EPIDEMIOLOGICAL STUDY OF SELECTED ZOONOTIC DISEASES IN SLOVAKIA
EPIDEMIOLOGICKÁ ANALÝZA VYBRANÝCH ZOONÓZ NA SLOVENSKU

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ABSTRACT
Background: Zoonoses are infections of animals (vertebrates) that are transmissible to humans by both direct and indirect contact. The etiological agent may be viruses, bacteria, fungi, parasites or prions. More than 200 diagnoses are currently classified as zoonoses. Increasing trends in incidence of zoonotic diseases were observed in previous years due to worldwide travel, globalization of markets, and human destruction of animal habitat. *Objectives:* The objective of the study is to conduct the epidemiological analysis of selected zoonoses- tick-borne encephalitis, Lyme disease, listeriosis and toxoplasmosis in Slovakia in time period of 2010–2019.
Methods: We quantified crude-morbidity rate and age-adjusted morbidity rate. We observed morbidity trend over last 10 years and morbidity in districts of Slovakia.
Results: We can observe an increasing trend in morbidity from tick-borne encephalitis (crude morbidity 1.70/100 000 in 2010 vs. 2.97/100 000 in 2019), with the maximum occurrence in Trenčín and Žilina districts. In Lyme disease, we found a stable trend in morbidity, while copying the epidemiological situation of tick-borne encephalitis. Listeriosis as one of the most common food-borne zoonosis has a stabilized morbidity trend, with a crude morbidity value of 0.34/100 000 in 2019. In toxoplasmosis, we observed a slightly decreasing trend (crude morbidity rate 2.55/100 000 in 2010 vs. 1.74/100 000 in 2019).
Conclusion: Epidemiological overview of zoonotic diseases with surveillance are essential tools in decision-making for implementing timely preventive and control measures.

Key words: Tick-borne encephalitis. Lyme disease. Listeriosis. Toxoplasmosis.

ABSTRAKT
Východiská: Zoonózy sú infekcie zvierat (stavovcov), ktoré sú prenosné na človeka priamym ale aj nepriamym kontaktom. Etiologickým agens môžu byť vírusy, baktérie, huby, parazity alebo prióny. Viac ako 200 diagnóz je v súčasnosti klasifikovaných ako zoonózy. V uplynulých rokoch boli zaznamenané rastúce trendy vo výskyte zoonotických chorôb v dôsledku celosvetového cestovania, globalizácie a deštrukcie biotopov zvierat ľudskou činnosťou.
Ciele: Cieľom štúdie je vykonať epidemiologickú analýzu vybraných zoonóz – kliešťovej encefalitídy, lymskej boreliózy, listeriózy a toxoplazmózy na Slovensku za obdobie rokov 2010–2019.
Metodika: Kvantifikovali sme hrubú mieru chorobnosti a vekovo štandardizovanú chorobnosť. Pozorovali sme trend chorobnosti za posledných 10 rokov a chorobnosť v jednotlivých okresoch Slovenska.
Výsledky: Môžeme pozorovať stúpajúci trend chorobnosti na kliešťovú encefalitídu (hrubá chorobnosť 1,70/100 000 v roku 2010 vs. 2,97/100 000 v roku 2019), pričom najvyšší výskyt je v Trenčianskom a Žilinskom kraji. Pri lymskej borelióze sme zistili ustálený trend chorobnosti, pričom maximálne hodnoty výskytu kopírujú epidemiologickú situáciu kliešťovej encefalitídy. Listerióza ako jedna z najčastejších zoonóz prenášaných potravinami má stabilizovaný trend výskytu, s hodnotou hrubej chorobnosti 0,34/100 000 v roku 2019. U toxoplazmózy sme zaznamenali mierne klesajúci trend výskytu (hrubá chorobnosť 2,55/100 000 v roku 2010 vs. 1,74/100 000 v roku 2019).
Záver: Epidemiologický prehľad výskytu zoonotických chorôb spolu so surveillance sú nevyhnutnými nástrojmi pre rozhodovanie na zavedenie včasných preventívnych a kontrolných opatrení.

Kľúčové slová: Kliešťová encefalitída. Lymská borelióza. Listerióza. Toxoplazmóza

INTRODUCTION

Human-animal contact has always led to the transmission of infectious diseases called zoonoses. Zoonoses are the group of infectious diseases that are transmissible from an animal to a human being. The causative zoonoses agents are viruses, bacteria and parasites. Methods of transmission from animals to human being are direct contact with the infected animal, alimentary transmission and transmission via vector [1]. In the past, zoonoses have caused the majority of infectious diseases cases, and even today they have a significant presence in the number of new cases of infectious diseases. They represent a major public health problem around the world due to our close relationship with animals in agriculture, as companions and in the natural environment [2].

