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Clinical-epidemiological characteristics of acute bacterial meningitis in children of Khmelnitskyi region (Podilsky region, Ukraine): fifteen-year-long

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Acute bacterial meningitis (ABM) leads to a significant number of complications and high mortality.

The aim — to analyze the etiological structure, epidemiological, socio-demographic features and complications in ABM in children of Khmelnitskyi region during 2004–2018.

Materials and methods. The analysis of 346 cases of ABM, of which 217 boys and 129 girls was conducted. The etiology of meningitis was determined by bacterioscopy, bacteriological sowing, latex agglutination and polymerase chain reaction. Complications were revealed based on the clinical picture and computed tomography and мagnetic resonance imaging. The processing of the results was carried out using analytical method, t-criterion and constructing 95% confidence interval.

Results. The disease started with fever 346 (100%), neck stiffness 289 (83.5%) and vomiting 273 (78.9%), less common, alteration of consciousness 28 (8.1%) and seizures 9 (2.6%). The high level of the cytosis were observed in meningococcal (5801.3±4856.7 cells/mm^3) and Hib meningitis (5152.6±4153.1 cells/mm^3), the lowest level was in pneumococcal meningitis (2601.0±1839.6 cells/mm^3). The highest level of liquor protein was in pneumococcal meningitis (179.0±51.0 mg/dl), and the lowest level was in meningococcal meningitis (102.0±49.0 mg/dl) and Hib meningitis (112.0±56.0 mg/dl). The etiological factor was established in 121 (35.0%) of patients. 52 (15.4%) of patients had neurological complications.

Conclusions. The majority (58.1%) of ABM are in children under the age of 3. The main causative agent remains *N. meningitidis* — 57.9%, the second place is *S. pneumoniae* — 21.5%, the third *Hib* — 9.9% of cases. Frequent complications were brain edema 32 (61.5%), seizures 19 (36.5%) and hydrocephalus 8 (15.4%).

The study was conducted in accordance with the principles of the Declaration of Helsinki. The research protocol was approved by the Local Ethics Committee of the institution mentioned in the work. Informed consent of the children's parents was obtained for the research.

No conflict of interests was declared by the authors.

Keywords: children, bacterial meningitis, epidemiology, etiology.

Клініко-епідеміологічна характеристика гострих гнійних менінгітів у дітей Хмельницької області (Подільський регіон, Україна): п'ятнадцятилітнє епідеміологічне спостереження

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Гострий бактеріальний менінгіт (ГБМ) призводить до значної кількості ускладнень та високої летальності.

Ціль — проаналізувати етіологічну структуру, епідеміологічні, соціально-демографічні особливості та ускладнення при ГБМ у дітей Хмельницької області за 2004–2018 рр.

Матеріали та методи. Проведено аналіз 346 випадків ГБМ, з яких 217 хлопчиків та 129 дівчаток. Етіологія менінгіту визначалася методами бактеріоскопії, бактеріологічного посіву, латексної аглютинації та полімеразної ланцюгової реакції. Ускладнення визначалися на підставі клінічної картини, комп'ютерної та магнітно-резонансної томографії. Обробка результатів проводилася з використанням аналітичного методу, t-критерію та побудови 95% довірчого інтервалу.

Результати. Захворювання почалося з лихоманки 346 (100%), ригідності шиї 289 (83,5%) та блювання 273 (78,9%), рідше, зміни свідомості 28 (8,1%) та судом 9 (2,6%). Високий рівень цитозу відзначений при менінгококовому (5801,3±4856,7 клітин/мм^3) та Hib-менінгіті (5152,6±4153,1 клітин/мм^3), найменший — при пневмококовому менінгіті (2601,0±1 мм^3). Найвищий рівень білка в ліквbooрі був при пневмококовому менінгіті (179,0±51,0 мг/дл), а найнижчий — при менінгококовому менінгіті (102,0±49,0 мг/дл) та менінгіті, викликаному Hib (112,0±56,0 мг/дл). Етіологічний фактор встановлено у 121 (35,0%) хворих. У 52 (15,4%) пацієнтів були неврологічні ускладнення.

