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PRACA POGLĄDOWA
REVIEW

Tick-borne encephalitis on the horizon – a call to action for Poland

Kleszczowe zapalenie mózgu na horyzoncie – apel o podjęcie działań dla Polski

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ABSTRACT

Tick-borne encephalitis (TBE) is a viral infection of the central nervous system caused by viruses belonging to the family *Flaviviridae*. The disease manifests with a range of symptoms, including fever, dizziness, nausea, vomiting, and neurological complications, such as meningoencephalitis and paralysis. These symptoms can have severe and long-lasting consequences for human health, potentially leading to permanent neurological damage or even death. Recent epidemiological trends reveal a marked and alarming increase in TBE cases across Poland and the Baltic states, signaling an emerging public health threat in these regions. This article aims to highlight the growing prevalence of TBE in Poland, examining environmental and socio-economic factors contributing to the virus's spread. Additionally, it outlines proposed strategies for the implementation of an effective control and prevention plan that includes public awareness campaigns, vaccination programs, and tick control measures. By presenting comprehensive data on TBE transmission, incidence rates, and the socio-economic burden of the disease, this article underscores the critical importance of preventing the spread of TBE and safeguarding public health.

KEYWORDS

encephalitis, ticks, epidemiology

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STRESZCZENIE

Kleszczowe zapalenie mózgu (*tick-borne encephalitis* – TBE) to wirusowe zakażenie ośrodkowego układu nerwowego wywołane przez wirusy należące do rodziny *Flaviviridae*. Choroba charakteryzuje się szeregiem objawów, w tym gorączką, zawrotami głowy, nudnościami, wymiotami i powikłaniami neurologicznymi, takimi jak zapalenie opon mózgowo-rdzeniowych i paraliż. Objawy te mogą mieć poważne i długotrwałe konsekwencje dla zdrowia ludzi, potencjalnie prowadząc do trwałego uszkodzenia neurologicznego, a nawet śmierci. Najnowsze trendy epidemiologiczne wskazują na znaczny i alarmujący wzrost liczby przypadków TBE w Polsce i krajach bałtyckich, co sygnalizuje zagrożenie dla zdrowia publicznego w tych regionach. Celem artykułu jest zwrócenie uwagi na rosnącą częstość występowania TBE w Polsce poprzez analizę czynników środowiskowych i społeczno-ekonomicznych przyczyniających się do rozprzestrzeniania się wirusa. Ponadto przedstawiono proponowane strategie wdrażania skutecznego planu kontroli i zapobiegania, obejmujące kampanie informacyjne, programy szczepień i środki kontroli kleszczy. Przedstawiając kompleksowe dane na temat transmisji TBE, wskaźników zapadalności i obciążenia społeczno-ekonomicznego związane z chorobą, podkreślono kluczowe znaczenie zapobiegania rozprzestrzenianiu się TBE i ochrony zdrowia publicznego.

SŁOWA KLUCZOWE

zapalenie mózgu, kleszcze, epidemiologia

INTRODUCTION

Tick-borne encephalitis (TBE) is a viral infection transmitted by the bites of *Ixodes ticks ricinus*, with potentially serious consequences for human health [1]. Although historically common in some regions, including Central and Eastern Europe, recent trends indicate an alarming increase in TBE cases in Poland [2]. In the years 1993–2008, there was significant growth in the number of TBE cases, especially in the northeastern part of Poland [3]. As climate change alters habitats and human encroachment brings humans closer to tick habitats, the incidence of tick-borne diseases is on the rise. Exploring the factors driving this increase and elucidating strategies for prevention and control are paramount in mitigating the public health burden posed by ticks. The prevalence and distribution of tick-borne encephalitis virus (TBEV) have been studied using surveillance strategies. Their results have revealed higher rates in eastern Poland and the Baltic states. This highlight growing public health concerns due to the rising incidence of TBE. Most cases occur during the period of greatest tick activity, in Central Europe mainly from April to November [4,5,6].

DISCUSSION

Aetiology

Neurotropic TBEV was identified as the causative agent of TBE by Zilber [7] more than 75 years ago. It is a spherical, lipid-enveloped (+)ssRNA virus that belongs to the genus *Flavivirus* in the family *Flaviviridae*. The mature virion consists of 3 structures: capsid (c), membrane proteins (m) and coat proteins (e). The E protein plays a decisive role in the virus life cycle. It participates in both the binding of the virus to the host cell, thus enabling its penetration into the intracellular space, and in the release of the nucleocapsid into the cell cytoplasm [6,7].

