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CLINICAL FEATURES AND COMPLICATIONS OF BACTERIAL MENINGITIS IN CHILDREN

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Relevance: Bacterial meningitis (BM) remains a significant cause of neurological complications and high mortality among children.

Aim: to study the clinical features of BM in children to optimize the diagnosis and etiopathogenetic therapy.

Methods: The object of the study is children diagnosed with meningitis, treated at the Multidisciplinary City Children's Hospital No. 3 in Astana, for the period from 2015 to 2023. Study design: prospective, control - case. Methods included clinical examination, complete blood count, cerebrospinal fluid test, CT and brain MRI. Descriptive statistics and Pearson's method were used for statistical processing.

Results: Introduction of the PCV13 vaccine led to a fourfold decrease in the incidence of pneumococcal meningitis, while cases of meningococcal meningitis declined 1.6 times from 2014 to 2023. The main clinical manifestations in children with BM included high fever (80–90% of patients, with febrile temperatures ranging from 38.7°C to 39.9°C), neurological deficits, and complications: seizures and cognitive impairment developed in 50% of children. Hypertensive syndrome was observed in 81.8% of children with pneumococcal meningitis (PM), and in 55.6% of meningococcal meningitis (MM) cases among children under one year old. Pneumococcal CNS involvement was characterized by focal symptoms in 45.5% of young children, while such changes were statistically significantly lower in MM cases—threefold less (16.7%, $p \leq 0.001$). Spearman's correlation analysis in the PM group showed a strong direct positive relationship between the following variables: delayed medical consultation and hospital stay duration ($r=0.7$; $p \leq 0.001$), delayed diagnosis and hospital stay duration ($r=0.7$; $p \leq 0.001$).

Conclusion: PCV13 vaccination has significantly reduced the incidence of pneumococcal meningitis, which presents most severely, with early neurological complications in 41.5% of cases, cerebral edema in 90.9% of infants, and hypertensive syndrome in 81.8%. Early diagnosis and timely treatment contribute to the prevention of both early and late neurological complications.

Keywords*: bacterial meningitis, viral meningitis, neurological complications, pneumococcal conjugate vaccine, pneumococcal infection, meningococcal infection.*

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Резюме

КЛИНИЧЕСКИЕ ОСОБЕННОСТИ И ОСЛОЖНЕНИЯ БАКТЕРИАЛЬНЫХ МЕНИНГИТОВ У ДЕТЕЙ

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Актуальность: Бактериальные менингиты (БМ) остаются значимой причиной неврологических осложнений и высокой смертности среди детей.

Цель исследования: изучение клинических особенностей БМ у детей для оптимизации диагностики и этиопатогенетической терапии.

Методы: Объект исследования - дети с диагнозом "менингит", пролеченные в Многопрофильной городской детской больнице №3 в г.Астана, за период с 2015 по 2023 гг. Дизайн исследования: проспективный, контроль – случай. Методы включали клинический осмотр, общий анализ крови, анализ спинномозговой жидкости, КТ и МРТ головного мозга. Для статистической обработки использовались описательная статистика и метод Пирсона.

Результаты: Введение вакцины ПКВ13 привело к четырехкратному снижению заболеваемости пневмококковым менингитом, в то время как случаи менингококкового менингита уменьшились в 1,6 раз с 2014 по 2023 годы**.** Основные клинические проявления у детей с БМ включали высокую температуру (80-90% пациентов, с фебрильной температурой от 38,7°C до 39,9°C), неврологические дефициты и осложнения: судороги и когнитивные нарушения– развивались у 50% детей. Гипертензионный синдром наблюдали в 81,8 % случаях в группе детей с ПМ, в 55,6% случаях при ММ у детей до 1 года. Пневмококковое поражение ЦНС характеризовалось развитием очаговой симптоматики в 45,5% случаев у детей раннего возраста, при ММ данные изменения зарегистрированы статистически достоверно меньше в 3 раза (16,7% p≤0,001). Корреляционный анализ по методу Спирмена в группе детей с ПМ продемонстрировала сильную прямую положительную связь между показателями: поздней обращаемости и количеством койко-дней (r=0,7;p≤0,001), поздней диагностикой и количеством койко-дней (r=0,7;p≤0,001).

Заключение: Вакцинация ПКВ13 привела к значительному снижению заболеваемости пневмококковым менингитом, который протекает наиболее тяжелее с ранними неврологическими осложнениями в 41,5% случаев, отеком головного мозга у детей первого года жизни в 90,9%, гипертензионным синдромом в 81,8%. Ранняя диагностика и своевременное лечение способствуют предотвращению ранних и поздних неврологических осложнений.

Keywords**: bacterial meningitis, viral meningitis, neurological complications, pneumococcal conjugate vaccine, pneumococcal infection, meningococcal infection**.

Для цитирования:

Баешева Д.А., Жумагалиева Г.Д., Кошерова Б.Н., Турдалина Б.Р., Алтынбекова А.В., Кубекова С.Ж., Жузжасарова А.А., Утегенова А.М., Жармаганбетова Б.О., Сейдуллаева А.Ж. Клинические особенности и осложнения бактериальных менингитов у детей // Наука и Здравоохранение. 2025. Vol.27 (2), С.87-98. *doi 10.34689/SH.2025.27.2.011*

Түйіндеме

БАЛАЛАРДАҒЫ БАКТЕРИАЛДЫҚ МЕНИНГИТТІҢ КЛИНИКАЛЫҚ ЕРЕКШЕЛІКТЕРІ

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Өзектілігі: Бактериялық менингит (БМ) неврологиялық асқынулардың және балалар арасындағы жоғары өлім-жітімнің маңызды себебі болып қала береді.