Висновки. Більшість ОБМ (58,1%) припадає на дітей віком до 3 років. Основним збудником залишається *N. meningitidis* — 57,9%, на другому місці *S. pneumoniae* — 21,5%, на третьому — *Hib* — 9,9% випадків. Частими ускладненнями були набряк мозку 32 (61,5%), судоми 19 (36,5%) та гідроцефалія 8 (15,4%).

Дослідження виконано відповідно до принципів Гельсінської декларації. Протокол дослідження ухвалено Локальним етичним комітетом зазначеної в роботі установи. На проведення досліджень отримано інформовану згоду батьків, дітей.

Автори заявляють про відсутність конфлікту інтересів.

Ключові слова: діти, бактеріальний менінгіт, епідеміологія, етіологія.

Introduction

Acute bacterial meningitis (ABM) is considered as one of the most dangerous infectious diseases, which leads to a significant number of complications and high mortality [1]. It meets a frequency of 2–5 per 100 thousand people in Western Europe and can be tens of times higher in less developed countries [10]. ABM is among the top ten causes of death related to infectious diseases in the world, the mortality rate of which is 20–30% [10,12]. In 30–50% of those who recovered they have permanent neurological complications [10].

Approximately 70% of cases of meningitis occur in children under the age of 5 years and in adults over the age of 60 [11].

ABM in children is associated with a significant risk of cognitive impairment, mental retardation and hearing impairment that persist in adolescence and can impair training, lead to behavioral disorders and social functioning [2].

Almost all bacterial pathogens have the potential to cause meningitis in human, however the relatively small number of pathogens (i.e. *Streptococcus B*, *Escherichia coli*, *Listeria monocytogenes*, *Haemophilus influenzae b (HIb)*, *Streptococcus pneumoniae* and *Neisseria meningitidis*) accounts for the majority of ABM cases in newborns and children, although the causes this association remains incompletely understood [15].

More than 90% of ABM cases in the world cause three major pathogens: *Hib*, *Streptococcus pneumoniae* (*S. pneumonia*) and *Neisseria meningitidis* (*N. meningitides*). However, the introduction of protein conjugated vaccines against these three pathogens in some countries has changed the epidemiology of bacterial meningitis [3,11,17]. In the United States there is a tendency to reduce morbidity and mortality for pneumococcal and meningococcal meningitis which are associated with the introduction of appropriate vaccination [9].

Thus, etiological agents, climatic and epidemiological factors that contribute to meningitis vary according to country and area. Determining these factors is crucial for monitoring and preventing this problem [14].

The aim of the study — to analyze the etiological structure, epidemiological, socio-demographic features and complications in ABM in children of Khmelnitsky region during 2004–2018.

Materials and methods

It was conducted a prospective analysis of 346 cases of ABM in children undergoing treatment at the Khmelnytskiy Infectious Diseases Hospital for the period from 2004 to 2018 of which 217 boys and 129 girls.

The diagnosis was based on clinical data (presence of intoxication, cerebral and meningeal syndromes) and liquor analysis (cytosis with predominance of neutrophils).

Establishment of the etiological pathogen of meningitis was carried out until 2007 by the bacteriological method. Starting from 2007, the research was carried out at the Central Sanitary and Epidemiological Station of Ukraine (Kyiv) by polymerase chain reaction (PCR) method using a set of reagents “Ampli Sens” *Neisseria* ssp, *Haemophilus* ssp, *Streptococcus* ssp produced by the State Research Center of the Central Research Institute of Rospotrebnadzor. Simultaneously with the PCR method bacterioscopy techniques were used to treat smear of liquor with coloring of Gram material, bacteriological cultures of blood and liquor and the method of latex agglutination.

Complications from the central nervous system were manifested on the basis of a clinical picture of their development (paresis of extremities, convulsions, etc.) and by additional research methods mainly computed tomography (CT) and мagnetic resonance imaging (MRI) both during the acute period of the disease and during the early reconvalescence. In the study we used an analytical method. The processing of the results was carried out by means of determining the standard deviation of the arithmetic mean ($M\pm\sigma$), Student’s criterion and constructing a 95% confidence interval (CI) for the difference of averages.

