has been reported to range from 46.7–71.1% (Behera et al., 2021; Senthilkumar et al., 2023). Our studies have shown that 33,053 sera from dogs were examined during the period 2003–2022, among which antibodies to *Leptospira* were detected in 57868 animals (17.5%). In fact, this species of animal had the highest seropositivity rates, which once again confirms the significant potential of dogs as reservoirs and sources of the infectious agent.

According to research conducted by Murillo et al. (2020), domestic cats are considered risk factors for human transmission of leptospirosis. PCR-based epidemiological studies have confirmed that cats can serve as reservoirs of the bacteria and potentially contribute to human infection (Dorsch et al., 2020; Murillo et al., 2020; Azócar-Aedo, 2023). In Ukraine, out of 747 cat sera tested during the period of 2003–2022, 98 (13.1%) were found to be positive for leptospirosis. These findings suggest that cats are often underestimated as a significant source of the pathogen for human infection, especially considering the relatively small number of tested cats compared to the estimated population of approximately 7.5 million cats in Ukraine. By Worldatlas Ukraine is ranked among the top 10 countries worldwide with the highest number of pet cats (www.worldatlas.com/articles/countries-with-the-most-pet-cats-globally.html). Large-scale epidemiological studies have indicated that the prevalence of leptospirosis among cats can reach up to 11.1% of their total population (Rodriguez et al., 2014). European scientists have identified cats as reservoir hosts of the leptospirosis pathogen, while dogs are considered accidental hosts in this context. These findings highlight the importance of recognizing the role of domestic cats in leptospirosis transmission and emphasize the need for further research and preventive measures involving this animal species.

Cattle are carriers of *Leptospira* and can become chronic carriers of the bacteria after infection, as noted by Levett (2001). In Ukraine, 3,704,116 cattle biological samples were tested during the analyzed period, of which 151,903 (4.1%) were positive for Leptospira antibodies. Although the overall percentage of positive results cannot be considered significant, cattle pose a significant risk as a source of infection for humans. This is because not only the meat of infected animals, but also milk can serve as a potential factor in the transmission and spread of *Leptospira*. Therefore, it is extremely important to take into account the role of cattle in the epidemiology of leptospirosis and implement appropriate measures to reduce the risk of human transmission (Pyskun, 2019).

Pigs have been identified as potential latent carriers of the *Leptospira* pathogen and can serve as a source of infection for humans, as noted by Schommer et al. (2021). In Ukraine, a total of 2,367,501 samples from pigs were examined during the period 2003–2022, with 49,153 (2.1%) testing positive for *Leptospira*. Although the percentage of positive results may not be considered significant, the concern arises from the fact that approximately half of the pig population (around 3 million animals) is kept in private households with limited sanitation conditions. This raises concerns about the potential risk of transmission from pigs to humans. The importance of pigs in the epidemiology of leptospirosis in Ukraine has been previously demonstrated (Ukhovskyi, 2022), and these findings align with that understanding. It is crucial to address the role of pigs in the transmission of *Leptospira* and implement appropriate measures to minimize the risk of infection in both pig farming and household settings.

Small ruminants, such as sheep and goats, have been implicated in the epidemiology of leptospirosis due to the potential excretion of bacteria in their urine, even though most of these animals are asymptomatic carriers of the bacteria, as noted by Haji Hajikolaei et al. (2022). Despite vaccination efforts, some studies have highlighted that small ruminants can still become infected through environmental exposure from infected animals, becoming a source of infection for other animals and humans, particularly when vaccinated with vaccines lacking serovars relevant to the local region, as discussed by Senthilkumar et al. (2023). Seroprevalence studies have indicated a level of 7.4% in sheep and 24.8% in goats, according to Zamora et al. (1975). In our analysis, we examined a total of 224,215 sheep and goats, which constitutes a small proportion of the overall population of these animal species. Furthermore, it is concerning that the number of these species in Ukraine is dramatically decreasing. Among the tested animals, only 1,545 (0.68%) were found to be positive for Leptospira.

Horses are known to carry various serovars of the *Leptospira* pathogen, with *Icterohaemorrhagiae* leptospirae being commonly detected and associated with acute systemic diseases, as documented by Verma et al. (2012). Studies have shown that horses can exhibit seropositivity rates of up to 80%, as reported by Roqueplo et al. (2013). In our analysis, a total of 167,595 horse sera were examined during the study period, revealing that 13,277 (7.9%) tested positive for leptospirosis. It is noteworthy that the majority of seropositive animals were identified in previous years, indicating a decline in recent cases. The substantial reduction in the horse population by more than 10 times compared to 1995–1997 also contributes to the decrease in the number of studies conducted and the overall decline in leptospirosis rates in this species.

