

ORIGINAL PAPER

Acute bacterial meningitis in Polish children – assessment of risk factors of neurological complications

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ABSTRACT

Introduction: Bacterial meningitis remains a potential problem for contemporary pediatrics, as regards both treatment and further care of patients with long-term complications. The aim of this study is to identify the most common neurological complications of acute bacterial meningitis among children and their main risk factors of occurrence.

Material and methods: We analyzed data on cases of children with bacterial meningitis hospitalized in The Infectious Diseases Department in St. Joseph Children's Hospital in Poznan, between 2010 and 2020. We considered *Streptococcus pneumoniae* and *Neisseria meningitidis* as etiological factors. Data on neurological complications were obtained during follow-up visits and as a result of telephone surveys.

Results: We identified 75 patients (1 month up to 17 years of age) with acute bacterial meningitis with the etiological factors *Streptococcus pneumoniae* and *Neisseria meningitidis*; 2 of them died as a result of infection (2.66%). Data on short and long-term complications were obtained from 59 patients. We observed complications among 42 children; the most frequent complications were cognitive impairment (31.37%), subdural effusion (17.19%), focal neurological deficits (15.6%), and hearing disorders (14.0%). Patients with neurological complications showed a higher frequency of lower count of neutrophils $< 13.8 \times 10^3/\mu\text{l}$ ($p < 0.01$), a lower hemoglobin level $< 12.0 \text{ g/dl}$ ($p < 0.00$), and platelet levels above $340 \times 10^3/\mu\text{l}$ ($p < 0.02$). Risks factors of neurological complications occurrence were irritability at admission ($p < 0.04$), age of patients under 34 months (95 CI%: 0.58–0.86), and length of hospitalization over 14 days (95 CI%: 0.70–0.92).

Conclusions: Despite the introduction of protective vaccination, bacterial meningitis is still a life-threatening disease that leads to significant neurological consequences. It is important to recognize patients with risk factors of neurological complications to provide them with multidisciplinary medical care later in life.

KEY WORDS:

risk factors, pediatrics, bacterial meningitis, neurological complications.

INTRODUCTION

Acute bacterial meningitis (ABM) is a severe infectious disease that primarily affects children. Despite the adequate healthcare facilities, widespread use of antibiotics, and vaccines against common pathogens, morbidity, and mortality rates are high in developing and developed countries [1]. The mortality rate varies 5–30%,

depending on the study. Neurological sequelae occur in 15–50% of cases [2–5]. Hearing disorders, hydrocephalus, focal neurological deficits, epilepsy, and also subtle neurological deficits, such as behavioral changes, learning difficulties, and attention deficit disorder, were observed in children after bacterial meningitis in the past [3, 4, 6–9]. Among the pediatric population, the occurrence of long-term neurological complications determines one's fur-

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ther development and achievements. One of the leading objectives is the early recognition of patients with ABM at higher risk of complication development to ensure proper healthcare by a multidisciplinary team after being discharged from the hospital [9]. This study aims to evaluate neurological sequelae and identify risk factors of ABM among pediatric patients in Poland, based on clinical and laboratory variables.

MATERIAL AND METHODS

An observational study was conducted to identify the risk factors for neurological complications in children with ABM. The study group was made up of children, hospitalized with bacterial meningitis at The Infectious Diseases Department in St. Joseph Children's Hospital in Poznan, between January 2010 and December 2020. Inclusion criteria were: diagnosis of pneumococcal or meningococcal meningitis, age 1 month to 17 years at the time of hospitalization. The etiology of the disease was confirmed by a positive test result of cerebrospinal fluid (CSF) or blood culture detecting microbial genetic material with PCR in the CSF/blood analysis.

We excluded cases of unknown etiology or caused by different pathogens. Analysis was based on the medical records and routine tests, performed during hospitalization, which included: onset period and symptomatology, general examinations results, imaging tests, blood tests, and cerebrospinal fluid examinations.

Early complications were observed during hospitalization, and data on late complications were obtained during follow-up visits and as a result of telephone surveys. Cognitive impairments were recognized by psychologists according to current standards. We excluded 16 patients who failed to obtain data on late complications.