Life cycle

The assembly and maturation of TBEV particles represent complex processes, similar to other flaviviruses, yet with some unique features. While the structural characterization of virion maturation is well-documented for many mosquito-borne flaviviruses, limited data are available for TBEV. Particularly the early events of particle production remain elusive, compounded by the predominant study of the TBEV life cycle in mammalian cells despite its intimate association with ticks. The entry into host cells involves receptor-mediated endocytosis, with laminin-binding protein and αVβ3 integrin identified as major receptor candidates in mammalian cells [8]. However, receptor candidates in tick cells are yet to be identified, suggesting potential alternative mechanisms of entry. Additionally, attachment factors like heparan sulfate facilitate virus-cell interactions, influencing infection outcomes. Once inside the cell, the pH-dependent conformational changes in the virion facilitate membrane fusion and the release of the viral RNA into the cytosol. Replication and translation occur at the endoplasmic reticulum, with viral and host enzymes cleaving the polyprotein to yield structural and non-structural proteins. The assembly of new virions involves the formation of nucleocapsids encapsulating the viral RNA, followed by budding into the endoplasmic reticulum lumen [9]. Maturation, marked by furin-mediated cleavage of the pr peptide from prM, renders the virion infectious. While extensively studied in mammalian cells, the maturation and egress of TBEV particles may differ in tick cells, suggesting potential variations in the virus life cycle across different host environments. Further research is warranted to fully elucidate these intricate processes [10].

Symptoms of tick-borne encephalitis

In TBEV infection, the TBE incubation period ranges from 2 to 28 days and is usually 7–14 days. This is the period between the virus entering our body and the appearance of the first symptoms [11]. The symptoms of the disease are very diverse – from asymptomatic to severe forms of encephalitis with nerve paralysis and loss of consciousness. In most cases, the disease has a mild course, but long-term neurological and psychiatric sequelae are observed. In approximately 75% of patients with TBE caused by the European subtype of TBEV, the disease has a typical biphasic course. The initial phase correlates with viral load and usually presents with non-specific symptoms such as fever, headache, body aches, fatigue, general malaise, anorexia, and nausea. Then the second phase commences, which is the occurrence of meningitis or TBE [12]. Most patients with a monophasic course of the disease show involvement of the central nervous system, including meningitis, while a minority have fever with headache but without meningitis [12,13].

Current picture of the epidemiology of TBE in Poland

According to research, in Poland between 2016 and 2020 there was a constant increase in the incidence of tick-borne diseases [14]. Only the years of the COVID-19 pandemic was there a deviation from the norm [15]. As research shows, the Warmian–Masurian Voivodeship, together with the Lesser Poland and Podlaskie Voivodeships, is at the forefront in terms of the incidence of Lyme disease and TBE [16].

While Lyme disease occurs throughout the country, TBE is limited to only the northeast of the country. No evidence has been found that the Warmian–Masurian Voivodeship has conditions that significantly favor the development of ticks and the TBEV, but the reason for the dominance of the Warmian–Masurian Voivodeship may be that the factor which favors the high activity of *I. ricinus* ticks in this region is the high humidity of the forest litter and undergrowth, which is caused by the large number of lakes in this area [17]. An important factor contributing to the increased number of cases in the mentioned areas are the average hospitalization conditions and the poor spread of preventive measures, including vaccinations [16,17].

The data from the National Institute of Public Health – National Institute of Hygiene (NIPH – NIH) for 2019 shows that there were 265 cases of TBE in Poland, translating to an incidence rate of 0.65 cases per 100,000 persons per year. This incidence rate, however, was not uniform across the country; it was significantly higher in the Podlaskie Voivodeship, with an incidence rate of 6.17 per 100,000 persons per year, and in the Warmian–Masurian Voivodeship, with an incidence rate of 1.75 per 100,000 persons per year [18].

Regarding viral meningitis, in 2018 Poland reported 1226 cases, of which 1108 (90%) were classified as either other specified or unspecified. Viral meningitis is an inflammation of the protective membranes covering the brain and spinal cord, known collectively as the meninges. The high percentage of cases classified as unspecified or other specified suggests potential challenges in the accurate diagnosis of viral meningitis, which could be due to the overlap of its symptoms with those of other neuroinfections, limitations in diagnostic technology or expertise, and the nonspecific nature of many viral infections [19].