Зерттеудің мақсаты: диагностика мен этиопатогенетикалық терапияны оңтайландыру үшін балалардағы БМ клиникалық ерекшеліктерін зерттеу.

Зерттеу әдістері: Зерттеу нысаны 2015-2023 жылдар аралығында Астана қаласындағы №3 көпсалалы қалалық балалар ауруханасында емделген менингит диагнозы қойылған балалар болды. Зерттеу дизайны: перспективалық, жағдайды бақылау. Әдістерге клиникалық тексеру, жалпы қан анализі, цереброспинальды сұйықтықты талдау, мидың КТ және МРТ кіреді. Статистикалық өңдеу үшін сипаттамалық статистика және Пирсон әдісі қолданылды.

Нәтижелері: PCV13 вакцинасын енгізу пневмококкты менингитпен сырқаттанушылықтың 4 есеге төмендеуіне әкелді, ал менингококкты менингит жағдайлары 2014 жылдан 2023 жылға дейін 1,6 есеге азайды. БМ бар балалардағы негізгі клиникалық көріністерге жоғары температура (температурасы 80-90 %-ға дейін фебрильді науқастардың 80-90 %-ы 3.8°C дейін) жатады. 39,9°C), неврологиялық тапшылықтар мен асқынулар: балалардың 50%-ында құрысулар және когнитивті бұзылулар дамыған. Гипертониялық синдром ПМ бар балалар тобында 81,8% жағдайда, 1 жасқа дейінгі балаларда ММ бар 55,6% жағдайда байқалды. Пневмококк ОЖЖ зақымдануы жас балаларда 45,5% жағдайда ошақты симптомдардың дамуымен сипатталды; ММ-де бұл өзгерістер статистикалық түрде 3 есеге аз тіркелді (16,7% p≤0,001). ПМ бар балалар тобында Спирман әдісін қолданатын корреляциялық талдау көрсеткіштер арасында күшті тікелей оң байланысты көрсетті: кеш жіберілген және емханадағы күндер саны (r=0,7; p≤0,001), кеш диагноз және ауруханадағы күндер саны (r=0,7; p≤0,001).

Қорытынды: ПКВ13 вакцинасы 41,5% жағдайда ерте неврологиялық асқынулармен ең ауыр пневмококкты менингитпен, өмірдің бірінші жылындағы балаларда церебральды ісінумен 90,9%, гипертониялық синдроммен 81,8% аурушаңдықтың айтарлықтай төмендеуіне әкелді. Ерте диагностика және уақтылы емдеу ерте және кеш неврологиялық асқынулардың алдын алуға көмектеседі.

Түйінді сөздер: *бактериялық менингит, вирустық менингит, неврологиялық асқынулар, пневмококкты конъюгаттық вакцина, пневмококк инфекциясы, менингококк инфекциясы.*

Дәйексөз үшін:

Баешева Д.А., Жумагалиева Г.Д., Кошерова Б.Н., Турдалина Б.Р., Алтынбекова А.В., Кубекова С.Ж., Жузжасарова А.А., Утегенова А.М., Жармаганбетова Б.О., Сейдуллаева А.Ж. Балалардағы бактериалдық менингиттің клиникалық ерекшеліктері // Ғылым және Денсаулық сақтау. 2025. Vol.27 (2), Б. 87-98. *doi 10.34689/SH.2025.27.2.011*

Introduction

Bacterial meningitis (BM) remains a significant cause of high morbidity, mortality, and frequent residual neurological complications worldwide, often requiring emergency medical intervention. The most common etiological agents in the development of BM are *Streptococcus pneumoniae, Haemophilus influenzae* type b (Hib), and *Neisseria meningitidis* [16]. Currently, the incidence and mortality rates are decreasing with the introduction of vaccines against the three most prevalent central nervous system (CNS) pathogens*: Haemophilus influenzae type b, Streptococcus pneumoniae, and Neisseria meningitidis* [16,17].

According to the World Health Organization (WHO, 2015), neurological complications in patients with BM are observed in 15% of cases in developed countries, while the mortality rate reaches 5% [13]. However, the incidence and related mortality of BM continue to rise in developing countries [20].

BM is characterized by severe clinical manifestations, with a mortality rate of up to 30%. Among survivors, approximately 50% of children may develop short- and long-term neurological complications [5]. Short-term complications include neurological deficits and subdural empyema, while long-term consequences may involve hearing loss, seizures, cognitive impairment, and hydrocephalus. These complications arise as a result of the host's immune response to the release of bacterial toxins, leading to neuronal damage. Risk factors for their development include early age, male sex, unfavorable premorbid background, and lack of vaccination [21]. Vaccination is the primary method of preventing BM and its complications. Alongside urgent pathogenetic therapy, timely antibiotic administration plays a crucial role in reducing the risk of neurological complications [9].

Recently, due to the lack of significant differences in the clinical course of BM, the importance of differential diagnosis has increased [10]. This is one of the pressing issues in neuroinfections, due to the frequent polyetiological nature of BM, progressive development of life-threatening conditions, and the appearance of neurological complications that are difficult to treat. Therefore, diagnosis and interpretation of clinical symptoms require adequate etiotropic therapy targeting the specific causative pathogen.

Thus, BM represents a serious medical and social issue in pediatrics, deserving special attention and requiring further study, with necessary monitoring of the prevalence and antibiotic resistance of *N. meningitidis, S. pneumoniae*, and *Hib*. In the Republic of Kazakhstan, only a limited number of scientific studies have been conducted on BM in children.

Objective of the study: To investigate the clinical features of bacterial meningitis in children to optimize diagnosis and etiopathogenetic therapy.