The calculations were made using Statistica 12 by StatSoft and PQStat by PQStat Software. The level of significance was $\alpha = 0.05$. The result was considered statistically significant when $p < \alpha$. For variables with a normal distribution and equal variances, we used Student's *t*-test for unrelated samples, and for samples not having equal variances, the Cochran-Cox test. In case of non-compliance with the normal distribution, the Mann-Whitney *U* test

was used. A multivariate logistic regression model was used to identify risk factors for developing neurological complications. The study was approved by the Human Research Ethics Committee of Poznan University of Medical Science.

RESULTS

During the study period, 75 children were hospitalized with meningococcal or pneumococcal meningitis at The Infectious Diseases Department in St. Joseph Children's Hospital in Poznan. The study group consisted of 59 children who met the study criteria. There were 22 females and 37 men, aged 3 months to 17 years. The mean age of hospitalized patients diagnosed with bacterial meningitis was 55 months (median of 27 months). All patients received empirical antibiotic therapy and intravenous corticosteroids in the first days of treatment. After identifying the etiological factor and obtaining an antibiogram, the treatment was changed to targeted. None of the patients were vaccinated against the causative bacteria (meningococcus or pneumococcus). 37 patients required at least one follow-up visit after discharge from the hospital. The remaining patients were referred for further care to specialist clinics (neurology, audiology). Complications were surveyed 1–10 years after hospitalization (mean 4.6 years).

The dominant etiology was *Neisseria meningitidis*, which accounted for 76.27% of cases; serogroups B and C were the most common. The observed complications along with their frequency and ethology are listed in Table 1. Neurological complications were observed in 42 patients, 59.52% of whom were male. Seizures occurred before and during hospitalization as one of the short-term complications, mostly without negative consequences. However, in some cases, they were an early symptom of developing epilepsy, diagnosed by neurologists after completing the treatment. Children with cognitive impairments presented learning disabilities, concentration and language difficulties, and as a result demonstrated delayed school readiness, had to repeat classes, required learning support and speech therapy.

Complications were observed more frequently in *Neisseria meningitidis* infections, but the differences were

TABLE 1. Complications after bacterial meningitis among children

Parameters	<i>Neisseria meningitidis</i>	<i>Streptococcus pneumoniae</i>	Total
Cognitive impairment (%)	28.21	41.67	31.37
Subdural effusion (%)	16.00	21.43	17.19
Focal neurological deficits (%)	14.00	21.43	15.60
Hearing disorders (%)	13.16	16.67	14.00
Hydrocephalus (%)	2.00	21.43	6.25
Abscess (%)	2.00	14.29	4.69
Epilepsy (%)	2.56	0.00	1.96
Mortality (%)	3.33	0.00	2.66

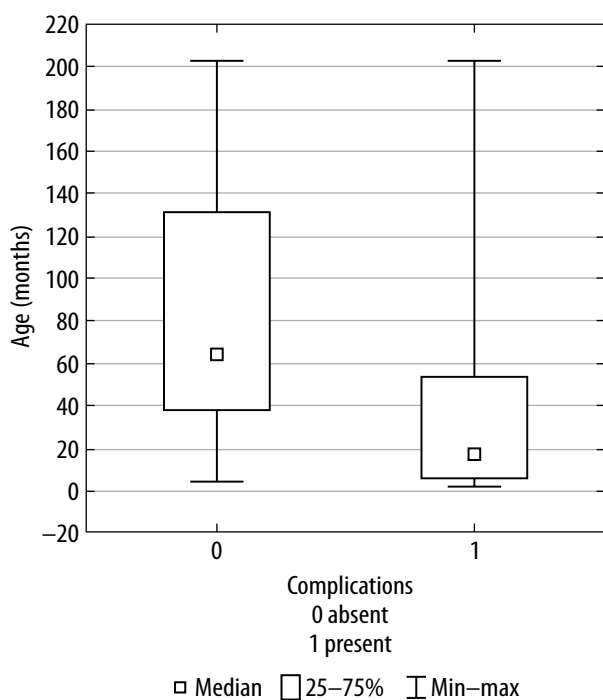


FIGURE 1. Complications depending on age

not statistically significant ($p < 0.73$). When analyzing the occurrence of individual complications, patients with *Streptococcus pneumoniae* infection had a 13-fold greater chance of developing hydrocephalus ($p < 0.03$). With other complications, the etiological factor did not significantly increase the risk of their occurrence.

