

## ORIGINAL ARTICLE

## RETROSPECTIVE ANALYSIS OF LEPTOSPIROSIS MORBIDITY IN IVANO-FRANKIVSK REGION (EPIDEMIOLOGICAL AND CLINICAL CHARACTERISTICS)

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Oleksandra Ya. Pryshliak, Tetiana O. Nikiforova, Zoriana R. Tylishchak, Oleksandr P. Boichuk, Nadiya V. Vaskul, Oksana V. Kopchak, Andriy L. Protsyk

IVANO-FRANKIVSK NATIONAL MEDICAL UNIVERSITY, IVANO-FRANKIVSK, UKRAINE

### ABSTRACT

**The aim:** To perform a retrospective analysis of leptospirosis morbidity in Ivano-Frankivsk region, to give the etiological characteristics of leptospirosis according to clinical-laboratory parameters, to determine the peculiarities of the course, prognostic features.

**Materials and methods:** Data of the State Enterprise "Ivano-Frankivsk Regional Laboratory Center of the Ministry of Health of Ukraine", reports and abstracts of medical records of the Regional Clinical Infectious Diseases Hospital for 2009-2018 were used. Clinical observation of patients, analysis of general-clinical, biochemical, and serological indices were carried out.

**Results:** The leptospirosis morbidity in Ivano-Frankivsk region during 2009-2018 was higher than in general in Ukraine. Activation of foci of leptospirosis *L. pomona* and grippotyphosa in 2009-2013, decrease of *L. grippotyphosa* and increase of *L. pomona* foci and "new" *L. autumnalis*, *australis*, *bataviae*, *cynopteri* in 2014-2018 were noted. The emergence of leptospirosis *L. autumnalis*, which had a high virulence and caused a severe course, was noted.

**Conclusions:** The leptospirosis morbidity in the Ivano-Frankivsk region over the past 10 years has exceeded the incidence in Ukraine and varied within 0.62-2.2 per 100,000. During the last 5 years, the serological structure has changed: *L. pomona* (27.7%) prevailed, *L. grippotyphosa* decreased (2.1%), *L. bataviae* and *cynopteri*, *autumnalis* increased (by 8.5%). Seasonality is shifted in the autumn-winter period (November-February) (*L. grippotyphosa*, *australis*, *pomona*, *canicola*). According to forecasts, leptospirosis induced by *L. autumnalis* was most adverse. Leptospiroses of serogroups *L. australis*, *bataviae*, *cynopteri* had a mild course, there were fewer complications.

**KEY WORDS:** Leptospirosis, seasonality, focus, serogroup, Ivano-Frankivsk region

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### INTRODUCTION

The pandemic distribution of leptospirosis causes considerable attention to this disease. The disease is registered more than in 80 countries of the world and ranks third in terms of natural-focal diseases [1, 2, 3]. A lot of attention has been paid to the study of leptospirosis in Ukraine: epidemiology has been studied in different geographical areas, natural foci have been identified, and the link between morbidity and the farming system, clinical manifestations, treatment methods [4, 5] have been determined. The difficult economic situation in Ukraine led to the destruction of the system of sanitary-veterinary control of the population of rodents – the main sources of leptospirosis pathogens. Also, the etiological structure of morbidity, periodicity and seasonality has significantly changed [6]. Due to the severity of the clinical course and indicators of lethality, leptospirosis is one of the first places in infectious pathology. The mortality rate of the disease in Ukraine in recent years is about 10%. High mortality is associated with the toxic effect of the pathogen on the important organs of the human being (kidney, liver, heart) [3, 7, 8, 9].