Materials and Methods

Study design: Prospective, case-control. The study population consisted of patients aged 1 month to 15 years with a clinical diagnosis of "meningitis," who received treatment in the intensive care unit and infectious disease departments No. 1 and 6 of the State Municipal Enterprise on the Right of Economic Management "Multidisciplinary City Children's Hospital No. 3" (MCCH No. 3) under the Akimat of Astana. This study was conducted as part of the scientific project "Development of Early Diagnosis and Preventive Measures for Hearing Loss Following Bacterial Meningitis in Children" (grant number AR05135091), funded under the 2018–2020 grant program. The project was carried out at the Department of Pediatric Infectious Diseases of the Astana Medical University and at the Life Sciences Center of the Private Institution "National Laboratory Astana" of Nazarbayev University, Astana.

The main study group included patients with an etiologically confirmed diagnosis of "bacterial meningitis." These patients were subdivided into two subgroups: children with pneumococcal meningitis (PM, n=26) and children with meningococcal meningitis (MM, n=83). The comparison control group consisted of patients with an etiologically confirmed diagnosis of "enteroviral meningitis" (EM, n=90). The diagnosis of bacterial meningitis (BM) was confirmed by identifying *N. meningitidis, S. pneumoniae*, or *Hib* from nasopharyngeal swabs, blood, and cerebrospinal fluid. Enteroviral meningitis was verified by PCR testing of stool samples. Clinical studies were conducted in accordance with national clinical protocols: "Diagnosis and Treatment of Meningococcal Infection in Children" approved by the Republican Center for Health Development, Ministry of Health and Social Development of the Republic of Kazakhstan, April 10, 2019, (Protocol No. 63), "Bacterial Meningitis in Children and Adults" (approved by the Republican Center for Health Development, Ministry of Health and Social Development of the Republic of Kazakhstan, June 9, 2016, Protocol No. 4, Protocol No. 9). The research methods included clinical examination, complete blood count (CBC: hemoglobin, leukocytes, neutrophils, platelets, ESR), urinalysis, blood biochemistry (CRP), procalcitonin test, cerebrospinal fluid (CSF) analysis, bacteriological cultures, CT and MRI of the brain, and consultations with a neurologist. A detailed analysis of patients' medical records was conducted (forms 003/u and 003–2/u). All observed patients had not been immunized with the pneumococcal vaccine (PCV), or with hexavalent or pentavalent *vaccines containing Hib*.

Statistical data processing was performed using SPSS IBM Statistics 23. The following parametric methods were used: descriptive statistics (mean, standard deviation). Sample size calculation was based on the following assumptions: 95% confidence interval, 80% power, 5% significance level, and a two-sided significance test. Descriptive statistics and Pearson's correlation method were applied.

The study was reviewed and approved by the Ethics Committee of the "Life Sciences Center" of Nazarbayev University (September 22, 2017, Protocol No. 20).

Results

Analysis of annual reports from MCCH No. 3 revealed that from 2014 to 2023, following the introduction of the PCV13 vaccine, the number of hospitalized cases of pneumococcal meningitis decreased by 4.2 times (from 26.4% to 6.2%) (Figure 1). Over the same period, there was only a trend toward a reduction in meningococcal meningitis

cases—by 1.6 times (from 27.6% to 16.5%). The proportion of BM cases with an unidentified etiology remained relatively constant throughout the observation period, ranging from 42.5% to 33.7%.

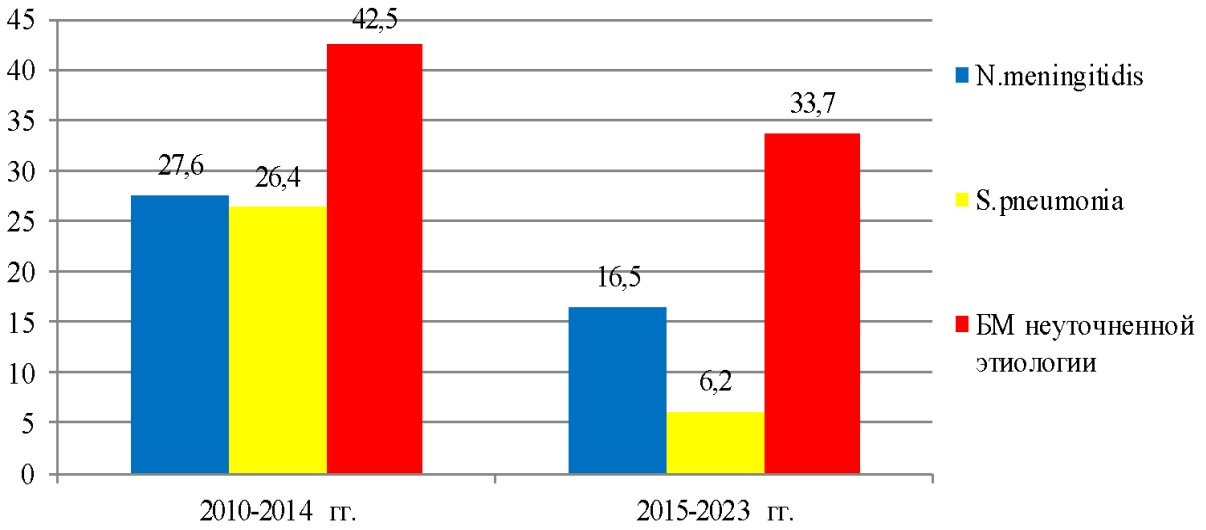
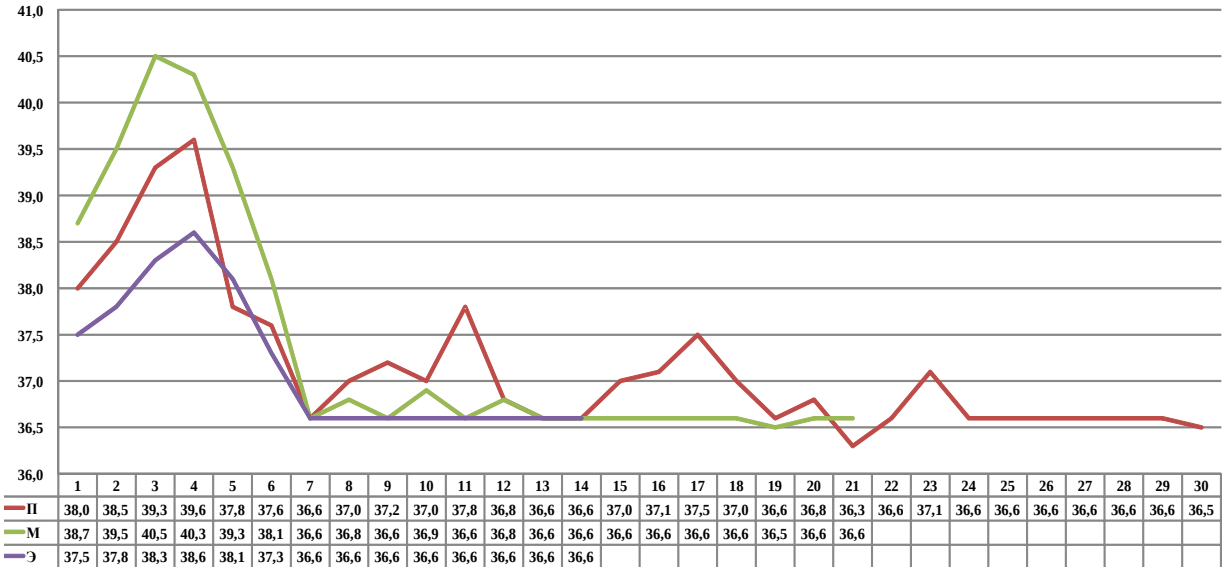