The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Local Ethics Committee for participant. Informed consent of the children’s parents was obtained for the research.

Results and discussion

Analyzing the dynamics of the incidence of ABM in children, it can be noted mainly its stable nature with slight annual fluctuations and a noticeable outbreak of infection in 2007–2008 as shown in figure 1. According to the diagram, the peak incidence occurred in 2007 and 2008, while a noticeable decline in incidence has been observed since 2014 with the lowest rates in 2017–2018. A similar trend with a decrease in the incidence rate can be associated primarily with the introduction in Ukraine to children under 1 year of age, starting in 2006, of routine vaccination against *Hib*-in-

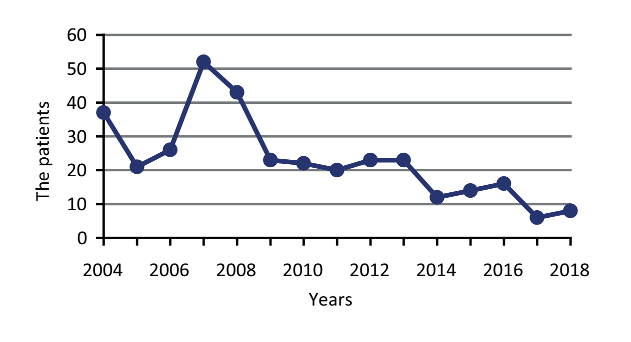

Fig. 1. Dynamics of sickness for ABM in children of Khmelnitskyi region during 2004—2018

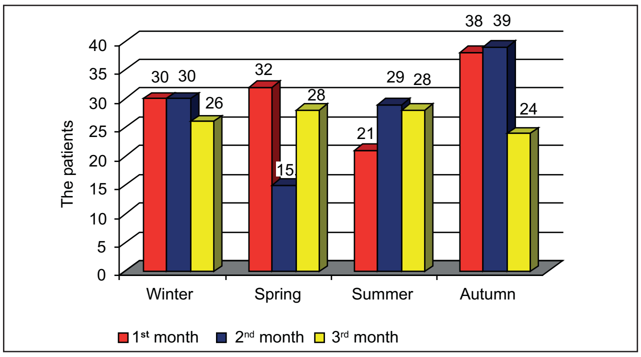

Fig. 2. The seasonal morbidity of ABM in children in Khmelnytskyi Region from 2004 to 2018

fection and, as a result, a decrease in the proportion of meningitis caused by *Hib*-infection, as well as socio-demographic factors (especially migration of the population and a decrease in the number of children in the region).

ABM in children practically equally arose in all seasons with slight variations depending on the month. The lowest incidence was observed in April 15 (4.3%) and the highest in September and October (by 38 (10.9%) end 39 (11.3%), respectively), (Fig. 2). In general, the highest seasonal increase in the incidence of ABM in children is in the autumn period and it is 101 (29.2%) of the total annual incidence.

An increase in the incidence of ABM in children in the autumn is most likely due to seasonal climatic changes, an increase in the number of respiratory diseases and an increase in contacts with other children in kindergartens and schools.

In the Egyptian study the highest morbidity in the ABM was observed in the autumn and winter periods [2]. In Italian observations the maximum number of cases of ABM (63.5%) occurred for the period from October to March [5].

The average age of children with ABM disease was 4.26±0.26 years. According to age categories the incidence of ABM was distributed as follows: in the first year of life 112 (32.4%) children suffered from illness, 89 (25.7%) from 1 to 3 years old, 61 (17.6%) from 4 to 11 years old, from 8 to 12 years old — 40 (11.6%) and from 13 to 18 years old — 44 (12.7%). Thus, the overwhelming majority of ABM was found in children aged 1 month to 3 years 201 (58.1%) especially before 1 year 112 (32.4%). Similar data was obtained in other studies [1,13].