Leptospirosis is the most widespread in the Western and Central regions of Ukraine, and the highest level is registered in the Lviv, Ivano-Frankivsk, Ternopil and Rivne

regions. The peculiarity of the Ivano-Frankivsk region is determined by its physical-geographical location, favorable weather conditions and composition of the fauna, which provides the prerequisites for the formation of the natural and anthropogenic foci of leptospirosis [5, 10]. Earlier in Ukraine and in the region the *Leptospira* of serovar *L. icterohaemorrhagiae* dominated, but from 2010 the leading place was occupied by *Leptospira L. grippotyphosa*, *L. pomona*, *L. canicola* and *L. hebdomadis* [5, 11]. It is believed that diseases caused by *Leptospira* of different serogroups have a single pathogenesis and pathological anatomy, clinical course, but this situation is not entirely accurate [12, 13]. Studies performed by us during 2009-2013 show the activation of the cells of *L. pomona* leptospirosis, as well as the occurrence of sporadic cases of *L. autumnalis* leptospirosis, which was characterized by high virulence and severity of the course of the disease. Some cases of leptospirosis of serogroups *L. australis* and *L. bataviae* had a mild course [14]. Taking into account the high morbidity, lethality of leptospirosis, the diversity of serovariants of pathogens, the emergence of new foci, more careful study of regional peculiarities of the epidemiological trend and clinical manifestations of this disease.

## THE AIM

To perform a retrospective analysis of the morbidity of leptospirosis in the Ivano-Frankivsk region, to give the etiological characteristics of leptospirosis according to clinical-laboratory parameters, to determine the peculiarities of the course, prognostic signs.

## MATERIALS AND METHODS

There were used data of the State Enterprise "Ivano-Frankivsk Regional Laboratory Center of the Ministry of Health of Ukraine", reports of the Regional Clinical Infectious Diseases Hospital (RCIDH), hospitalization records of patients treated in RCIDH for the period from 2009 to 2018 inclusive. The clinical observation of patients, analysis of general-clinical and biochemical parameters, serological results of the examination were performed.

## RESULTS AND DISCUSSION

The Ivano-Frankivsk region is located in the west of Ukraine and borders on Lviv, Ternopil, Chernivtsi and Zakarpatska. In the south it has a state border with Romania, where there is also high leptospirosis morbidity. By the nature of the relief, the region is divided into three parts: plain, foothill, and mountainous. The flat part – area near the river Dniester – is adjacent to the Dniester River. Here the forest-steppe dominates – the agricultural area of the region. In the middle part – the foothills – the forest landscape with broad-leaved forests prevails. The mountainous part of the region is occupied by the Eastern Carpathians. The region is in the zone of moderately continental climate, the most humid in Ukraine (humidity coefficient is 1.5-3.0). The average annual precipitation – is from 600 to 1550 mm. Water resources are represented by superficial (rivers, lakes, reservoirs) and underground waters. There are three water reservoirs in the region (Burshtyn, Chechva, Kniahynyn) with an area of 1670 hectares. The rivers with a length of up to 10 km – 8128, over 10 km – 188, and over 100 km – four, prevail: Dniester (1362 km), Prut (910 km), Limnytsa (122 km), Svicha (107 km). The prevalence of the population occupied by agricultural labor and geographical peculiarities contribute to the spread of pathogens of leptospirosis among rodents, animals and human infection.

The morbidity of leptospirosis in Ivano-Frankivsk oblast and in Ukraine over the last 10 years (2009-2018) is represented in Table I.

From the data in Table I, it is evident that the leptospirosis morbidity in the Ivano-Frankivsk region was higher than in the whole Ukraine in all years except 2012. The high rates were in 2010, 2014 and 2018 (2.71, 2.27, 2.26 per 100 thousand of population respectively).

Retrospective data on the incidence of leptospirosis in the region from 1980 to 2018 are represented in Figure 1.