Factors contributing to the growth in TBE cases in Poland

The significant rise in TBE cases is not only owing to improved diagnosis of the disease. The increase in the incidence of TBE can be divided into:

1. Factors that favor the development of ticks: changes in land development, the transformation of agricultural fields into fallow lands and forest areas, current climate changes, other factors affecting the main hosts of ticks – small and medium-sized mammals [20].
2. Factors conducive to multiplication of the virus in a given area: optimal conditions for maintaining a large rodent population, the coexistence of appropriate climatic conditions in subsequent seasons.
3. Factors favoring contacts between ticks and humans: the popularity of tourist areas, favorable weather conditions, professional status and the availability of vaccines [21].

The observed impact of climate change is reflected in the increase in the incidence of tick-borne diseases. Among them, the most spectacular is the expansion in the range and incidence of TBE [19,20]. According to research conducted by the Medical University of Białystok, model parameters describing the impact of temperatures in individual months on the annual incidence of TBE were estimated based on annual data from the period 1972–2004. A clear rise in the number of cases of TBE was shown, starting in 1993. The relationship between the air temperature thresholds at which ticks increase their activity and the incidence of TBE is evident. This model also proves that temperature is not the only weather factor that determines tick activity. It shows the general tendency of the phenomenon over a long period [20,21,22,23].

In the discussed trend of the growing number of TBE cases, an important factor is the tourist popularity of endemic areas [24]. The relationship between recreational and tourist activity and the incidence of tick-borne diseases can be seen by analyzing the number of registered cases of Lyme disease before and in 2020, which was the year of the COVID-19 pandemic and numerous related restrictions. The ban on entering the forest and widespread quarantines could have reduced the number of infections at that time [24,25].

An additional aspect contributing to the spread of TBE is socio-economic status. The lower economic status of part of the population living in endemic areas increases the likelihood of working outdoors and collecting forest undergrowth for their own needs and for economic purposes [26,27].

Strategies for controlling TBEV infections in Poland

Observing the growth in TBEV infections described above, the question arises: how can we control the virus and prevent its transmission? In the prevention of TBE infections, it is recommended to wear clothing that protects the body sensitive to tick bites, use repellents and remove ticks from the skin as quickly as possible (e.g. by taking a shower after visiting a forest or meadow and thoroughly examining the entire body) [27]. Although recommended PPE seems obvious for preventing tick-borne diseases, including TBE, the effectiveness of some measures is limited, questionable, or has not been adequately evaluated. An additional problem is that only a small percentage of exposed people use the recommended procedures in their everyday lives [28,29,30,31]. Because TBEV can be transmitted through food, pasteurization and avoiding the consumption of unpasteurized milk and dairy products prevent infection in humans [31].

The most effective method of preventing TBE is a vaccine. Currently, two vaccines prepared from isolated European TBEV strains are used in Europe: FSME-INJECT (by Baxter AG, Vienna, Austria) and the Encepur vaccine (by Chiron-Behring, Marburg, Germany). The primary vaccination consists of two doses of the vaccine administered one month apart and a third dose administered one year later. Booster doses are recommended every 3–5 years, which allows 96–98% of vaccinated people to achieve immunity [18,27].

CONCLUSIONS

As Poland faces a growing threat of TBE, a coordinated and multi-faceted approach is crucial to effectively control and ultimately eliminate the spread of this potentially devastating disease.

By implementing the proposed strategies and supporting international cooperation, Poland can make significant steps towards protecting its population against the growing threat of tick-borne infections. As the incidence of TBE increases in Poland, there is an urgent need to develop comprehensive strategies that include public education on prevention methods, such as avoiding high-risk areas or wearing protective clothing outdoors; improving access to vaccinations; strengthening vector control measures; and supporting further research to better understand local differences in affected regions. Although efforts are underway to address this issue through national surveillance systems and research focusing on the epidemiology and clinical presentation of TBE, debates continue regarding the most effective strategies to control the spread of TBE. Some argue that increased environmental management may be necessary to reduce tick populations, while others emphasize vaccination as a key measure.