The impact of climate changes, especially global warming has improved living conditions for *Ixodes ricinus*, which led to increasing trend of new cases of tick-borne encephalitis and Lyme disease [3]. In 1986, 20 new cases of tick-borne encephalitis were diagnosed in Slovakia per a year, while in 2016, there were confirmed almost 200 of new cases [4]. Tick-borne encephalitis is a viral infectious disease involving the central nervous system. The disease clinically manifests as meningitis, encephalitis, or meningoencephalitis. The incidence of long-term neurological consequences is in 30 to 60 % of patients and permanent neuropsychiatric consequen-

ces are observed in 10 to 20 % of infected patients. Clinically serious cases have been observed in younger and middle-aged adults in recent years with mortality rate from 1 % to 3 %. Convalescence period is usually very long with high costs on health-care provider level [5].

In Slovakia, the morbidity of Lyme disease was 5.00/100 000 in 1989, 19.08/100 000 in 2010 and 21.08/100 000 in 2016. Long-term trend of Lyme disease morbidity is increasing in Slovakia.

Arthritis caused by borreliosis mostly affects large joints – knee and elbow. Other manifestations may be encephalitis, encephalopathy and polyneuropathy – these occur mainly in adults. In addition to common rashes (erythema migrans), lymphocytoma may occur in a row, usually on the ear lobe or breast. Bannwarth syndrome is similarly rare in Europe as a complication [6]. In 10–20 % of patients who have overcome Lyme disease, symptoms such as fatigue, muscle and joint pain, speech disorders, cognitive impairment, impaired short-term memory and concentration continue to appear [7].

Listeriosis as one of the most common food-borne zoonosis in Slovakia is important and continuous public health problem. Listeriosis lethality can reach up to 30 %, especially in less developed regions. Prevalence in Europe in 2016 was 0.5/100 000 (2536 cases) with a mortality rate of 16.2 % [8]. In 2016, up to 99.2 % of patients with listeriosis had to be hospitalized – listeriosis was the disease with the highest rate of hospital admission. The most common complication or consequence of listeriosis is septicaemia and meningitis. Other common complications are encephalitis, brain abscess and endocarditis. In pregnant women, it often takes place under the image of influenza with subsequent premature birth or miscarriage, or congenital disease – granulomatosis infantiseptica [9]. Listeriosis is one of the diseases with the highest level of economic burden among all infectious diseases, also due to the relatively low number of cases [10].

Toxoplasmosis is one of the most common zoonoses in Slovakia and based on a national seroprevalence survey, it is one of the most common (10–85 %) diseases in humans. In Slovakia, in 1986 prevalence was 6.0/100 000, while in 2016, prevalence decreased to 2.4/100 000. Despite the downward trend in incidence, toxoplasmosis is still a common and dangerous disease, especially for pregnant women and immunocompromised patients [11]. Toxoplasmosis in most immunocompetent patients is carried out inaparently with non-specific flu-like symptoms. In immunocompromised patients (especially patients with HIV– as an opportunistic infection) brain abscess is frequently observed. In an epidemiological study conducted in Mexico, toxoplasmosis accounted for up to 42 % of opportunistic infections in HIV patients and toxoplasmosis encephalitis has been reported in 1–5 % of HIV patients [12]. Congenital form of toxoplasmosis can cause harm to the foetus depending on the period of infection [13].

These zoonotic diseases are public health threat due to the increase in the number of new cases, due to the clinical severity with long-term and permanent consequences leading to disabilities and lower health-related quality of life and economic burden.

STUDY OBJECTIVE

Main aim of our study was to conduct epidemiological analysis of selected diagnosis of zoonotic diseases (tick-borne encephalitis, Lyme disease, listeriosis and toxoplasmosis) in Slovakia in period of years 2010-2019 with specific objectives: 1) to find out trend of crude morbidity rate and age-adjusted morbidity rate of selected zoonotic diseases; 2) to quantify age-adjusted morbidity rate of selected zoonotic diseases by districts of Slovakia.

METHODS

The design of our study is cross-sectional study, one of the observational designs. This design allows to measure the occurrence of a disease in population considering demographic characteristics of the given groups related to the specific environment.

Observed study group consisted of patients diagnosed with laboratory confirmation of following zoonotic diseases by ICD 10 [14] in time period of years 2010-2019 in Slovakia:

- A84 – Thick-borne viral encephalitis,
- A69.2 – Lyme disease,
- A32 – Listeriosis and
- B58 – Toxoplasmosis.