A similar trend, in which the greatest incidence occurs in children under 1 year old and from 1 year to 3 years and which can be traced in studies in other countries can be explained by the immaturity of the immune system and central nervous system (especially the blood-brain barrier). Also, the risk of the disease increases in the presence of an unfavorable premorbid background (prematurity, previous intrauterine hypoxia, anemia) and concomitant diseases, which are very often observed in this age category. In our study, premorbid background and concomitant pathologies were observed in 92 (46%) patients under 3 years of age and were mainly represented by anemia 66 (71.7%), perinatal CNS lesions 15 (16.3%), and malnutrition 9 (9.8%) and etc.

According to the received data the number of male patients who were ill with ABM was 212 (62.7%), while the female population was 126 (37.3%) which corresponded to the ratio of boys to girls 1.7:1.

The etiological factor of ABM was established in 121 (35.0%) patients (Fig. 3). The detection of pathogens of ABM in other countries and regions varies slightly and does not always reaches even an average level which can be due to many factors. According to the study [16] the average level of detection of ABM in the country was 37.1%, among which the detection of meningococcal etiology was 41.8% and meningitis of nonmeningococcal etiology was not more than 32% [16]. At the same time, in Italy the detectability of the pathogens of the ABM reached 65.9% [5].

Figure 3 shows that *Neisseria meningitidis* remains the main pathogen among children with ABM which was detected in 70 (57.9%) cases. The second ranked place is *S. pneumoniae*, which was detected in 26 (21.5%) patients. The third place was usually *Haemophilus influenzae*, which was detected in 12 (9.9%) patients. *Staphylococcus aureus* 5 (4.2%) was a notable percentage among the pathogens and other agents were isolated in rare cases.