Complications were significantly more frequent among patients under 34 months of age (sensitivity 66.67%, specificity 76.47%; 95 CI%: 0.58–0.86) (Figure 1).

The length of hospitalization was significantly longer in patients with complications, and also antibiotic therapy was longer in those patients. The proposed cut-off point was 14 days (sensitivity 76.19%, specificity 82.35%; 95 CI%: 0.70–0.92). 44.1% of patients required hospitalization in the intensive care unit, but this did not increase the risk of complications ($p < 0.15$).

The relationships between the results of selected laboratory tests and the occurrence of complications are presented in Table 2. The hemoglobin level was significantly different in people with and without complications; the proposed cut-off point was 12.0 g/dl (sensitivity 92.86%, specificity 47.06%) (Figure 2). Neutrophil count was significantly lower in patients with complications; the cut-off point was $13.8 \times 10^3/\mu\text{l}$ (sensitivity 66.67%, specificity 88.24%) (Figure 3). Complications were observed significantly more often in patients with platelet levels above $340 \times 10^3/\mu\text{l}$ (sensitivity 66.67%, specificity 76.47%) (Figure 4).

Complications were observed less frequently in patients with petechiae ($p < 0.02$, OR = 4.32) and headaches ($p < 0.03$, OR = 3.35). Children with irritability were 3.58 times more likely to develop complications ($p < 0.04$, OR = 3.58). The presence of other symptoms (vomiting, meningeal signs, fever, seizures) and the patient’s general condition upon admission did not significantly affect the incidence of complications.

DISCUSSION

In our study, any complications (short-term or long-term) were observed in 71% of patients. The mortality

TABLE 2. Risk factors of neurological complication occurrence after bacterial meningitis

Parameters	Complications		p-value
	Yes (n)	No (n)	
Age (months)	17.5 (42)	64.0 (17)	0.01*
Length of stay (days)	18.1 (42)	11.8 (17)	0.00↑
PCT [ng/ml]	24.35 (34)	19.45 (14)	0.86*
CRP [mg/l]	223.58 (42)	212.0 (17)	0.75↑
Hgb [g/dl]	10.5 (42)	11.6 (17)	0.00↑
Total leukocytes (count)	15.2 (42)	22.1 (17)	0.13*
Neutrophils (count)	11.5 (42)	18.0 (17)	0.01*
Platelets (count)	283.5 (42)	202.0 (17)	0.02*
Fibrinogen [g/l]	7.9 (39)	6.45 (16)	0.09↑
D-dimer [ug/l]	2460.0 (36)	16.14 (16)	0.13*
Glycemia [mg/dl]	120.0 (38)	110.0 (17)	0.43*
Protein [g/l] in CSF	1.97 (42)	1.7 (17)	1.00*
Total leukocytes in CSF	1940.5 (42)	4481.0 (17)	0.28*
Glucose [mg/dl] in CSF	32.0 (41)	20 (17)	0.75*