We have collected data retrospectively from Epidemiological Information System of Slovakia. For the diagnosis listed above, we observed number of cases on yearly basis and district of residence.

To analyse epidemiological situation of selected zoonotic diseases, we quantify crude and age-adjusted morbidity rate. A morbidity rate is a measure of the frequency of a disease occurrence in a defined population during a specified time interval.

The mathematic formula for the morbidity of a defined population, over a specified period of time, is: number of cases occurring during a given time period divided by size of the population among which the cases occurred × 10 n. Data necessary for computing the crude morbidity rate were obtained from Epidemiological Information System of Slovakia (number of cases) and National Statistical Office of Slovakia (size of the population in period of years 2010-2019 and size in age groups also). Age-adjustment is a statistical process applied to rates of disease, death, injuries or other health outcomes which allows to control the effects of differences in population age distributions. There are two basic methods of age-adjustment or so called standardization: the direct and indirect method. In our study, we used the direct method. The process of age-adjustment by the direct method changes the amount that each age group contributes to the overall rate, so that the overall rates are based on the same age structure. Rates that are based on the same age distribution can be compared to each other without the presence of confounding by age. Adjustment is accomplished by first multiplying the age-specific rates of disease by age-specific weights. The weighted rates are then summed across the age groups to give the age-adjusted rate. This sum is divided by the total standard population to obtain the age-adjustment. In this study, we used European standard population [15].

To meet specific objective of the study, we observed the trend of crude and age-adjusted morbidity rate of selected zoonotic diseases in period of years 2010–2019. For demonstration of this, line graphs with trend-lines were used to find increasing, decreasing or stable trend of disease morbidity.

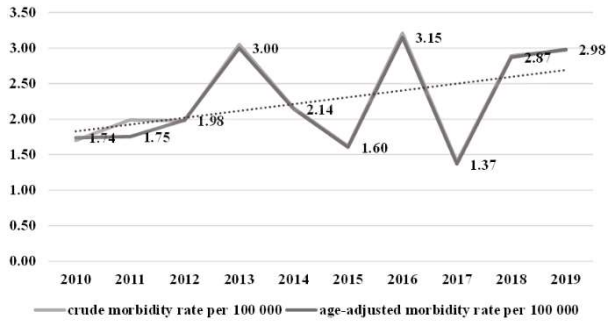
We computed the averages of age-adjusted morbidity rate for each diagnosis of zoonosis for 8 districts that creates Slovakia: Bratislava, Trnava, Trenčín, Nitra, Žilina, Banská Bystrica, Prešov and Košice district.

For data computing, we used MS Excel 2016 for graphic demonstration, program R 3.5.2 for crude and age-adjusted morbidity rates quantification and program Quantum GIS 3.16.1 for morbidity rates presentation by districts of Slovakia.

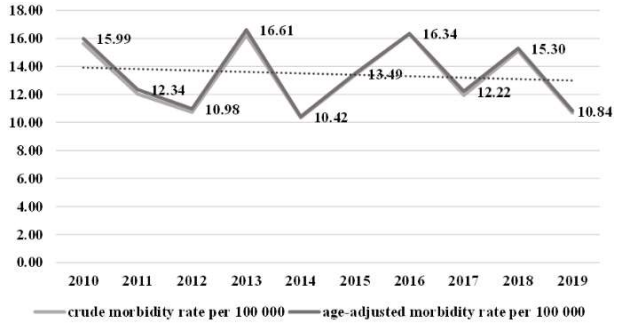
RESULTS

Trends of crude morbidity rate and age-adjusted morbidity rate of observed zoonotic diseases

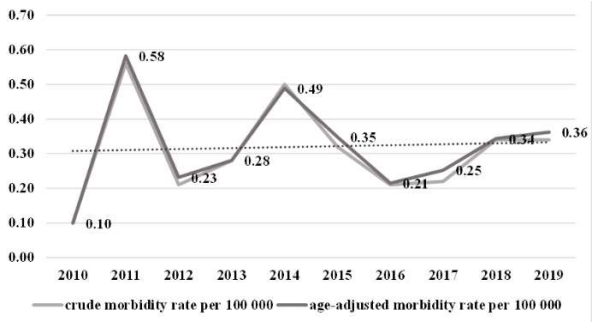
When following tick-born encephalitis morbidity, there is fluctuation in disease occurrence in the years with increasing trend. In 2010, crude morbidity rate was 1.70/100 000 and age-adjusted morbi-