Numerous studies have substantiated the role of wildlife as a reservoir of leptospirosis infection for domestic animals, as documented by Vieira et al. (2018). Browne et al. (2022) analyzed 86 large-scale epidemiological studies and identified over 80 wild animal species affected by *Leptospira* pathogens, primarily in the United States and Brazil. The reduction of wildlife habitats has facilitated the bidirectional transmission of the pathogen between farmed animals and wildlife (Matthias et al., 2008; Petrakovsky et al., 2014). Seropositivity rates of up to 72.0% have been observed in deer, specifically *Cervus timorensis*, as reported by Roqueplo et al. (2013). Additionally, wild animals have exhibited seroprevalence rates of up to 70.0% (Zamora et al., 1975). Notably, seropositivity rates of 13.6% were detected in wild boars based on sera collected over a nearly two-year period (Cilia et al., 2020). The majority of wildlife studies have focused on terrestrial animals such as wild boars and raccoons; however, there have been reports of *Leptospira* carriage in aquatic species like sea lions and manatees, as well as reptiles including boas and crocodiles, as noted by Vieira et al. (2018). Leptospirae have also been isolated from poikilothermic animals such as frogs and toads, as evidenced by studies conducted by Gravekamp et al. (1991) and Haake & Levett (2015). In Ukraine, during the analyzed period, 22,125 sera samples from wild boars were tested, with 483 (2.2%) yielding positive results. Similarly, among 8,277 tested roe deer, 32 (0.38%) showed seropositivity. Overall, 10,094 other wild animals were tested, with 40 cases (0.39%) testing positive. While seropositivity in various wildlife species within our territories has been confirmed, the percentage of seropositive wildlife remains relatively low.

The use of inactivated vaccines (whole-cell or membrane) containing one or more pathogenic strains (serovars) of *Leptospira* is a common practice in veterinary medicine to prevent leptospirosis primarily in cattle, pigs, and dogs, as outlined in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals. These vaccines elicit a protective response by inducing the production of antibodies against leptospiral lipopolysaccharide (Adler & de la Peña Moctezuma, 2010). To ensure the effectiveness of vaccination programs, epidemiological studies are conducted to determine the prevalence of different *Leptospira* serovars/serogroups in various animal species (Chapman et al., 1990; Adler & de la Peña Moctezuma, 2010). However, it is important to note that vaccines do not provide long-term immunity, and they may not confer cross-protection against *Leptospira* serovars not included in the vaccine formulation. Furthermore, there are no global vaccination programs established at either the country or global level.

Analysis indicates that the patterns of seropositivity among animals, including farm animals, domestic animals, and wildlife, align with the incidence rates of human leptospirosis. This finding supports the idea that *Leptospira* carriers serve as the primary source and reservoir of the pathogen for humans. Throughout the analyzed period, a total of 7,937 people were reported as infected. The research results suggest that the number of animals seropositive for leptospirosis does not always correlate with the number of human cases in all regions. This discrepancy, where regions with low seropositivity exhibit a high incidence of human cases, highlights significant shortcomings in the prevention and control system for this disease in those particular areas.

Leptospirosis is a significant infectious pathology that affects the welfare of animals and, through them, humans. After all, the transmission of the pathogen between species is the leading problem of leptospirosis. The analysis of the epizootic situation shows how many species of wild and farm animals are involved in the reservoir of the pathogen and the subsequent transmission of the pathogen to humans. Therefore, the causative agents of this zoonosis pose a global threat and require the implementation of the One Health principles of cooperation between the public administration sector, veterinary medicine, environmental agencies and health authorities to control this disease (Schneider et al., 2013; Pal et al., 2021). Leptospirosis is a bright example of this principle, as the connection between animals and natural ecosystems, and ultimately between humans and animals, is fully traced. Therefore, inter-sectoral and interdisciplinary control strategies should be improved in this area to develop common approaches and improve forecasting (Rabinowitz et al., 2013; Schneider et al., 2015). It is impossible to eradicate the components of the epizootic process of leptospirosis in the natural environment, so a significant number of animals and humans are involved in the epizootic and epidemic process. This leads to the conclusion that the disease is extremely closely related to environmental conditions, and the question of eradication of leptospirosis may not be raised at all. It can only be about prevention and control of this infection.