Retrospectively, in the dynamics of morbidity in leptospirosis, three periods can be distinguished: from 1980 to 1988 – during some years the disease has not been registered or there have been sporadic cases. Since 1988,

the rise in the morbidity with a maximum in 1992 – 7.56 per 100 thousand of population, and a gradual decrease before 2000 – 2.34 per 100 thousand of population. Since then, the intensive index varies within the 3.48-0.62 per 100 thousand. Fluctuations indicate a certain periodicity of the increase in leptospirosis morbidity (3 years), which is related to the level of infection of domestic and agricultural animals, the number of rodents, the sanitary condition of settlements, the volume of deratization.

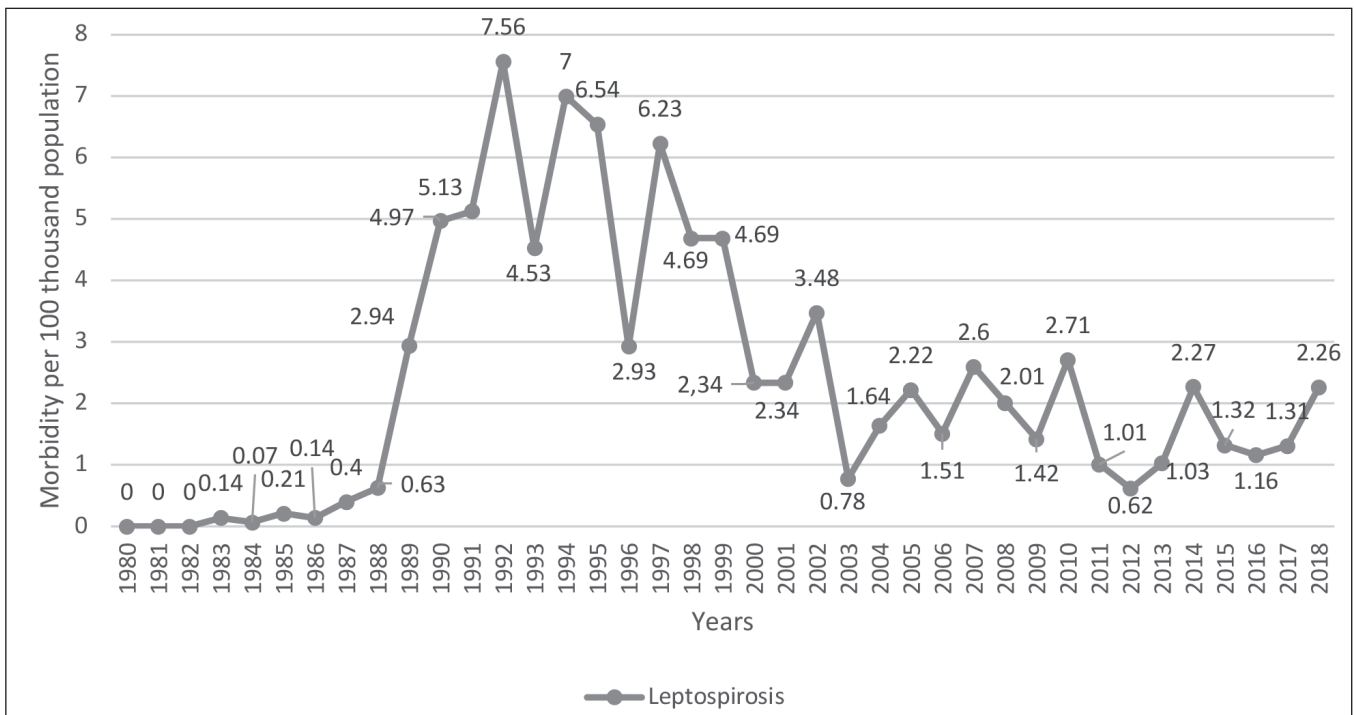
Territorial distribution of leptospirosis morbidity in the region has its own peculiarities. Primarily, the incidence was recorded the area near the Dniester river: Halych (2011 – 4.54 per 100 thousand), Kolomyia (2010 – 6.59 per 100 thousand), Dolyna (2012 – 2.92 per 100 thousand), Tysmenytsia (2013 – 2.32 per 100 thousand) areas. Gradually, the morbidity spread to the foothills where a dense river network is developed. In mountainous regions (Verkhovyna, Nadvirna), very rare cases were registered. The number of foci increases, there were added Tlumach (2016 – 4.12, 2018 – 6.29 per 100 thousand), Snyatyn (2016 – 3.15, 2018 – 10.76 per 100 thousand), Horodenka districts (2016 – 3.83, 2018 – 4.11 per 100 thousand). Over the past 5 years, mortality in the region was an average 0.32 per 100 thousand, in Ukraine – 0.12 per 100 thousand of population.