Author's contribution

Study design – P. Ziobro, J. Zientek
Data collection – P. Ziobro, J. Zientek
Manuscript preparation – P. Ziobro, J. Zientek, J. Fiegler-Rudol
Literature research – P. Ziobro, J. Zientek, J. Fiegler-Rudol
Final approval of the version to be published – K. Lau

REFERENCES

1. Monath T.P., Heinz F.X. Flaviviruses. In: B.N Fields, D.M. Knipe, P.M. Howley [ed.]. Fields virology. 3rd ed. Vol. 1. Philadelphia: Lippincott-Raven Publishers, 1996, pp. 961–1034.
2. Süss J. Tick-borne encephalitis 2010: epidemiology, risk areas, and virus strains in Europe and Asia – an overview. Ticks Tick Borne Dis. 2011; 2(1): 2–15, doi: 10.1016/j.ttbdis.2010.10.007.
3. Czupryna P., Moniuszko A., Pancewicz S.A., Grygorczuk S., Kondrusik M., Zajkowska J. Tick-borne encephalitis in Poland in years 1993-2008 – epidemiology and clinical presentation: A retrospective study of 687 patients. Eur. J. Neurol. 2011; 18(5): 673–679, doi: 10.1111/j.1468-1331. 2010.03278.x.
4. Mansfield K.L., Johnson N., Phipps L.P., Stephenson J.R., Fooks A.R., Solomon T. Tick-borne encephalitis virus – a review of an emerging zoonosis. J. Gen. Virol. 2009; 90(Pt 8): 1781–1794, doi: 10.1099/vir.0.011437-0.
5. Lindquist L., Vapalahti O. Tick-borne encephalitis. Lancet 2008; 371(9627): 1861–1871, doi: 10.1016/S0140-6736(08)60800-4.
6. Kaiser R. Tick-borne encephalitis. Infect. Dis. Clin. North Am. 2008; 22(3): 561–575, doi: 10.1016/ j.idc.2008.03.013.
7. Zilber L.A. Spring-summer tick-borne encephalitis. Arkhiv Biol. Nauk. 1939; 56: 255–261.
8. Protopopova E.V., Sorokin A.V., Konovalova S.N., Kachko A.V., Netesov S.V., Loktev V.B. Human laminin binding protein as a cell receptor for the tick-borne encephalitis virus. Zent. Bakteriol. 1999; 289: 632–638, doi: 10.1016/S0934-8840(99)80021-8.
9. Füzik T., Formanová P., Růžek D., Yoshii K., Niedrig M., Plevka P. Structure of tick-borne encephalitis virus and its neutralization by a monoclonal antibody. Nat. Commun. 2018; 9(1): 436, doi: 10.1038/s41467-018-02882-0.
10. Pulkkinen L.I.A., Butcher S.J., Anastasina M. Tick-borne encephalitis virus: A structural view. Viruses 2018; 10(7): 350, doi: 10.3390/v10070350.
11. Dumpis U., Crook D., Oksi J. Tick-borne encephalitis. Clin. Infect. Dis. 1999; 28(4): 882–890, doi: 10.1086/515195.