In general, researchers point out that the inclusion of risk factors for the disease depends on the characteristics of the environment (water, moist soils, etc.) in which a certain number of reservoir animals are located, so the significant variability in seropositivity in individual years explains this situation (Perez et al., 2011; Traxler et al., 2014; Dhewantara et al., 2019). Other risk factors are associated with areas with high precipitation, forests, overpopulated regions, poverty, low educational attainment, and lack of sanitation facilities (Santos et al., 2017; Gutiérrez et al., 2019). Ukrainian scientists point out that during 1994–2014, the most at-risk group in the overall leptospirosis incidence was agricultural workers, land reclamation workers, and people engaged in private farming (Hopko, 2017). The author also notes that for the period from 2008 to 2017 in Ukraine, the highest incidence rate was in 2010 (1.38 per 100 thousand people, 622 cases), the lowest – in 2015 (0.7 per 100 thousand, 301 cases). Hopko (2019) also highlights that the infection rates of cattle, pigs, dogs, and cats have an impact on the incidence of leptospirosis in humans.

In general, animals that test positive for the pathogen are those that have survived exposure to *Leptospira* and subsequently serve as reservoirs of the infection. The presence of antibodies merely indicates that the studied animals have been exposed to the pathogen. It has been reported that the prevalence of leptospirosis is considerably higher in rural areas, where a significant number of animals are kept (Erdinc et al., 2006; Alavi & Khoshkho, 2014; Dorsch et al., 2020), which is consistent with our findings from the analysis of the epidemiological and epidemic situation. Towards the end of the previous century, two zones with a high incidence of leptospirosis in humans emerged in Ukraine. The first zone encompassed the territories of Zakarpattia, Chernivtsi, Ivano-Frankivsk, Ternopil, and Khmelnytskyi regions, while the second zone extended along the Dnipro River (Chernihiv, Kyiv, Cherkasy, Kirovohrad, and Mykolaiv regions) (Hopko, 2019).

Thus, the complexity of controlling leptospirosis lies in the epizootic and epidemiological features of the disease. After all, pathogens are able to develop symbiotic relationships with many host animals (when Leptospirae persist in the kidneys for months without causing active disease in the host). In addition, wild animals form an active reservoir of the pathogen and are active sources of the pathogen for farm animals (Haake & Levett, 2015; Rajapakse, 2022).

The State Service of Veterinary Medicine is responsible for planning preventive measures and ensuring the monitoring and control of potential carriers of the pathogen. Epidemiologists play a crucial role in investigating human infection cases and strengthening preventive measures to mitigate the spread of the disease among humans. The primary objective of this analysis is to improve the epidemiological situation of leptospirosis in farm animals, leading to a reduction in the number of infected domestic animals and, consequently, in human cases. Our research findings demonstrate a wide distribution and prevalence of leptospirosis among various species of farm and wild animals. The disease is endemic among domestic animals and affects all species.

Conclusion

Our research has established a significant prevalence of leptospirosis in various animal species in Ukraine. During the period 2003–2022, 6,543,934 samples of biological materials from farm, small and wild animals were tested for leptospirosis, of which 222,323 or 3.33% were positive. During the analyzed period, 7937 people fell ill with leptospirosis. Significant incidence was recorded in Zakarpattia – 674 people, Lviv – 564, Kherson – 576. The peak years in the incidence of leptospirosis were 2004 – 729 people, 2005 – 679, 2007 – 674, 2010 – 632 people. Currently, there is a positive trend of decrease in the incidence of leptospirosis. The peak of seropositivity among different animal species was in 2005–2012 (except for wild boars, in which the peak of seropositivity occurred in 2012–2020). In general, there was a 3.85–5.14-fold decrease in the number of animals tested for leptospirosis at the beginning and end of the analysis, which is explained by a significant reduction in the number of different animal species in the country. Leptospirosis carrier animals are reservoirs and sources of the pathogen not only for animals but also for humans, they complicate the epidemic situation with this disease in our country.

Considering the challenging epizootic and epidemic situation of leptospirosis in Ukraine, it is necessary to improve preventive measures and raise public awareness about the disease, particularly in rural areas. Given the zoonotic nature of leptospirosis, it is imperative to prioritize the implementation of the One Health concept. This approach aims to identify the underlying factors driving the disease and enables effective prevention and control strategies for leptospirosis. By adopting a comprehensive and interdisciplinary approach, involving collaboration between veterinary medicine, public health, and environmental agencies, we can better understand and address the complexities of leptospirosis transmission and reduce its impact on both animal and human health.

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The authors declare that there is no conflict of interest.

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