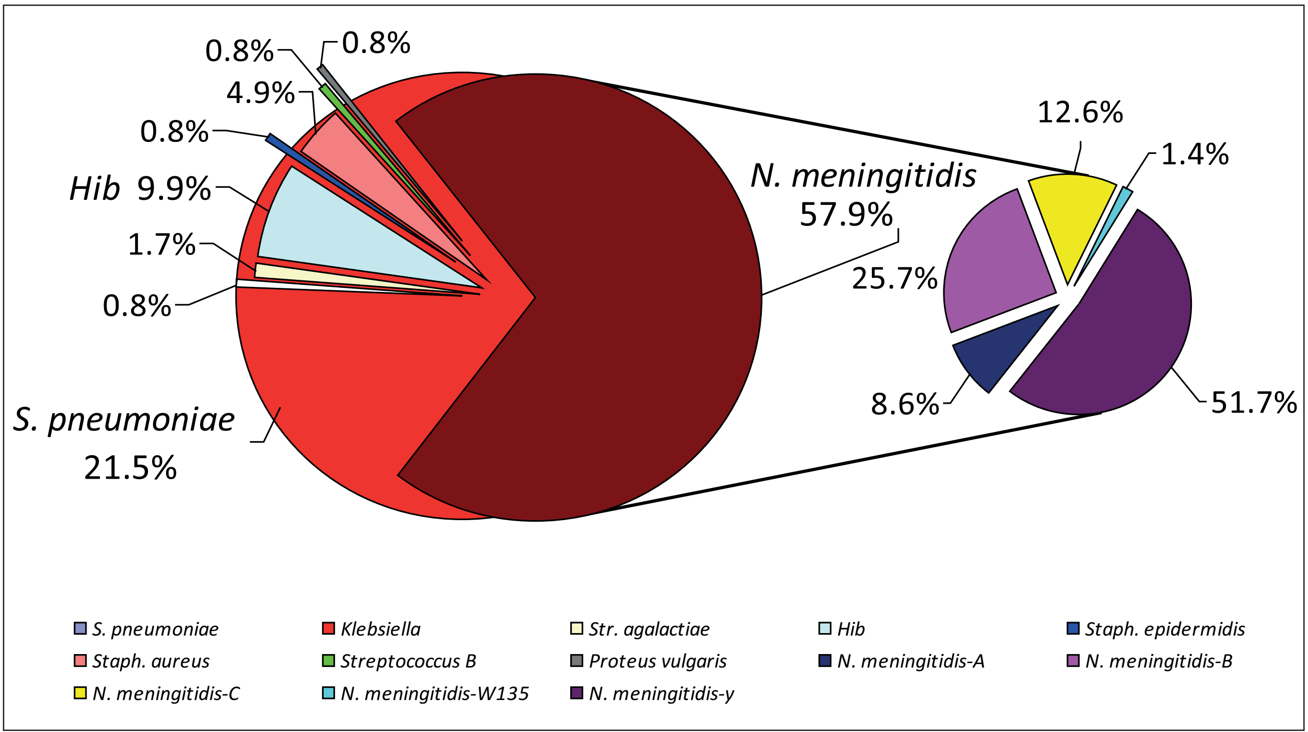

Fig. 3. The etiological structure of purulent meningitis in children in Khmelnytskyi region from 2004–2018

Since 2006 routine vaccination of children against *Hib*-infection has been carried out in Ukraine, at the same time vaccination against meningococcal and pneumococcal infections has not been carried out and is not carried out, therefore it is possible that these pathogens dominate the etiological structure of ABM both in the region and throughout the country.

It should be noted that 9 out of 12 children in whom *Hib* was identified were not vaccinated against this infection.

It should be noted that in 34 (48.3%) of cases it was detected the serogroup *N. meningitidis* where meningococcal serogroup B 18 (25.7%) was the most frequent and serogroups C 9 (12.6%) and A 6 (8.6%) were found to be less frequent. In only one case it was detected the meningococcal serogroup W135; in other cases the serogroup of the pathogen was not successful.

The method of PCR liquor was verified by the pathogen in 66 (54.5%) patients, by bacterioscopy of the smear of the liquor — in 45 (37.2%) patients, by latex agglutination method — in 5 (4.1%) and bacteriological sowing method of the material — in general 65 (53.7%) patients. The method of bacteriological cure of the liquor was verified in 42 (64.6%) patients, the sowing of blood — in (23.2%) patients and in 4 (6.1%) patients the causative agent was sown posthumously from the shells of the brain.

Among the above-mentioned verification methods only one method detected a pathogen in 74 (61.1%) patients with two methods simultaneously in 38 (31.4%) patients and at the same time in three methods in 9 (7.5%) patients.

The received data from the etiological factor in most cases coincide with the data obtained in other regions and countries.

However, in some countries the etiological structure of ABM differs from the usual which can be explained by the use of appropriate vaccines against the main pathogens of meningitis as well as geographical features and socio-demographic factors.

Quite different data were obtained in China. The main causative agent of ABM was also *S. pneumoniae* 33.2% but *E. coli* 10.9% took the second place and *Enterococcus* 10.0% took the third place which could be explained by the fact that the group of patients was predominantly composed of children under the age of 1 where these pathogens can often be the cause of ABM [13].

In our study the bacterial culture of *N. meningitidis* was detected in 34 patients, *S. pneumoniae* — in 13 and *Hib* — in 7 patients. Accordingly, a study was conducted on sensitivity to antibiotics. In the course of the research it was determined that *N. meningitidis* was in most cases susceptible to most antibacterial agents namely: chloramphenicol, ampicillin, penicillin, ceftriaxone, meropenem, ofloxacin, amicacin, and gentamicin. In two (5.8%) cases *N. meningitidis* serotype B was not susceptible to vancomycin and in two (5.8%) cases they were moderately susceptible to vancomycin and clindamycin.

S. pneumoniae was almost always susceptible to chloramphenicol, ampicillin, penicillin, ceftriaxone, meropenem, ofloxacin, amicacin, vancomycin, ciprofloxacin, levofloxacin and rifampicin. In three (23.0%) cases *S. pneumoniae* was not susceptible to ofloxacin and in one (7.7%) case – to chloramphenicol.

Hib was susceptible to chloramphenicol, ceftriaxone, amoxicillin, levofloxacin, cefaperazone and doxycycline. In two (28.5%) cases *Hib* was not susceptible to ceftriaxone, amicacin, ampicillin and imipenem.