Figure 1. Proportion of pediatric BM cases at MCCH No. 3 before (2010–2014) and after the introduction of PCV13 in Astana (2015–2023).

Since 2009, no cases of meningitis caused by Haemophilus influenzae type b have been recorded, which is likely associated with the introduction of the Hib vaccine in Kazakhstan in 2008. High and prolonged fever was one of the first and most common symptoms observed in children with meningitis. Table 15 presents the dynamics of body temperature increases, which were recorded in all patients included in the study. Febrile temperatures were observed across all study groups (80–90%) and were characterized by a rise in body temperature from 38.7°C to 39.9°C. It is noteworthy that hectic fever was identified in one-third of patients with meningococcal meningitis (MM). Subfebrile temperature was recorded in 40% of children under the age of one year with pneumococcal meningitis (PM). In the group of children over 5 years old with enteroviral meningitis (EM), febrile temperature predominated in 55.2% of cases, while hectic fever occurred in only 18.4%.

A common feature of meningitis of various etiologies is the resistance of the febrile response to antipyretic treatment. In cases of unfavorable BM progression, body temperature sometimes dropped to normal or subfebrile levels after a brief spike or even without a spike at all. This may have been associated with the development of septic shock [32, p. 105]. We conducted a detailed analysis of the dynamics of the febrile response in pediatric meningitis cases, taking into account the average duration of hospitalization, which was 32±6 days for PM, 17±4 days for MM, and 10±2 days for EM ($p \leq 0.05$).

In the MM group, the temperature curve was characterized by an acute onset with a sharp rise from febrile to hectic levels (38.3°C to 39.3°C), peaking on days 3–4, followed by normalization of body temperature by the end of the illness under the influence of antibacterial therapy (Figure 2).



	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
П	38,0	38,5	39,3	39,6	37,8	37,6	36,6	37,0	37,2	37,0	37,8	36,8	36,6	36,6	37,0	37,1	37,5	37,0	36,6	36,8	36,3	36,6	37,1	36,6	36,6	36,6	36,6	36,6	36,6	36,5
М	38,7	39,5	40,5	40,3	39,3	38,1	36,6	36,8	36,6	36,9	36,6	36,8	36,6	36,6	36,6	36,6	36,6	36,6	36,5	36,6	36,6									
Э	37,5	37,8	38,3	38,6	38,1	37,3	36,6	36,6	36,6	36,6	36,6	36,6	36,6	36,6																

Figure 2. Temperature Curve Dynamics in Meningitis.

In patients with pneumococcal meningitis (PM), the highest body temperature was recorded on day 4, followed by a decrease on days 6–7. Subsequently, despite ongoing etiotropic therapy, unlike in meningococcal meningitis (MM), there was a wave-like pattern of sub-febrile temperature fluctuations from day 8 to day 23 of hospitalization, with brief intervals (1–2 days) of temperature normalization. In general, body temperature normalized in most PM patients (56%, n=13) between days 11–16, and only in 8.6% (n=2) by day 30 of illness.

Hypothermia in PM was characterized by resistance to antipyretic therapy and sharp fluctuations in body temperature, indicating a dysfunction of central thermostatically mechanisms, consistent with our earlier findings [51, p. 63]. In enteroviral meningitis (EM), during the first 1-2 days of illness, the temperature remained at sub-febrile levels and transitioned to febrile (38.3°C) by day 3. The peak febrile response (38.6°C) was observed on day 4 of hospitalization, with stabilization by day 6 and no recurrence of hypothermia.

