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ORIGINAL PAPER

Retrospective Analysis of Meningococcal Disease in Transcarpathian Region of Ukraine

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Abstract

Background: Meningococcal infection (MI) is one of the most significant bacterial infections in children, it is characterized by a life-threatening and unpredictable fulminant course in the structure of infectious diseases. MI in Ukraine represents an important cause of mortality. The Transcarpathian region is located on the western boundary of Ukraine with 4 European countries. Such location of the district and its geopolitical issues related to immigration plays a crucial role in disease transmission and serve as a gate to infectious diseases to and from European Union. **Methods:** This was a retrospective study that included 32 patients with a confirmed diagnosis of meningococcaemias. The data were obtained from patients' electronic medical records (EMR). Data collected included demographic, clinical, and laboratory. Continuous variables were expressed as means with standard deviations. Categorical variables were summarized as counts and percentages. **Results:** Meningococcal morbidity in the Transcarpathian region was higher than in the whole of Ukraine in all researched years. Primarily, the highest incidence was recorded in the Perechyn district and in Uzhhorod city. 53% of all cases of MI occur in the period from December to February. The main constant clinical manifestation of the disease was skin symptoms. **Conclusions:** The incidence rate of MI is an important problem for public health and may pose a threat to neighboring countries. The methods for the prevention of meningococcal infection include antimicrobial chemoprophylaxis following identification of an index case, use of droplet precautions, vaccination prior to exposure, and avoidance of exposure.

Keywords: Meningococcal Disease; Infectious Disease Epidemiology; Neisseria Meningitidis; Invasive Meningococcal Disease

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INTRODUCTION

Neisseria meningitidis is a leading cause of invasive bacterial disease around the world[1]. The disease can appear sporadically, with seasonal variations and outbreaks, and it frequently appears suddenly, progressing rapidly to death[2,3]. *N. meningitidis* invasion into the human bloodstream causes invasive meningococcal disease (IMD), which can result in meningococcaemia and septic shock, purpura fulminans, meningococcal meningitis (MM), pneumonia, arthritis, and pericarditis[4]. Meningococcal infections can be fatal in 10% of cases, with up to 36% of survivors developing permanent sequelae; they are a significant cause of morbidity and mortality in infants and young children, as well as a serious public health problem[4-7].

There is a significant decrease morbidity and mortality of MI (meningococcal infection) for the last 40 years in Ukraine. Between 1983 and 2015 the incidence of MI decreased by 7.2 times[8]. In 2012 in Ukraine, IMD incidence (0.75 per 100,000) was comparable to the one of EU (0.7 per 100,000). However, death rate in Ukraine (0.09 per 100,000) was higher than in the European Union (0.06 per 100,000). Also, this has to consider that half of the cases of MI in Ukraine are not bacteriologically confirmed[9].

According to the Department of Epidemiological Surveillance and Prevention of Infectious Diseases of the Transcarpathian regional center for control and prevention of diseases, the incidence of meningococcal infection in the Transcarpathian region increased from 1.03 per 100,000 in 2015 to 3.34 per 100,000 in 2018.

The purpose of this study is to establish epidemiological and clinical features of patients with meningococcaemia in the Transcarpathian region.

MATERIALS AND METHODS

This was a retrospective, observational, single-center study, which included all consecutive patients with a confirmed diagnosis of meningococcaemias, at Transcarpathian Regional Clinical Infectious Diseases Hospital, between January 2016 and December 2018.

The data were obtained from patients' electronic medical records (EMR), including patients with clinical and laboratory-confirmed meningococcaemia. Data collected included demographic, clinical, and laboratory, and was anonymized so that patients could not be identified.

Epidemiological data were collected from national and regional health reports, as well as additional information from online reports.

Continuous variables were expressed as means with standard deviations. Categorical variables were summarized as counts and percentages. All analyses were performed using SPSS.

RESULTS

Epidemiology features

The Transcarpathian region is a western administrative division of Ukraine, which borders with four European countries such as Poland, Slovakia, Hungary, and Romania. The number of Ukrainian migrants in neighboring European countries accounts for a large population[10]. Such location of the district and its geopolitical issues related to migration in connection with the Russian invasion of Ukraine plays a crucial role in disease transmission and serves as a gate to infectious diseases in European Union.