In 305 (88.1%) children the disease was overwhelming as meningitis whereas meningoencephalitis was diagnosed in 41 (11.9%) children. There was no significant difference in the incidence between the children of the countryside and the city. Mostly children living in urban areas 186 (53.8%) in comparison with rural children 160 (46.2%), were ill that corresponding to a ratio of 1.2:1.

In 346 (100%) of cases, the disease began with fever. Very frequent symptoms of ABM were neck stiffness 289 (83.5%) and vomiting 273 (78.9%). Seizures was almost always manifested by tonic-clonic epileptic seizures and was observed in 9 (2.6%) of patients for the first day of the disease, subsequently they developed in another 10 (2.9%) of patients. Focal neurological signs were presented in the form of development of limb paresis in 4 (13.8%) patients, cranial nerve involvement in 5 (17.2%) patients, oculomotor disorders in 15 (51.8%) patients, limb tone disorders, anisoreflexia, and the presence of pathological reflexes in another 5 (17.2%) patients. The clinical manifestation of ABM is presented in table.

Table

Clinical manifestation of acute bacterial meningitis in children

Clinical symptoms	Number of patients	%
Fever	346	100
Headache	124	35.8
Vomit	273	78.9
Neck stiffness	289	83.5
Kernig's sign	176	50.8
Brudzinski's sign	122	35.2
Hyperesthesia	130	37.6
Irritability	36	10.4
Alteration of consciousness	28	8.1
Seizures	9	2.6
Focal neurological signs	29	8.4
Septic shock	21	6.0
Petechial rash	56	16.2

The development of similar clinical symptoms characteristic of ABM in different ratios is also noted in studies by other authors.

The highest level of cytosis with the predominance of neutrophils was observed in meningitis caused by *N. meningitidis* which was 5801.3±4856.7 cells/mm³ and significantly exceeded the cytosis level in meningitis caused by *S. pneumoniae* in which it reached 2601.0±1839.6 cells/mm³ ($p<0.001$) (95% CI, 1246.5 to 5154.0 cells/mm³). It was slightly lower and statistically insignificant ($p>0.05$) than with meningococcal meningitis it was observed the cytosis at meningitis induced *Hib* which was 5152.6±4153.1 cells/mm³, however cytosis was significantly superior in meningitis induced *S. pneumoniae* ($p<0.01$), (95% CI, 597.7 to 4505.4 cells/mm³). The high level of cytosis in meningitis caused by *N. meningitidis* and *Hib* can be explained by a significant inflammatory reaction of the body in response to the release of bacterial endotoxin, the main factor of the emergence of toxic toxic shock, which is released only when the bacteria are destroyed, which is especially characteristic of meningococcus and other gram-negative bacteria. The toxic effect of endotoxin stimulates the cells of the immune system, which leads to the release of a large number of inflammatory mediators and cytokines with the development of a pronounced inflammatory response.

The level of protein of the liquor was the highest in meningitis caused by *S. pneumoniae* and was 179.0±51.0 mg/dl in comparison to meningitis induced *N. meningitidis* where its level was 102.0±49.0 mg/dl ($p<0.001$), (95% CI, 54.0 to 99.0 mg/dl) and meningitis induced *Hib* where the protein level was 112.0±56.0 mg/dl ($p<0.05$), (95% CI, 29.0 to 104.0 mg/dl).

This difference can be explained by the fact that meningitis caused by *S. pneumoniae* has a more severe course and it is much more often causes damage of the brain substance with the development of neurological complications and the tendency to abscess. Similar changes in contrast to gram-negative pathogens are associated mainly with the action of exotoxin bacteria. In studies by J.S. Braun et al. (2007) it was shown that it is pneumolysin that is the key factor in the development of neuronal damage and death in pneumococcal meningitis [8].