In our observations, signs of intoxication in infants included irritability, restlessness, lethargy, weakness, and refusal to breastfeed. Notably, the latter is classified as a general danger sign in the Integrated Management of Childhood Illness (IMCI) guidelines and serves as an indication for urgent care. As presented in Table 1, irritability and restlessness were more commonly recorded in children under 1 year of age across all groups—ranging from 60.0% to 75%. In children over 1 year, weakness and lethargy were noted in 75% of those with PM, compared to only 25% and 32.4% in the MM and EM groups, respectively-supporting the more severe clinical course of PM. One of the most significant indicators of CNS infection in infants was refusal to breastfeed, observed in 85.7% of PM patients, 60% of MM patients, and 60% of EM patients under 1 year of age.

Table 1.

Intoxication Syndrome in Children with Meningitis (Absolute numbers and percentages by age group).

Clinical Symptoms	PM (n=26) abs/%			MM (n=83) abs/%			EM (n=90) abs/%		
	0-11mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y
	n=14	n=12	n=0	n=20	n=31	n=29	n=10	n=37	n=43
Irritability, restlessness	9	7	0	15	13	13	6	12	12
	64,2	58,3	0,0	75	65	44,8	60,0	32,4	27,9
Lethargy, weakness	8	9	0	6	8	9	2	12	11
	57,5	75	0,0	30	25	31,3	20,0	32,4	25,5
Refusal to breastfeed	12	8	0	12	4	0	6	0	0
	85,7	57,5	0,0	60	13	0,0	60	0,0	0,0

A key clinical aspect in the disease course is the presence of symptoms indicating CNS involvement—such as changes in psycho-emotional state and consciousness—which serve as equivalents of hydro-cephalic-hypertensive syndrome [27]. According to IMCI guidelines, in infants, painful irritability is a high-evidence marker of CNS involvement. Hypertensive syndrome (see Table 2) was observed across all groups, but was more pronounced in PM and MM than in EM. Intense headache (88.6%; 91.7% in children over 1 year with MM; 59.1% with EM) was mostly localized in the frontal-temporal region and usually lasted no more than 5±1.5 days. Only patients with PM had prolonged headache durations. Vomiting was present at disease onset in most patients and was typically frequent, repetitive, and non-relieving (PM – 91.6%, MM – 64.5%, EM – 43.9%), predominantly in children over 1 year of age. In infants under 1 year, hypertensive syndrome manifested as: High-pitched neurological cry (PM – 64.2%, MM – 45%, EM – 50%), Regurgitation (PM – 58.3%, MM – 35%, EM – 30%), Bulging and tense anterior fontanelle (PM – 100%, MM – 65%, EM – 20%).

Meningeal signs indicate inflammation of the pia mater and spinal nerves. Table 3 presents meningeal signs in children with bacterial meningitis (BM). These signs were particularly pronounced in PM and MM among children older than 1 year, especially in those over 5 years of age. Muscle tone changes caused by CNS infection in PM, MM, and EM were primarily observed as nuchal rigidity: PM: 92.8% and 100%, MM: 90%, 100%, and 100%, EM: 70%, 83.7%, and 88.3%. Brudzinski's upper sign was more frequently identified in children older than one year: PM – 58.3%, MM – 35.4%, EM – 12.9%. Among infants, positive Kernig's and Lessage's signs were also detected. In our study: Kernig's sign: PM – 57.1%, MM – 50%, EM – 20%, Lessage's sign: PM – 71.4%, MM – 50%, EM – 20%.

Assessment of consciousness was performed using the Glasgow Coma Scale (GCS), which evaluates the level of consciousness and coma in children. Scoring is based on three parameters: eye opening (E, score 1–4), verbal response (V, score 1–5), and motor response (M, score 1–6). Thus, the minimum score is 3 (Grade III coma), and the maximum is 15 (clear consciousness).

Upon admission to the hospital, among children with pneumococcal meningitis (PM), clear consciousness was observed in every second infant (58.3%) and in 83.3% of children aged 12–59 months. However, between days 2–5, there was a progression in the level of impaired consciousness, ranging from somnolence to stupor (see Table 4). In meningococcal meningitis (MM), clear consciousness was observed in most children across all age groups (85%, 87.1%, and 89.6%), and, unlike the PM group, further deterioration of consciousness was recorded only in isolated cases. In viral meningitis , no impairment of consciousness was registered either upon admission or during hospitalization.

Table 2.

Hydro-cephalic-Hypertensive Syndrome in Children with Meningitis.

Clinical Symptoms	PM (n=26) abs/%			MM (n=83) abs/%			EM (n=90) abs/%		
	0-11 mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y
	n=14	n=12	n=0	n=20	n=31	n=29	n=10	n=37	n=43
Headache	12	11	0	0	27	28	0	24	23
	85,7	91,6	0,0	0,0	87	96,4	0,0	64,8	53,4
High-pitched neurological cry	9	9	0	9	9	27	5	0	15
	64,2	75,0	0,0	45	29	93,1	50,0	0	34,8
Repeated vomiting	7	11	0	15	20	29	1	16	22
	45,5	91,6	0,0	75	64,5	100,0	10	43,2	51,6
Regurgitation	6	2	0	7	5	0	3	4	0
	58,3	16,6	0,0	35	16,1	0,0	30,0	10,8	0,0
Bulging and tense anterior fontanelle	14	6,0	0	13,0	15,0	0	2,0	6,0	0
	100	50,0	0,0	65	48,3	0,0	20,0	16,2	0,0
Hyperesthesia	10		0	12	17	22	4	24	15009
	83	75	0,0	60	54,8	75?8	40	64,8	20,9
Photophobia	10	10	0	15	7	17	3	10	15
	83	83,3	0,0	75	22,5	58,6	30,0	27	34,8
Seizures	9	8	0	5	6	4	0	0	0
	83	66,7	0,0	25	19,3	13,7	0,0	0,0	0,0

Table 3.