There is a clear summer-autumn seasonality of leptospirosis – from July to October. On average, the increase in morbidity begins to be recorded from July each year (9.2% from average annual) with a clear peak in September (24.6% from average annual) and October (10.8% from average annual). Seasonality is due to agricultural activity in summer (June-July) and harvesting in autumn (September), as well as infection through water. The second peak of morbidity is observed in December (12.3%), coincides with the migration of mouse rodents from the environment into the outbuildings.

In RCIH over the past 10 years, 161 patients with leptospirosis were treated (85.7% of the diagnosis was confirmed serologically), 11 persons died (mortality rate – 6.8%). To evaluate changes in the etiological spectrum, patient charts for 2009-2013 and 2014-2018 were analyzed.

The basis of the etiological spectrum in the first group (63 serologically confirmed cases) were: *L. pomona* (22.92%) and *L. grippotyphosa* (22.92%), *L. icterohaemorrhagiae* (16.6%), *L. canicola* – 10.42 %, there were new *Leptospira* which were not previously registered: *L. autumnalis* (10.42%), *L. australis* (6.28%), *L. bataviae* (6.28%), *L. cynopteri* (4.16%).

In 2014-2018 (75 serologically confirmed cases), in the etiological composition of leptospirosis there was a shift. *L. pomona* also prevailed – 27.7%, but *L. grippotyphosa* decreased to 2.1%, *L. icterohaemorrhagiae* and *L. canicola* were often met (by 12.8%), *L. bataviae* and *L. cynopteri* *L. autumnalis* (by 8.5%) were registered more often, there were single cases of *L. tarassovi* and *L. australis* (by 2.1%). In part of patients in 2018 (15.9% of all), 2-3 *Leptospira* were detected in diagnostic titers (1:200-1:800). Among them the "new" *Leptospira* prevailed that were not pre-



**Fig. 1.** Leptospirosis morbidity in Ivano-Frankivsk region for the period of 1980-2018 (per 100 thousand population)

**Table I.** Leptospirosis morbidity in Ivano-Frankivsk region and Ukraine for the period of 2009-2018 (per 100 thousand population).

Years	Ivano-Frankivsk region		Ukraine		Relative indicator of the comparison of the intensity index
	Absolute value	Per 100 thousand population	Absolute value	Per 100 thousand population	
2009	20	1.42	438	0.95	1.50
2010	38	2.71	632	1.37	1.98
2011	15	1.01	314	0.68	1.49
2012	9	0.62	316	0.7	-0.89
2013	14	1.03	320	0.79	1.30
2014	31	2.27	474	1.04	2.18
2015	18	1.32	301	0.7	1.89
2016	16	1.16	321	0.76	1.53
2017	18	1.31	322	0.78	1.68
2018	31	2.26	273	0.64	3.53

viously found – *L. javanica*, or were rarely registered – *L. bataviae*, *L. cynopteri*, *L. autumnalis*, often in conjunction with *L. icterohaemorrhagiae*. Of all the fatal cases in 2018, one is due to a combination of 3 serovariants: *L. icterohaemorrhagiae*, *L. grippityphosa* and *L. pomona*.