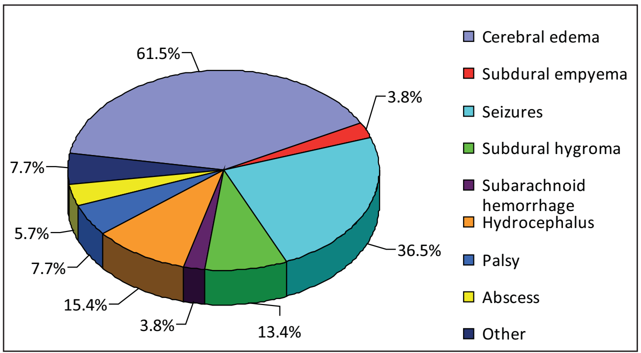

Fig. 4. General complications of ABM in children from the central nervous system

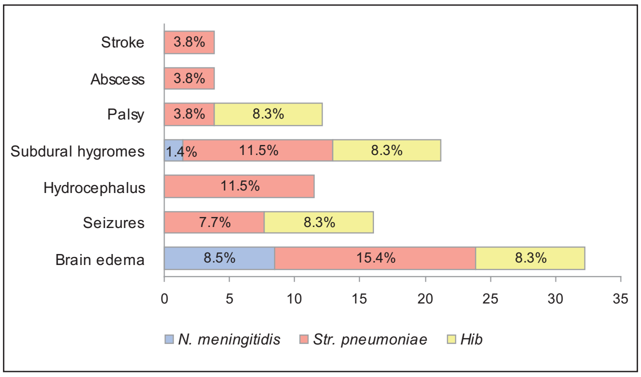

Fig. 5. Complications of the CNS caused by the main pathogens of ABM

A similar trend was observed with the levels of sugar in liquor. At the lowest level it was detected in meningitis induced *S. pneumoniae* and it was 1.91±0.35 mmol/l, while in meningitis induced *N. meningitidis* the sugar level was 2.41±0.47 mmol/l ($p<0.01$), (95% CI, 0.29 to 0.70 mmol/l) and with meningitis caused by *Hib* 2.35±0.34 mmol/l ($p<0.01$), (95% CI, 0.19 to 0.68 mmol/l) compared with pneumococcal meningitis. There was no significant difference between the level of liquor sugar between meningococcal meningitis and meningitis induced *Hib*.

According to the European Federation of Neurological Societies (EFNS) the neurological complications of ABM occur in 30–50% of cases. Chronic fatigue, depression and sleep disturbance are often found in reconvalescents of meningitis. Cognitive dysfunction, behavioral disorders, convulsions, and motor disorders are common complications of meningitis in adults and children. Delay in growth and mental development are delayed complications of ABM found in children. Chronic fatigue, depression and sleep disturbance are common in reconvalescents of meningitis [10].

In a study by M.C. Atti et al. (2014) in 34.1% of cases of ABM there was at least one complication of the course of pathology, in 7.1% there were severe complications [5]. The most serious and frequent complications arise in meningitis caused by Streptococcus pneumoniae with a high mortality rate of up to 36% of cases [7]. In 40% of cases of pneumococcal meningitis there are neurological complications of which the most frequent are behavioral disorders (22.9%) [4].

According to G. Berberian et al. (2014) complications of pneumococcal meningitis occurred in 50% of patients and the lethal end was observed in 10% of cases. In 22% of cases pneumococcal meningitis was secondary, most often as a result of pneumonia, otitis and sinusitis [6].

In our observation, in 52 (15.4%) patients, both acute and late neurological complications of the disease were observed, a significant part of which were severe (Fig. 4).

Of severe infections which complicated the course of the disease the brain edema 32 (61.5%), epileptic seizures 19 (36.5%) and hydrocephalus 8 (15.4%) were common. Subdural hygromes 7 (13.4%), paresis of extremities 4 (7.7%), abscess formation 3 (5.7%), subarachnoid hemorrhage, hearing impairment and subdural empyema were detected (by 2 (3.8%), respectively). Among other lesions 4 (7.7%) isolated cases were parenchymal and subdural hemorrhages, ischemic stroke, visual impairment with the development of amaurosis and ventriculitis. In 18 (34.6%) patients several complications were observed at the same time.

In our study the most severe and frequent complications occurred in meningitis caused by *S. pneumoniae* compared to other bacterial meningitiditis agents (Fig. 5).

Thus, the most severe cerebral complications were observed in meningitis caused by *S. pneumoniae* and *Hib*.