Meningeal Symptoms in Studied Children.

Clinical Symptoms	PM (n=26) abs/%			MM (n=83) abs/%			EM (n=90) abs/%		
	0-11mo.	12-59mo	5-15y	0-11mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y
	n=14	n=12	n=0	n=20	n=31	n=29	n=10	n=37	n=43
Nuchal rigidity	13	12	0	18	31	31	7	31	38
	92,8	100,0	0,0	90,0	100,0	100,0	70,0	83,7	88,3
Brudzinski's upper sign	3	7	0	1	11	17	0	4	35
	21,4	58,3	0,0	5	35,4	54,8	0,0	12,9	81,3
Brudzinski's lower sign	0	5	0	0	8	11	0	0	2
	0	41,7	0,0	0,0	25,8	31	0,0	0,0	5,2
Kernig's sign	8	5	0	10	11	12	2	0	0
	57,1	41,7	0,0	50,0	35,4	41,3	20,0	0,0	0,0
Lessage's sign	10	2	0	10	10	10	2	0	0
	71,4	16,7	0,0	50,0	27,0	34,4	20,0	0,0	0,0

Table 4.

Assessment of Consciousness in Children with Meningitis upon Admission (Glasgow Coma Scale).

Clinical State	PM (n=26) abs/%			MM (n=83) abs/%			EM (n=90) abs/%		
	0-11mo.	12-59mo.	5-15y	0-11mo.	12-59mo.	5-15y	0-11m.	12-59mo.	5-15y
	n=14	n=12	n=0	n=20	n=31	n=29	n=10	n=37	n=43
Clear (15 points)	6	10	0	17	27	26	10	37	43
	58,3	83,3	0,0	85	87,09	89,6	100	100	100
Somnolent (11–14)	3	1	0	2	2	2	0	0	0
	21,5	8,3	0,0	20	6,4	6,8	0,0	0,0	0,0
Stupor (9–10)	3	0	0	0	0	0	0	0	0
	24,4	0,0	0,0	0	0,0	0,0	0,0	0,0	0,0
Coma (≤8 points)	0	0	0	0	0	0	0	0	0
	0,0	0	0,0	0,0	0,0	0,0	0,0	0,0	0,0

Analysis of clinical data in patients with meningitis revealed that the most common complications were: hypertensive syndrome, hydrocephalus, paresis, and divergent strabismus. The frequency of complications varied by group. Hypertensive syndrome was most frequently observed in the PM group among infants (92.5%) - twice as high as in MM (65%) - and only in 10% of EM cases. In children over 1 year, this complication occurred 1.6 times more often in PM (78.5%) than in MM (48.3%), while in children over 5 years with MM, the rate was 17.2%. The second most common complication was hydrocephalus: 28.5% in PM, and 3.2% in MM (in children over 1 year). Divergent strabismus was observed in 7.1% of PM cases in infants and was not registered in other groups.

Table 5.

Neurological Complications of BM in Children.

Complications	PM (n=26) abs/%			MM (n=83) abs/%			EM (n=90) abs/%		
	0-11 mo.	12-59 mo.	5-15 y	0-11 mo.	12-59 mo.	5-15 y	0-11 mo.	12-59 mo.	5-15 y
	n=14	n=12	n=0	n=20	n=31	n=29	n=10	n=37	n=43
Hypertensive syndrome	13	9	0	13	15	5	1	1	1
	92,5	78,5	0,0	65	48,3	17,2	10	2,7	2,3
Hydrocephalus	4	1	0	0	1	0	0	0	0
	28,5	8,3	0,0	0,0	3,2	0,0	0,0	0,0	0,0
Paresis	3	0	0	2	0	1	0	0	0
	21,5	0	0,0	10	0,0	3,4	0,0	0,0	0,0
Divergent strabismus	1	0	0	0	0	0	0	0	0
	7,1	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0

To investigate the correlation between clinical-diagnostic parameters and disease outcomes, Spearman's correlation method was used. In the PM group, a strong direct positive correlation was found between the following parameters: Delayed hospital admission and length of hospital stay (r=0.7; p≤0.001), Delayed diagnosis and length of stay (r=0.7; p≤0.001), Length of hospital stay and neurological complications (r=0.7; p≤0.05), Poor outcome and disease severity (r=0.7; p≤0.05), Disease severity and consciousness impairment (r=0.7; p≤0.05), Consciousness suppression and somnolence (r=0.7; p≤0.05).

Table 6.

Correlation Between Clinical Course and Poor Outcome in PM, MM, and EM.

1 - Correlation Pair	2 - Correlation Pair	Correlation strength and P*		
		PM	MM	Em
Delayed admission	Length of stay	0,7	0,5**	–0,1
Delayed diagnosis	Length of stay	0,7	0,5**	0,2*
Length of stay	Neurological complications	0,7	0,6**	–
Poor outcome	Disease severity	0,7	0,4**	–
Disease severity	Consciousness	0,7	0,1	–
Consciousness suppression	Somnolence	0,7	0,0	–
Disease severity	Combined antibiotic therapy	0,7	0,1	–0,1
Neurological complications	Poor outcome	0,6	0,9**	–
Neurological complications	Disease severity	0,6	0,4**	–
Neurological complications	Consciousnes	0,6	0,1	–
Admission temperature	Admission cytosis	0,6	0,0	0,1
Poor outcome	Combined antibiotic therapy	0,6	0,09**	–
* – p≤,001; ** – p≤0,05				

The dependent variable selected for analysis was the dichotomous variable "meningitis outcomes." For pneumococcal meningitis (PM), this variable included three possible outcomes: "discharged without complications," "discharged with neurological complications," and "transferred to another hospital." For meningococcal meningitis (MM) and enteroviral meningitis (EM), two outcomes were considered: "discharged without complications" and "discharged with neurological complications," thus indicating a probable future assignment of a patient to one of these two or three outcome groups.