The morbidity of meningococcal disesase in Transcarpatian region and in Ukraine over the 2016-2018 is represented in Figure 1. From the data in Figure 1, it is evident that the meningococcal morbidity in the Transcarpatian region was higher than in the whole Ukraine in all researched years. The high rates were in 2018 (3.34 per 100 thousand of population, which exceeds the relative morbidity in Ukraine by 5.3 times) (Table 2).

Territorial distribution of meningococcal morbidity in the region has its own peculiarities. Primarily, the highest incidence was recorded in the Perechyn district (11.0 per 100 thousand) and in Uzhhorod city (7.7 per 100 thousand). The incidence was slightly lower in Uzhhorod and Velykobereznyansky district (2.8 per 100 thousand) (Fig. 2). There was no case of meningococcal infection in Volovets and Svalyava districts.

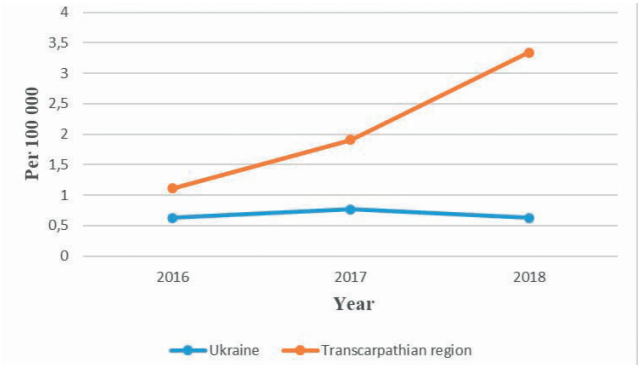

Figure 1. Incidence dynamic of meningococcal disease in Transcarpathian region compare to Ukraine

Table 2. Incidence of meningococcal disease in the Transcarpathian region by district (2015–2018).

Years	Transcarpathian region		Ukraine		Relative indicator of the comparison of the intensity index
	Absolute value	Per 100 thousand population	Absolute value	Per 100 thousand population	
2016	14	1.11	270	0.63	1.76
2017	24	1.91	326	0.77	2.48
2018	42	3.34	269	0.63	5.30

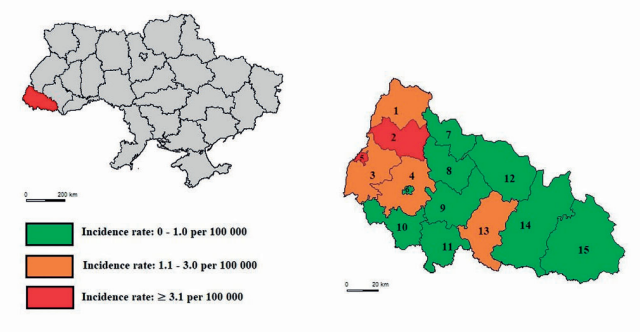

Figure 2. Meningococcal morbidity in Transcarpathian region and Ukraine for the period of 2016-2018 (per 100 thousand population).
Districts and city of Transcarpathian region: 1 – Velykobereznyansky district; 2 – Perechyn district; 3 - Uzhhorod district; 4 - Mukachevo district; 5 – Uzhhorod city; 6 – Mukachevo city; 7 - Volovetsky district; 8 - Svalyavsky district; 9 - Irshav district; 10 - Berehiv district; 11 - Vynogradivskyi district; 12 - Mizhhirsky district; 13 - Khust district; 14 - Tyachiv district; 15 - Rakhiv district.

There is a clear winter-spring seasonality of meningococcal disease – from December to April. On average, the increase in morbidity begins to be recorded in December (25% from average annual). 53% of all cases of meningococcal infection occur in the period from December to February.

According to data from the Department of Epidemiological Surveillance and Prevention of Infectious Diseases of the Transcarpathian regional center for control and prevention of diseases, all meningococci species isolated from patients were classified as serogroup type B.

Demographic and clinical characteristics

As shown in Table 1, men dominated – 65%, of the population, aged from 0 to 63, and the largest group included individuals aged 5-10 (31%).