12. Lotric-Furlan S., Avsic-Zupanc T., Strle F. An abortive form of tick-borne encephalitis (TBE) – a rare clinical manifestation of infection with TBE virus. Wien. Klin. Wochenschr. 2002; 114(13–14): 627–629.
13. Bogovic P., Lotric-Furlan S., Strle F. What tick-borne encephalitis may look like: clinical signs and symptoms. Travel Med. Infect. Dis. 2010; 8(4): 246–250, doi: 10.1016/j.tmaid.2010.05.011.
14. Ferlenghi I., Clarke M., Ruttan T., Allison S.L., Schalich J., Heinz F.X. et al. Molecular organization of a recombinant subviral particle from tick-borne encephalitis virus. Mol. Cell 2001; 7(3): 593–602, doi: 10.1016/s1097-2765(01)00206-4.
15. Kmieciak W., Ciszewski M., Szewczyk E.M. Tick-borne diseases in Poland: Prevalence and difficulties in diagnostics. [Article in Polish]. Med. Pr. 2016; 67(1): 73–87, doi: 10.13075/mp.5893.00264.
16. Stefanoff P., Rosińska M., Zieliński A. Epidemiology of tick-borne diseases in Poland. [Article in Polish]. Przegl. Epidemiol. 2006; 60 Suppl 1: 151–159.
17. Kolpy I. Observations on the distribution and activity of Ixodes ricinus L. in the Warmia-Mazury lake region. [Article in Polish]. Wiad. Parazytol. 1961; 7: 915–918.
18. Kuchar E., Zajkowska J., Flisiak R., Mastalerz-Migas A., Rosińska M., Szenborn L. et al. Epidemiology, diagnosis, and prevention of tick-borne encephalitis in Poland and selected European countries – a position statement of the Polish group of experts. [Article in Polish]. Med. Pr. 2021; 72(2): 193–210, doi: 10.13075/mp.5893.01063.
19. Randolph S.E. Evidence that climate change has caused 'emergence' of tick-borne diseases in Europe? Int. J. Med. Microbiol. 2004; 293 Suppl 37: 5–15, doi: 10.1016/s1433-1128(04)80004-4.
20. Zajkowska J., Kondrusik M., Zajkowska O., Kuśmierczyk J., Czupryna P., Pancewicz S. Statistical analysis of influence of meteorological data on the incidence rate of tick-borne encephalitis in Bialystok. [Article in Polish]. Przegl. Epidemiol. 2008; 62(2): 453–460.
21. Brownstein J.S., Holford T.R., Fish D. A climate-based model predicts the spatial distribution of the Lyme disease vector Ixodes scapularis in the United States. Environ. Health Perspect. 2003; 111(9): 1152–1157, doi: 10.1289/ehp.6052.
22. Stefanoff P., Staszewska E., Ustrnul Z., Rogalska J., Łankiewicz A., Rosińska M. Ecologic study of the risk of tick-borne encephalitis in Poland – presentation of the method. [Article in Polish]. Przegl. Epidemiol. 2008; 62 Suppl 1: 112–121.
23. Witkowska D., Dzisko J., Lubińska M., Iwańczuk-Czernik K., Sowińska J. Borreliosis in humans in the region of Warmia and Mazury in 1999-2008. Medycyna Wet. 2010; 66(7): 484–488.
24. Diez-Roux A.V., Kiefe C.I., Jacobs D.R. Jr, Haan M., Jackson S.A., Nieto F.J. et al. Area characteristics and individual-level socioeconomic position indicators in three population-based epidemiologic studies. Ann. Epidemiol. 2001; 11(6): 395–405, doi: 10.1016/s1047-2797(01)00221-6.
25. Zajkowska J., Czupryna P. Tick-borne encephalitis – epidemiology, pathogenesis and clinical course, prophylaxis and treatment. Forum Zakażeń 2013; 4(1): 43–51, doi: 10.15374/fz2013012.
26. Hudopisk N., Korva M., Janet E., Simetinger M., Grgič-Vitek M., Gubenšek J. et al. Tick-borne encephalitis associated with consumption of raw goat milk, Slovenia, 2012. Emerg. Infect. Dis. 2013; 19(5): 806–808, doi: 10.3201/eid1905.121442.
27. Charrel R.N., Attoui H., Butenko A.M., Clegg J.C., Deubel V., Frolova T.V. et al. Tick-borne virus diseases of human interest in Europe. Clin. Microbiol. Infect. 2004; 10(12): 1040–1055, doi: 10.1111/j.1469-0691.2004.01022.x.
28. Bogovic P., Strle F. Tick-borne encephalitis: A review of epidemiology, clinical characteristics, and management. World J. Clin. Cases 2015; 3(5): 430–441, doi: 10.12998/wjcc.v3.i5.430.
29. Stanek G., Wormser G.P., Gray J., Strle F. Lyme borreliosis. Lancet 2012; 379(9814): 461–473, doi: 10.1016/S0140-6736(11)60103-7.
30. Vázquez M., Muehlenbein C., Cartter M., Hayes E.B., Ertel S., Shapiro E.D. Effectiveness of personal protective measures to prevent Lyme disease. Emerg. Infect. Dis. 2008; 14(2): 210–216, doi: 10.3201/eid1402.070725.
31. Corapi K.M., White M.I., Phillips C.B., Daltroy L.H., Shadick N.A., Liang M.H. Strategies for primary and secondary prevention of Lyme disease. Nat. Clin. Pract. Rheumatol. 2007; 3(1): 20–25, doi: 10.1038/ncprheum0374.