To construct the regression model, 15 variables were introduced using a stepwise inclusion method, comprising 8 continuous and 7 categorical predictors. The predictors were combined in a random sequence over several stages, after which a final logistic regression equation was selected based on its predictive accuracy. Following the forced inclusion of all factors into the model, the overall

significance level was p = 0.000, indicating that the model was statistically significant (p < 0.05).

To examine the influence of various factors on disease outcomes, a stepwise elimination procedure was employed to determine the minimal set of predictors, assessed by Nagelkerke's R^2. The coefficient of determination (R^2) indicates the proportion of variance in the dependent variable explained by the predictors included in the model. For predicting the outcomes of bacterial meningitis (BM), the final model demonstrated a Nagelkerke R^2 of 0.634 (63%), suggesting that 63% of the variability in BM outcomes could be attributed to the identified predictors.

Table 6 presents the final results of the stepwise inclusion of potential predictors, along with the significance levels, Wald statistics, the -2 Log Likelihood of the reduced model, and chi-square statistics. The likelihood ratio test reflects changes in the likelihood function when a specific predictor is excluded, expressed through the chi-square (χ^2) value. A significance level of p < 0.001 indicates that the included factors — vaccination status, term/preterm birth status, premorbid conditions, delayed diagnosis, hospital admission, and age — have a highly significant impact on the dependent variable (BM outcome).

The likelihood ratio tests demonstrated that the most influential predictors were vaccination status (p = 0.000), hospital admission (p = 0.001), delayed diagnosis (p = 0.005), age under one year (p = 0.003), low peripheral blood and cerebrospinal fluid (CSF) leukocyte counts (p = 0.005), elevated CSF protein levels (p = 0.000), and decreased CSF glucose levels (p = 0.000).

Table 6.

Results of constructing a logistic regression model.

Effect	Model fitting criteria	Likelihood Ratio Tests		
	–2 Log Likelihood of the simplified model	Chi-squared	d.f.	Stat.
Model	94,172[a]	0,000	0	
vaccination status	99,859[b]	28,799	4	,000
full-term and premature	72,353[b]	1,293	2	,646
premorbid background	72,524[b]	1,463	2	,591
late diagnosis	26,547[b]		8	,005
Hospital admissions over 48 hours	77,023[b]	5,963	6	0,001
age up to 1 year	75,435[b]	4,374	4	,003
Low levels of peripheral leukocytes in the blood and cerebrospinal fluid	82,489 [b]			0,005
high protein levels in cerebrospinal fluid	95,878 [b]	5,894	4	0,000
Decreased cerebrospinal fluid	92,789	4,564	4	0,000
Group	99,859[b]	28,799	4	,176
Notes 1[a]- indicators criteria for model fitting 2[b]- indicators criteria for model fitting				

Discussion

Currently, thanks to the development and widespread implementation of the 13-valent pneumococcal conjugate vaccine (PCV13), the incidence and mortality of pneumococcal meningitis (PM) in children have significantly decreased [7]. In Kazakhstan, following the introduction of Hib vaccination against Haemophilus influenzae type b in 2008, cases of meningitis caused by this pathogen were no longer registered. Since the launch of PCV13 in 2014, the incidence of this vaccine-preventable disease has also declined. Similar trends were observed in Astana: hospital admissions due to pneumococcal meningitis dropped 4.2-fold, and meningococcal meningitis decreased by 1.6 times. However, the proportion of bacterial meningitis (BM) cases with unidentified etiology remained consistent throughout the observation period.

In line with the aim of our study, we investigated the clinical features of BM in children to optimize diagnosis and etiopathogenetic therapy. The clinical manifestations of BM are non-specific and age-dependent. Some of the most concerning symptoms for parents and important diagnostic indicators of CNS involvement include: febrile response, headache, and vomiting unrelated to food intake and unrelieved by it [13].

In acute neuroinfections, fever usually rises rapidly to high levels—39°C or above—within several hours. The intensity and duration of the febrile response in PM differed from MM. In PM, we observed a wave-like elevation of sub-febrile temperatures from days 8 to 23 of hospitalization, with brief normalization intervals (1–2 days). In contrast, the temperature in MM responded more positively to treatment by days 5–8, with no subsequent rises. Overall, in PM, temperature normalization occurred between days 11–16 of illness, and only in 8.6% of cases by day 30. In EM, temperature normalized by days 4–5.

Review of medical records showed that MM had an acute onset (91±3.5%), with signs of intoxication including febrile and hectic fever, headache, and frequent vomiting, which was more common than in PM or EM (p≤0.05). These features likely contributed to earlier hospital admission.

Timely initiation of therapy plays a crucial role in patient outcomes, as delayed antibiotic treatment is associated with worse prognoses [3,14]. Mortality from BM in children ranges from 4% to 21%, while neurological sequelae affect one-third of survivors [14]. Nonetheless, rational use of antibiotics is important to limit the development of multi-drug

resistance, adverse effects, repeated hospitalizations, and rising treatment costs [20].