CRP – C-reactive protein, CSF – cerebrospinal fluid, PCT – procalcitonin

*Mann-Whitney U test

↑ Cochran-Cox test

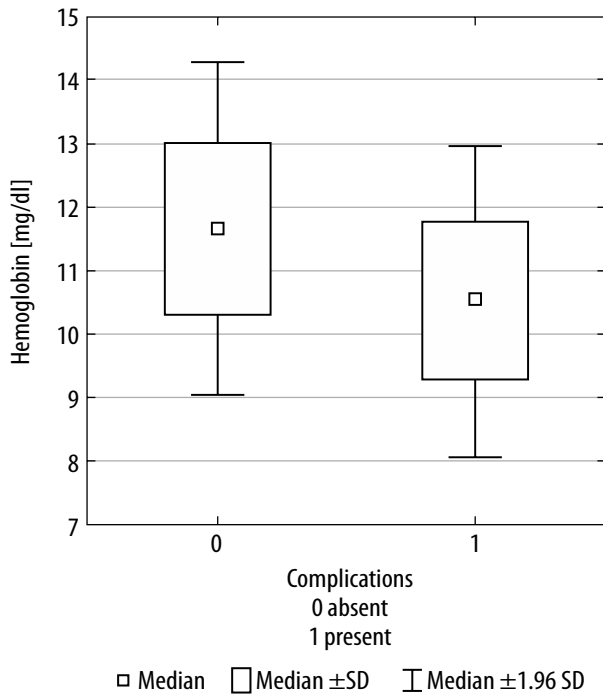


FIGURE 2. Complications depending on hemoglobin level

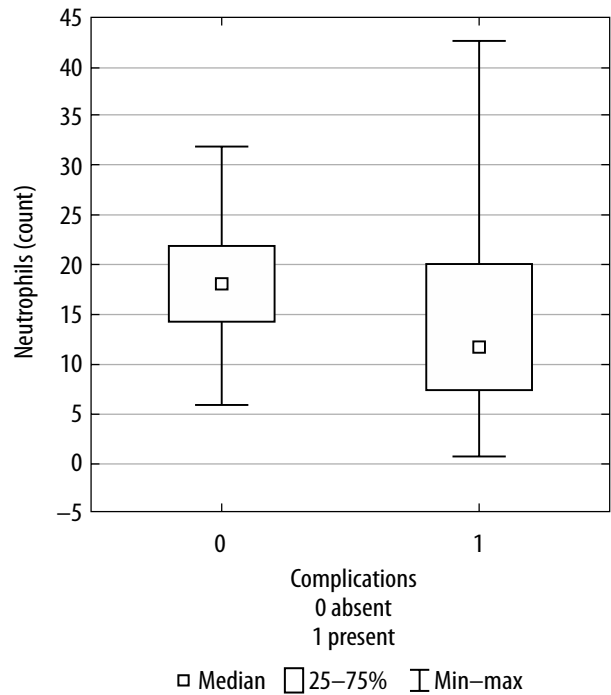


FIGURE 3. Complications depending on neutrophil count

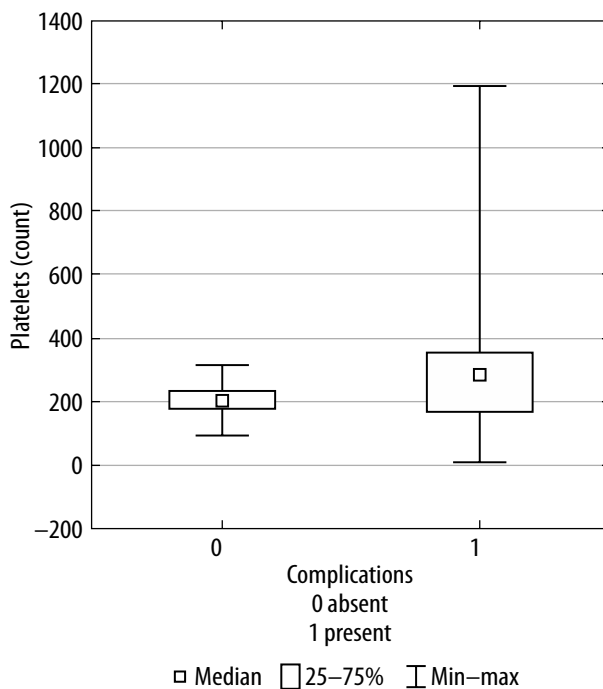


FIGURE 4. Complications depending on platelet count

rate was 2.7%. Previous publications indicate that childhood bacterial meningitis is associated with a 49% risk of serious neurological sequelae and a mortality rate of up to 14% [5, 10, 11]. In a recent research review (1970–2010), approximately 50% of children with ABM (between 1 month and 18 years of age) developed neurological deficits after 5 years of follow-up [5].