The outcome of the disease with full recovery was observed in 268 (77.4%) patients and in 78 (22.6%) patients the consequences of the disease were observed in the form of cerebroasthenic syndrome 67 (85.9%), autonomic dysfunction 4 (5.3%), and epilepsy 4 (5.3%), deafness 2 (2.6%), apallic syndrome, atactic syndrome and amaurosis 1 (1.3% each). It should be noted that all cases of deafness occurred with *Hib* meningitis.

Also during the study period 15 (4.3%) patients died, including boys 11 (73.3%) and 4 (26.7%) girls corresponding to 2.75:1 with a total annual mortality of 0.44 per 100 thousand children. After the introduction of vaccination against *Hib*-infection, there is also a decrease in mortality from ABM in children. If during the study period the highest mortality from ABM was observed in 2006 (1.62 per 100 thousand children), then the lowest mortality was observed in 2016 (0.41 per 100 thousand children).

In 11 (73.3%) patients the disease was overwhelming as meningoencephalitis. Almost all deceased causes of death were the development of cerebral edema with insertion into the large occipital opening, while in 4 (26.6%) patients occlusive hydrocephalus was detected, in 2 (13.3%) the brain abscess was detected and 1 (6.6%) subdural hemorrhage and ventriculitis were detected.

The majority 11 (73.7%) of deceased children were under 1 year old. In 9 (60.0%) dead patients the pathogen was detected of which 3 (33.3%) were *S. pneumoniae*, 3 (33.3%) children had *N. meningitidis*, and 1 (11.1%) kid had *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Proteus vulgaris*. In the other 6 (40.0%) children the pathogen was not identified.

Taking into account epidemiological data, during the study the prevalence of ABM among children in the Khmelnitskyi region was determined which in total was 10.0 per 100 thousand children per year. It can be noted that the obtained indicator is somewhat higher than the total European population which is probably related to the climatic conditions of the region and the absence of planned vaccination against major pathogens of the ABM (*N. meningitidis* and *S. pneumoniae*).

Conclusions

Over the past ten years, there has been a significant decrease in the disease by ABM in children, which is probably associated with the introduction in Ukraine, starting in 2006, of a planned vaccination against *Hib*-meningitis.

Mostly (58.1%) children with ABM aged 1 month to 3 years old, especially one year old (32.4%) are ill. The disease is more common in boys than in girls in the ratio of 1.7:1.

The etiological factor of ABM was established in 121 (35.0%) patients. *N. meningitidis* remains the major causative agent among children with ABM which was detected in 70 (57.9%) cases. The second place is *S. pneumoniae* — 26 (21.5%) cases. The third place was *Hib* which was detected in 12 (9.9%) patients. *Staphylococcus aureus* 5 (4.2%) was a notable percentage; other agents were isolated in rare cases.

All detected pathogens of ABM were sensitive to the main antibacterial preparations (ceftriaxone, penicillin, chloramphenicol, meropenem, etc.) which are used as a starting therapy in the treatment of ABM.

In 346 100% of cases, the disease began with fever. Very frequent symptoms of ABM were neck stiffness 289 (83.5%) and vomiting 273 (78.9%). The highest level of cytosis with neutrophil prevalence was observed in meningitis caused by *N. meningitidis* compared with pneumococcal meningitis ($p<0.001$). The level of cerebrospinal fluid protein was highest with pneumococcal meningitis compared with meningococcal meningitis and *Hib*-meningitis ($p<0.05$).

In our observation, neurological complications of the disease were observed in 52 (15.4%) patients. The most common complications were cerebral edema 32 (61.5%), epileptic seizures 19 (36.5%) and hydrocephalus 8 (15.4%). The most severe cerebral complications occurred in meningitis caused by *S. pneumoniae*. The outcome of the disease with full recovery was observed in 268 (77.4%) patients and the effects of the disease were observed in 78 (22.6%) patients.

During the study 15 (4.3%) patients died which corresponded to an annual mortality of 0.44 per 100 thousand children.

In the course of the study the prevalence of ABM among children in the Khmelnitskyi region was determined which in total was 10.0 per 100 thousand children per year.

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