Diagnosing BM can be challenging due to the absence of the full meningeal or meningoencephalitic syndrome. Only 41% of adult patients present with the "classic triad" of fever, neck stiffness, and altered mental status—and even less frequently in children and infants [19]. It is difficult to distinguish PM, MM, and EM based on clinical features alone [5], though there are differences in the severity and type of presenting syndromes. In our comparative analysis of BM and EM symptoms, key clinical signs of hydro-cephalic-hypertensive syndrome included: headache, neurological cry, vomiting, regurgitation, bulging and tense anterior fontanelle, hyperesthesia, and photo-phobia. Headache was most intense in PM (86.9%), followed by MM (82.7%) and EM (62%), mostly localized in the frontotemporal region. In PM patients, headache was more prolonged. BM in children over 1 year usually began with vomiting, while in infants, onset often included neurological cry (64.2%, 45%, and 50% in PM, MM, and EM respectively), regurgitation (58.1%, 35%, and 30%), and bulging fontanelle (100% in PM, vs. 65% in MM, and 20% in EM).

According to the literature, seizures occur in 20–30% of BM cases caused by S. pneumoniae and Hib [11]. In our data, 83% of infants with PM experienced seizures by days 3–4 of illness, often progressing to Grade I coma. Consciousness suppression (57.6%) and recurrent seizures (78.3%) were also frequently observed. In MM, seizures occurred in about a third of children (27.8%), while none were reported in serous meningitis of enteroviral etiology. These findings align with literature suggesting that altered consciousness is associated with poorer outcomes [15]. Among children with BM who developed neurological complications, 82% had altered mental status upon admission. Even in the absence of complications, 39% of BM patients showed changes in consciousness [2]. The longer a child remains unconscious, the higher the risk of adverse outcomes.

Neurological complications arise from the host's immune response to bacterial toxins, resulting in neuronal damage. Risk factors include young age, male sex, unfavorable premorbid background, lack of vaccination, and *S. pneumoniae* as the causative agent. Children with *pneumococcal meningitis* have a higher risk of neurological complications (75%) compared to those with *N. meningitidis* (25%) or Hib (20%) [4,17]. *S. pneumoniae* is also associated with a greater risk of symptomatic seizures, hydrocephalus, hearing loss, and intellectual disability compared to *N. meningitidis* or Hib [8,18]. According to our findings, early complications occurred in 41.5% of PM cases, 27% of MM cases, and 5.6% of EM cases (see Table 5). Literature indicates that 71% of infants (<1 year) with BM develop neurological complications, compared to 38% of children aged 1–5 and 10% of those aged 6–16 years [4]. Infants diagnosed with BM are at high risk of developing hydrocephalus, subdural effusion, seizures, hearing loss, and strabismus (4.3%) [1]. Hydrocephalus accounts for ~7% of BM in children and occurs mainly in neonates and infants (25%). In our study, hydrocephalus developed in 36.4% of children under 1 year, many of whom required surgical intervention in the form of periventricular shunting after CSF sanitation [1,2].

One significant risk factor for neurological complications is the time elapsed between symptom onset and the start of diagnostic and therapeutic care. In one study, children admitted within 48 hours of symptom onset had a lower rate of complications (40%) than those admitted later [9,22].

Our findings are consistent with published data: in PM patients, strong direct correlations were identified between late diagnosis and hospital stay ($r=0.7$; $p\leq0.001$), hospital stay and neurological complications ($r=0.7$; $p\leq0.05$), and between poor outcome and disease severity ($r=0.7$; $p\leq0.05$). In comparison, the MM group showed only one strong correlation—between late diagnosis and neurological complications ($r=0.8$; $p\leq0.001$). However, there is no universal definition of the time window in which CNS-related delayed clinical manifestations are likely to develop [19,22]. According to the systematic review by De Jonge RC, Van Furth AM, and Wassenaar M. (2010), a high risk of developing neurological complications in pneumococcal meningitis (PM) is observed in patients with unfavorable premorbid conditions, such as prematurity, congenital anomalies, and a disease duration exceeding 48 hours before hospital admission [23]. Based on their findings, prognostic indicators of bacterial meningitis (BM) severity include impaired consciousness, seizures, prolonged fever lasting more than seven days, absence of petechiae, shock, severe respiratory failure, peripheral circulatory insufficiency, male sex, and early age (under one year). Furthermore, laboratory markers — including low peripheral blood and cerebrospinal fluid (CSF) leukocyte counts, elevated CSF protein levels, and decreased CSF glucose concentrations — were identified as significant predictors of severe disease progression, leading either to a fatal outcome or to serious long-term neurological complications [23].

Our study yielded comparable results. Likelihood ratio tests demonstrated that the most significant predictors within our model included vaccination status ($p=0.000$), hospitalization ($p=0.001$), delayed diagnosis ($p=0.005$), age under one year ($p=0.003$), low peripheral blood and CSF leukocyte counts ($p=0.005$), elevated CSF protein levels ($p=0.000$), and decreased CSF glucose levels ($p=0.000$).

Conclusions

In Kazakhstan, following the introduction of Hib vaccination against Haemophilus influenzae type b in 2008, cases of meningitis caused by this pathogen have not been recorded. After the implementation of PCV13 vaccination against pneumococcal infection in 2014, the incidence of the disease has significantly decreased. In Astana, hospital admissions for pneumococcal meningitis declined by a factor of 4.2, and for meningococcal meningitis by 1.6 times. Among all types of bacterial meningitis (BM), pneumococcal meningitis remains the most severe, with early neurological complications reported in 41.5% of cases. A strong direct positive correlation was found in the group of children with PM between the following parameters: delayed hospital admission, delayed diagnosis, and length of hospital stay; as well as between disease severity, length of hospital stay, and neurological complications.

Conflict of Interest:

All authors have reviewed the content of the article and declare no conflict of interest.

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