In our research, we took into account the two commonest etiological factors: *Streptococcus pneumoniae* and *Neisseria meningitidis* [12, 13]. After the introduc-

tion of population-based immunization against *Haemophilus influenzae* in Poland, an invasive bacterial infection caused by *Haemophilus influenzae* is no longer a problem [14]. *Neisseria meningitidis* was responsible for the majority of infections. Vaccinations against *Neisseria meningitidis* are not compulsory in Poland; the vaccination rate is low (< 30% in children younger than 5 years). In 2017 in Poland population vaccinations against *Streptococcus pneumoniae* were introduced. Many studies have detected an increased risk of complications in pneumococcal infections, which we did not confirm in our study [11, 15–17]. Only cases of hydrocephalus were significantly more frequently observed in infections caused by *Streptococcus pneumoniae*. This is a result of a lower frequency of invasive infections caused by *Streptococcus pneumoniae*.

The prognostic factors of neurological abnormalities based on laboratory tests were: platelet count higher than $340 \times 10^3/\mu\text{l}$, neutrophil count less than $13.3 \times 10^3/\mu\text{l}$, hemoglobin level lower than 12 g/dl. This is in line with the previously published studies [9, 17–19]. In a study by Tsai *et al.* CSF cell counts below or equal to $200/\text{mm}^3$, and CSF protein concentrations higher than 330 mg/dl are warning signs of a bad outcome [20]. We did not observe the influence of the concentration of inflammatory markers in the blood and CSF examination results on the occurrence of complications.

One of the main factors increasing the risk of complications, confirmed in many studies, was the young age at the onset of the disease [9, 15, 16, 18, 19]. In the conducted study, complications were significantly more frequent in children younger than 34 months of age. This can be explained by the weaker response of the immature organism to a severe bacterial infection.

According to a study by Roine *et al.*, the presence of consciousness disorders on admission was a factor in poor prognosis [18]. Shingi *et al.* found in their study that the Glasgow Coma Scale below 8 increases the risk of long-term neurological sequelae [21]. In our study, we did not confirm these relationships; the patient's general condition and the presence of disturbances in consciousness did not significantly affect the occurrence of complications, although they were more often observed among patients with complications. Although irritability at clinical onset is rarely mentioned as a risk factor for complications in ABM, in the present study it was observed 3.5 times more often in patients with neurological disorders. Hearing loss is one of the commonest neurological complications in the course of ABM. Up to 31% of children develop unilateral or bilateral hearing impairment [22–24]. Hearing loss is more common in infections caused by *Streptococcus pneumoniae* (14–32%) compared to *Neisseria meningitidis* (2–23%) [24, 25]. In the conducted study, hearing loss was observed in 14% of children, more often in infections with *Streptococcus pneumoniae*, but the difference was not statistically significant.

In our study, the most frequent long-term complications were cognitive impairment (31.37%) such as behavioral problems, impaired school performance, and attention deficit disorder. Patients required participation in additional extracurricular activities and psychological counseling. In a Dutch study, it was found that 30% of children with ABM had a history of poorer academic performance, and problems with concentration, and repeated the class two times more often compared to healthy children with a similar socioeconomic background [26]. The Danish population study showed that adults who had a history of ABM in childhood have lower education and lower economic status compared to healthy peers [27]. Cognitive impairment is difficult to measure due to the lack of standardized tools; hence it is often underestimated.

CONCLUSIONS

Patients with neurological complications required longer hospitalization and prolonged antibiotic therapy, which was associated with the use of increased medical and technological resources, and higher costs of stay.

Despite the availability of vaccinations and effective treatment, bacterial meningitis is still a threat to the healthy development of pediatric patients in developed countries. Meningitis survivors often require multidisciplinary medical care later in life. Cognitive dysfunction, hearing impairment, epilepsy, and hydrocephalus often cause various degrees of disability, affecting daily activities. It is important to identify patients with risk factors for neurological complications at an early stage of the disease and to provide them with multidisciplinary care.

DISCLOSURE

The authors declare no conflict of interest.

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