The patient charts (epidemiological history, clinical manifestations and laboratory data) were analyzed for the comparison of diseases caused by different serogroups. Men dominated – 77.1%, rural population, aged from 22 to 82, the largest group included individuals aged 50-70. Children were two under 18 years of age, with leptospirosis *L. rhomona*, of moderate severity. There were no mild forms, medium severe – 10.4% (*L. pomona*, *L. cynopteri*), anicteric – 4.3% (*L. grippityphosa*, *L. pomona*, *L. australis*). The rest of the patients were diagnosed with a severe form.

The water route predominated in summer in patients with *L. pomona*, *L. bataviae*, *L. grippityphosa*: patients drank dirty water, swam in the river, the pond. In other cases, the infection was associated with the care of animals and the contact with rodents. Patients were admitted to RCIH from June to October, but few cases – in the inter-season period in April-May (*L. grippityphosa*, *L. icterohaemorrhagiae*) and in the autumn-winter period (November-February) (*L. grippityphosa*, *L. australis*, *L. pomona*, *L. canicola*). It's interesting, that *L. autumnalis* corresponded to its name and was registered only in September-October.

Most patients had a high temperature – 39-40°C; it was somewhat lower in patients with *L. australis* – 37.5-39°C. All patients had pain in the muscles, except for a few patients with *L. australis*, *L. pomona*. Nausea and vomiting

were noted in 21% of patients, most often with *L. grippotyphosa* and *L. canicola*. All patients had jaundice, except for single anicteric forms. High average values of bilirubin were in patients with *L. icterohaemorrhagiae*, *L. autumnalis*, *L. canicola*, –  $397.08 \pm 25.20$ ,  $485.89 \pm 41.22$ ,  $372.50 \pm 30.09$   $\mu\text{mol/l}$ , respectively. The protein spectrum (total protein and albumins) changed most in *L. grippotyphosa* and *L. autumnalis* (decreased to 45 g/l and 40%, respectively). The least damage to the liver was in patients with *L. australis* and *L. cynopteri* (bilirubin –  $108.36 \pm 9.90$ ,  $143.85 \pm 12.45$   $\mu\text{mol/l}$ ). The largest size of the liver was in patients with *L. autumnalis* ( $17.5 \pm 0.8$  cm), and the smallest one was in *L. canicola*, *L. grippotyphosa* ( $14.3 \pm 0.1$  cm). Anemia, leukocytosis, high ESR were in all patients, but *L. grippotyphosa* (leukocytosis –  $26.0 \pm 1.8 \cdot 10^9$ ), *L. icterohaemorrhagiae* (Hb –  $88 \pm 6.2$  g/l), *L. autumnalis* (ESR –  $57.0 \pm 4.2$  mm/h) gave the greatest shifts in average hematological indices. In patients with *L. pomona*, *L. cynopteri*, *L. bataviae*, these indices changed to a much lesser extent.

Acute renal failure (ARF) with polyuria phenomena was present in almost all patients. The most severe ARF was caused by *L. icterohaemorrhagiae* (urea –  $26.10 \pm 3.83$  mmol/l), *L. grippotyphosa* (creatinine –  $375.79 \pm 28.32$  mmol/l), and also *L. autumnalis*, *L. canicola*. Significantly lower were those in patients with *L. cynopteri* and *L. australis* (urea –  $17.98 \pm 0$ , creatinine –  $173.55 \pm 10.32$ , urea –  $19.08 \pm 1.67$ , creatinine –  $277.90 \pm 18.92$  mmol/l, respectively). Acute hepatic encephalopathy (precoma 1) and DIC syndrome were observed in 1 patient with *L. autumnalis* and in 1 patient with *L. grippotyphosa*. Infectious-toxic shock of the 1-2 degree was in 2 patients with *L. icterohaemorrhagiae* and in 1 patient with *L. canicola*. Hemorrhagic syndrome was most pronounced and more frequent in *L. grippotyphosa*, *L. icterohaemorrhagiae*, *L. autumnalis*. Reactive pancreatitis was observed in 76% of patients with different *Leptospira*, with the exception of *L. cynopteri*, *L. australis*, and was accompanied by an increase in the level of  $\alpha$ -amylase of blood, diastase of urine, hyperglycemia. Pneumonia was found in 34.8% of patients with different serovariants, complicated by pleurisy, hydrothorax, respiratory insufficiency. Cardiac damage (carditis, atrial fibrillation) was observed in leptospiroses *L. icterohaemorrhagiae*, *L. grippotyphosa*, *L. autumnalis*, *L. pomona*. Unfortunately, *L. javanica* was registered only in combination with other *Leptospira*, that did not give us the possibility to reveal its clinical peculiarities.