The main constant clinical manifestation of the disease was skin symptoms. Typical hemorrhagic rash (purpuric or petechiae) was observed in more than 81% of cases (Fig. 3). Leucocytosis (WBC ≥ 9×10^9/L) was observed in more than half of the cases (53%). More

Table 1. Demographic and clinical characteristics of patients with meningococcemi

Characteristic	Total patients n=32
1.Demographic	
Age (Years)	13.2 ± 15.8
0 - 3, n (%)	5 (15)
3 - 5, n (%)	5 (15)
5 - 10, n (%)	10 (31)
10 - 18, n (%)	8 (27)
≥ 18, n (%)	4 (12)
Gender (Male), n (%)	21 (65)
2.Signs and symptoms at admission	
2.1 Type of rash:	
Maculopapular, n (%)	0 (0)
Pupruric, n (%)	17 (53)
Petechiae, n (%)	9 (28)
No rash, n (%)	6 (19)
2.2 Headache, n (%)	9 (28)
2.3 Vomiting, n (%)	9 (28)
2.4 Cold hands and/or feet, n (%)	3 (9)
2.5 Fever ≥ 38 ^{0}C	5 (15)
3.Comorbidities at admission	
Rotavirus infection, n (%)	3 (9)
Giardiasis, n (%)	2 (6)
Pinworm infection, n (%)	4 (12)
Ascariasis, n (%)	4 (12)
Whipworm infection, n (%)	1 (3)
4.Laboratory findings	
WBC ($\times10^9$/L)	12.3 ± 8.8
GRA ($\times10^9$/L)	9.9 ± 8.8
5. Complications	
Disseminated intravascular coagulation (DIC), n (%)	2 (6)
Septic shock, n (%)	1 (3)

Figure 3. Hemorrhagic rash of a child with meningococcemia

than 43% of patients had a normal body temperature (36.5–37 ˚C) on admission, 15% had a temperature above 38 ˚C. Complications of meningococcal disease such as DIC and septic shock were observed in 6% and 3%, respectively.

DISCUSSION

Meningococcal infection remains a serious challenge to the health care system and epidemiological surveillance of the Transcarpathian region. The distribution of the disease shows the prevalence of cases in highly populated areas like the district capital. Most cases of meningococcal infection were in the border areas of the Transcarpathian region (Uzhhorod, Perechyn, Velykobereznyansky), which can pose a threat to neighboring countries. Most cases of meningococcal disease occur in the winter, which is quite typical[11,12].

Meningococcemia occurs in 20%–30% of meningococcal disease cases[6,4]. The classic sign of meningococcemia is petechial purpuric exanthema[13] According to available data petechiae or purpura are seen in 50% to 60% of patients. Twenty percent to 30% of children may not have a rash on presentation[14,15]. Our data obtained as a result of our research are similar. The absence of rashes (in 19%) poses a serious problem for doctors, as it makes it difficult to establish a diagnosis. A late diagnosis can lead to complications such as disseminated intravascular coagulation and purpura fulminans.

Only 2-11% of children with petechiae and fever have invasive meningococcal disease. Although most other children probably have viral infections, antibiotic therapy should be commenced without awaiting additional information[16]. Other causes may include the following: pneumococcal septicaemia, hemorrhagic viral fevers, rubella, immune thrombocytopenia, Henoch-Schönlein purpura, vitamin C deficiency, etc.

Microbiological diagnostics is an important method not only for confirming the etiology of an infection, but also for carrying out a sensitivity test to antibiotics. Increasing resistance of meningococci to antibiotics has been reported[17,18]. In Ukraine, the Gram staining method is widely used, however, negative results do not exclude the diagnosis of meningococcal infection. The latest available data in Transcarpathia indicate that all strains were of serogroup B. Therefore, large-scale vaccination against serogroup B will be useful for eliminating the outbreak of meningococcal infection in the Transcarpathian region.

CONCLUSION

The incidence rate of meningococcal infection is an important problem for public health and may pose a threat to neighbouring countries such as Romania, Hungary, Poland, and Slovakia. The main reason for the high morbidity is the lack of routine vaccination against meningococcal. The methods for the prevention of meningococcal infection include antimicrobial chemoprophylaxis following identification of an index case, use of droplet precautions, vaccination prior to exposure, and avoidance of exposure.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the

Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

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