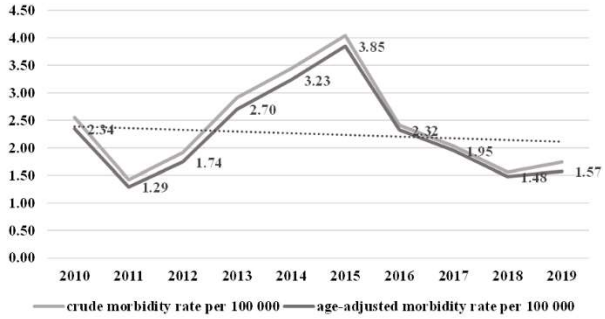
Graph 1 Trend of crude and age-adjusted morbidity rate of thick-borne encephalitis in Slovakia



Graph 2 Trend of crude and age-adjusted morbidity rate of Lyme disease in Slovakia



Graph 3 Trend of crude and age-adjusted morbidity rate of listeriosis in Slovakia



Graph 4 Trend of crude and age-adjusted morbidity rate of toxoplasmosis in Slovakia

Figure 1 Average age-adjusted morbidity rate of thick-borne encephalitis by districts of Slovakia for observed period of years 2010–2019

Figure 2 Average age-adjusted morbidity rate of Lyme disease by districts of Slovakia for observed period of years 2010–2019

Figure 3 Average age-adjusted morbidity rate of listeriosis by districts of Slovakia for observed period of years 2010–2019

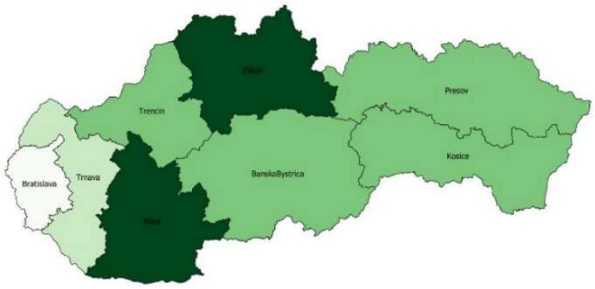


Figure 4 Average age-adjusted morbidity rate of toxoplasmosis by districts of Slovakia for observed period of years 2010–2019

dity rate was 1.74/100 000. Both values increased to 2.97/100 000 and 2.98/100 000 in year 2019 (Graph 1).

Over the observed period, highest crude morbidity rate (16.31/100 000) and the age-adjusted morbidity rate (16.34/100 00) of Lyme disease occurred in year 2016, while the lowest rate was in year 2012 (crude morbidity rate 10.73/100 000 and age-adjusted morbidity rate 10.98/100 000). There is the slightly decreasing trend of Lyme disease morbidity, with apparent differences over the 10-year follow-up (Graph 2).

Listeriosis morbidity showed stable trend in Slovakia over observed time period. Since lower values of morbidity rates in year 2010, there was significant increase in following year 2011, to 0.56/100 000 crude morbidity rate and 0.58/100 000 age adjusted morbidity rate. Similar sharp increase was reported in year 2014, 2015 and also in 2019 as the last observed year of our study (Graph 3).

There is slightly decreasing trend of toxoplasmosis morbidity rate in Slovakia during 10-year follow-up. Since 2012, we observed increase in toxoplasmosis morbidity rate annually till 2015, followed by decrease till 2019 as last observed year (Graph 4).

Quantification of age-adjusted morbidity rate of selected zoonotic diseases by districts of Slovakia

In 10-year follow-up, the highest average age-adjusted morbidity rate was reported from Trenčín district (50.58/100 000), Žilina district (46.43/100 000) and followed by Banská Bystrica district (34.07/100 000). This part of Slovakia, with the highest morbidity rates of encephalitis, is area with the most intense circulation of the vector Ixodes ricinus (Figure 1).

Occurrence of Lyme disease cases in Slovakia copies the geographical distribution of thick-borne encephalitis due to the same vector – thick Ixodes ricinus. Similarly, the highest average age-adjusted morbidity rate was reported from Trenčín district (237.07/100 000) and Žilina district (176.54/100 000) (Figure 2).

In 10-year study follow-up, majority of all cases due to listeriosis occurred in Nitra district (average

age-adjusted morbidity rate 6.20/100 000) and Trnava district (average age-adjusted morbidity rate 6.04/100 000) (Figure 3).

The highest age-adjusted morbidity of toxoplasmosis was reported in Žilina district (46.94/100 000), followed by Nitra district (44.63/100 000). The lowest age- adjusted morbidity rate was in Bratislava district (6.97/100 000), which is the most urbanized area in the country- and also area with lowest occurrence of animal host of toxoplasmosis agent in animal pets, especially cats (Figure 4).