Thus, in Ivano-Frankivsk oblast, the intensification of the foci of the leptospirosis of the serogroup *L. rhomona* and *L. grippotyphosa* in 2009-2013, the sharp reduction of *L. grippotyphosa* in 2014-2018 and the increase of the foci of *L. rhomona* and the “new” *Leptospira* *L. autumnalis*, *L. australis*, *L. bataviae*, *L. cynopteri*, *L. javanica*. The emergence of new foci of leptospirosis in foothill areas is explained by an increase in the number of infected rodents, mammals, domestic animals due to the infection of soil, water, unsatisfactory vaccination of domestic animals, the termination of both urban and field 2-time deratization. According to the clinical and laboratory features, one can distinguish etiologic differences

in leptospiroses, the occurrence of leptospirosis cases in the serogroup of *L. autumnalis*, which has high virulence, with the severity of the disease is not inferior to the traditional serogroups – *L. grippotyphosa* and *L. icterohaemorrhagiae*. Single cases of leptospirosis of serogroups *L. cynopteri* and *L. australis* have a mild course. These data require further investigation in terms of evidence.

## CONCLUSIONS

1. The morbidity of leptospirosis in the Ivano-Frankivsk region over the past 10 years has exceeded the level of morbidity in Ukraine and ranged from 0.62 to 2.2 per 100 thousand of population.
2. During the last 5 years the serological structure of leptospiroses in the Ivano-Frankivsk oblast has changed. The leading role in epidemiology was *L. rhomona* (27.7%). The topicality of *L. grippotyphosa* (2.1%) has decreased, the registration of *L. bataviae* and *L. cynopteri*, *L. autumnalis* (by 8.5%) has increased.
3. Periodicity of rise in leptospirosis morbidity was determined every 3 years. Seasonality is shifted in the autumn-winter period (November-February) (*L. grippotyphosa*, *L. australis*, *L. pomona*, *L. canicola*).
4. Prognostic most adverse is the course of leptospirosis caused by *L. autumnalis*. Leptospiroses of the serogroups *L. australis*, *L. bataviae*, *L. cynopteri* had a relatively easier course and much less complications.

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#### ORCID and contributionship:

*Oleksandra Ya. Pryshliak: 0000-0002-3256-5108<sup>F</sup>*  
*Tatiana O. Nikiforova: 0000-0002-5891-0168<sup>D</sup>*  
*Zoriana R. Tylishchak: 0000-0002-7891-2849<sup>B</sup>*  
*Oleksandr P. Boichuk: 0000-0003-0646-6533<sup>A</sup>*  
*Nadiya V. Vaskul: 0000-0002-5368-7948<sup>E</sup>*  
*Oksana V. Kopchak: 0000-0002-6352-6638<sup>C</sup>*  
*Andrii L. Protsyk: 0000-0003-2041-5337<sup>B</sup>*

#### Conflict of interest:

*The Authors declare no conflict of interest.*

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#### CORRESPONDING AUTHOR

##### **Oleksandr P. Boichuk**

Ivano-Frankivsk National Medical University  
 2 Galitska st., 76000 Ivano-Frankivsk, Ukraine  
 tel: +380506749109  
 e-mail: opboy@ukr.net

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