DISCUSSION

Zoonotic diseases are one of the most important public health challenges regarding the increasing incidence trends, epidemic potential of spreading, clinically severe symptoms leading to disabilities or deaths and also to high health-care related costs. The impact of climate changes, especially global warming, is basis to the expansion of ideal living conditions of tick named Ixodes ricinus to colder areas with higher altitudes. This causes the increasing trends in the number of new cases of tick-borne encephalitis and Lyme disease. We observed increasing trend in the incidence of tick-borne encephalitis in the years 2010-2019 in Slovakia. In 2010, crude morbidity rate was 1.70/100 000, age-adjusted morbidity was 1.74/100 000, while in 2019 these values increased to 2.97/100 000 (crude morbidity rate) and 2.98/100 000 (age-adjusted morbidity rate). Increasing trend in the incidence of tick-borne encephalitis has been also reported in Europe. Over the last 30 years, the number of cases per year in Europe has increased by up to 193 %. There are several reasons: climate changes which improved tick living conditions, increased popular outdoor activities in endemic areas of vectors, but also improved diagnostics options and notification [16]. During the period of 10 years, the highest values of the average age-adjusted morbidity rate for tick-borne encephalitis were reported in Trenčín district (50.58/100 000), Žilina district (43.47/100 000) and Banská Bystrica district (34.70/100 000). Avdičová et al. based on the epidemiological analysis of tick-borne encephalitis in Slovakia over the last 20 years, report that approximately 2/3 of the area of Slovakia represents a large endemic area of tick-borne encephalitis in reservoir animals and ticks as vectors. It is estimated that only 1% of ticks transmit encephalitis, yet the risk of the disease is high. Tick-borne encephalitis and Lyme disease are the most frequently diagnosed zoonosis in Slovakia [17].

In the period of years 2010-2019, we observed a stabilized trend in the morbidity rate of Lyme disease in Slovakia with a very slight decrease. In Poland, there has been an upward trend since 2002, with fluctuations over the years. The cause of the increasing trend is due to changes in climatic conditions of disease vector and due to improved laboratory capacity for disease confirmation [18].

During the observed period from 2010 to 2019, we could see a slightly increasing trend in the morbidity due to listeriosis, while in 2010 the crude morbidity rate was at the level of 0.10/ 100 000 and age-adjusted morbidity rate was at the level of 0.09/100 000. In 2008-2015, there was an increasing trend in Europe for the incidence of listeriosis, most notably in the age group over 75 years, and in the age group 25-44 years in women (related to infection in pregnancy) [8]. An increasing trend in the incidence of listeriosis has been observed, especially in connection with the consumption of contaminated fresh fruit and vegetables [19]. Another 8 European countries follow the same trend, especially in people over 60, and even more in population over 70 years. The cause of the increase in the number of cases is unknown [20].

Bobic et al. reported that the decreasing trend in the incidence of toxoplasmosis in the countries of south-eastern Europe is related to a Europe-wide decline in the number of cases per year. The decrease in the number of cases is related to the introduction of public health programs (health education), improved hygiene conditions on farms, and more frequent use of frozen meat compared to the consumption of raw meat. Especially more frequent use of frozen meat has resulted in a reduction in the incidence of toxoplasmosis in Albania and Serbia [21]. We observed the same epidemiological situation in Slovakia in our study. We found a slightly decreasing trend in the morbidity rate of toxoplasmosis over the 10-year period.

Further research is need to know epidemiological situation of zoonotic diseases for timely preventive and control measures. Especially study designs which allow to find causal interference and associations.

CONCLUSION

Many people who have spent some time in con-

tact with animals on their daily basis at urban or rural settings as part of their work duties or while enjoying different kinds of outdoor activities or unwillingly. However, animal species are the reservoir for pathogens transmissible to human population and causing diseases with range from mild to severe clinical symptoms, with high rate of long-term complications and deaths. From all zoonotic diseases, the most relevant are those who affect domestic animals and synanthropic living rodents. In general, the prevention of zoonotic disease, there are three main actions: the disposal of infection sources, the interruption of disease transmission routes and specific prophylaxis. Encroachment of animal habitats (for instance rodent control, the liquidation of animal farms, landscaping methods etc.) mean the most serious intervention form which is implemented strictly in accordance with epidemiological analysis.

Ethical approval of the research

This study was approved by ethical board of Faculty of Health Care and Social work, Trnava University in Trnava, Slovakia. Research and data analysis process did not deal with an individual patient diagnoses with chosen zoonotic diseases. All data have been de-identified and were not attributable to individual patients.

Conflict of interest

There is no conflict of interest. No kind of research funding was needed to conduct this study.

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